

Robinson Research Institute

Annual Report 2014



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

Our mission is to deliver world-class 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.

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Who we are

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.



RRI at a glance



\$16.5m+ funding in 2014



Research Themes



370+ publications



\$34,000+ raised for the Robinson Research Foundation



10 Research Priorities



Embedded in **5** SA hospitals



48Research Leaders



100+ PhD students



Affiliations the School of Paediatrics

and Reproductive Health



400+ Members



20+ Honours students



Collaborations multiple national and international



Message from the Deputy Vice-Chancellor Research



The University of Adelaide is committed to expanding and further investing into strategic research.

Our goal is to deliver world-class research and to translate our research findings to bring about improvements in people's lives. Our five research institutes are set-up to address national, state and global priorities, focussing on the key challenges of critical value to society. One of those 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 recognising that 'good health is everything' and that we are '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 generations. With over 400 talented scientists and clinicians, the Institute is advancing knowledge

and bridging the gap between research discoveries and clinical practice.

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

I would personally like to commend the members of the Institute for their commitment and drive to solving major health burdens that impact upon society across the globe. I am confident they 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

Message from the Chair



2014 was a year of consolidation, enhanced collaboration and preparation for the future.

As members embrace the model of collaboration, I am witnessing a renewed vitality and an emerging appetite to challenge the boundaries of research, tackle new areas and to develop diverse partnerships to enable this.

The Institute continues to lead the way and build on past strengths. It remains proactive in reviewing and adapting to the dynamic environment in which it operates. This year has seen investments in research funding programs re-focused and refined to deliver increased value to the research efforts and competitive standing of members.

Financial support for medical research continues to be a significant challenge. In 2014, the Federal Government announced it would establish a Medical Research Future Fund valued at \$20 billion by 2020. The deregulation of University fee structures is another key policy on the drawing board. At the time of writing this message the government reforms remain unresolved. We must keep the conversation alive and build broad understanding across

government and the community on the importance of investing in and raising funds for health, medical research and infrastructure.

I wish to acknowledge and thank each of the following:

- > RRI Board Members for their commitment, considered contributions and general 'value-add' to the Institute
- > RRI Members who have again made many great strides in their research work
- > RRI Director Professor Sarah Robertson, she has shown great leadership, tenacity and insight in progressing and implementing fundamental initiatives that are serving the interests of the Institute well, both now and into the future

The Institute has much to celebrate and much to look forward to in 2015. It will be exciting. It will be challenging.

Professor Jock Findlay Chair

Advisory Board



Prof Jock Findlay AO (Chair)



Prof Mike Brooks



Prof Alastair Burt



A/Prof Naomi Dwyer



Prof Julie Owens



Prof Sarah Robertson



Prof Paul Rolan



Prof Andrew Zannettino



Its been inspiring to get to better know many of our 400 people, and to devise concrete ways the Institute can support and enable their important work.

To discover, to understand, and to direct the benefit of new knowledge to improving the health and quality of life for children and families is our shared ambition. We have some of the most innovative and skilled researchers in the country. Our capacity to bring our collective abilities to bear on major questions spanning reproduction, pregnancy and childhood is unparalleled. The Institute affords us the vehicle to work collaboratively to tackle the important and difficult research questions that are beyond our scope as individual research groups, but tractable if we pull together.

Tackling the earliest phase of life is the key to solving many of the major health conditions affecting Australians and people across the globe. Focussing our efforts on conception, pregnancy, and the infant and child will deliver great dividends in community and population health. We are committed to ensuring that all intending parents plan good pregnancy health from before conception; to reduce the toll of preterm birth on conditions like preeclampsia and gestational diabetes that have life-long consequences; to alleviate the pregnancy disorders and early life events that contribute to non-communicable conditions including obesity, diabetes, allergy and neurological impairment; and to develop new interventions that protect children from infection, disability and neuro-developmental disorders.

In 2014 we were committed to refining our Institute goals and to develop mechanisms and programs to support delivery of the best possible outcomes. We now have a defined series of initiatives that assist researchers to develop large scale funding applications, to increase project competitiveness for national funding support, to provide seed funding and mentoring schemes to encourage our early career researchers, as well as a wide range of opportunities to help researchers communicate their research outcomes, publish in the best journals, and better engage with media.

These programs build on the Institute's investment in core facilities to underpin the research effort across all of the four Research Themes. We are now delivering advanced capability in gene manipulation through the GSEx Facility, in large-scale data analysis in the Bioinformatics Facility, in measuring a wide range of analytes through the Research Assay Service and in delivering coordinated epidemiological and mechanistic analyses through the Cohort and Intergenerational Studies Facility. New in 2014 were the SA Genome Editing Service, to fast-track development of genetic mouse models, and services to deliver Biostatistics support.

In 2014 we secured several new NHMRC and ARC project grants and fellowships, and were especially pleased with the award of two NHMRC Centres of Research Excellence in the Protection of Pancreatic Beta Cells and in Polycystic Ovary Syndrome.

In 2015 we will work towards establishing our new home in the Adelaide Nursing and Medical Schools building in the West End precinct. We look forward to reaping the benefits of new facilities, improved infrastructure and equipment, and greater opportunity to interact with other medical researchers in Adelaide's consolidated medical research precinct. The synergies and efficiencies to be realised will assist us in dealing with a difficult economic climate, and a contracting medical research funding base. With new partnerships there will be even better opportunities to strengthen our team-based approach to issues that have global significance.

The Institute is proud to foster and develop Adelaide's historic leadership in reproductive science and medicine. I am grateful to the University leadership for their investment in our research and confidence in our research excellence. We are supported by the fantastic work of the Institute office staff, not least the efforts of Institute Manager Ms Kate Irving. I also thank the Advisory Board, and particularly Chair Professor Jock Findlay, for encouragement and guidance.

I hope you enjoy this report, which highlights the diversity and impact of our research programs over the last 12 months. Our contributions continue to push the boundaries of human knowledge, and show the many ways we translate our discoveries to make a real difference in people's lives.

Professor Sarah Robertson

Executive Committee



Prof Sarah Robertson (Chair)



A/Prof Simon Barry



Prof Jenny Couper



Prof Jodie Dodd



Kate Irving



A/Prof Helen Marshall



Prof Julie Owens



Prof Claire Roberts



Prof Ray Rodgers



A/Prof Darryl Russell



A/Prof Michael Stark



Currently there is no effective treatment for whooping cough. Those who present to hospital with symptoms receive supportive treatment - which may include antibiotics, oxygen and intravenous fluid - and wait for the infection to pass. However, those with severe infection may need to be managed in the intensive care unit, and may be sick for up to 3-6 months. For some, the infection can lead to death. Ten Australian babies died in the last whooping cough epidemic.

Research led by Associate Professor Helen Marshall, who leads the Vaccines and Infectious Diseases Group, studied 120 children with whooping cough who were admitted to hospitals across Australia. They set out to find whether they could predict earlier the children who are more likely to become severely unwell from whooping cough.

"We found the most severe cases of whooping cough were in infants less than two months of age and those born prematurely, who had almost five times the risk of severe disease compared to older infants and those born at term."

"The dilemma is that those at highest risk of severe disease are too young to be protected by immunisation, as childhood vaccines in current national programs start at six to eight weeks of age," said Helen.

new approach.

"By immunising pregnant mothers against whooping cough, the mother transfers protective antibodies to the fetus which protect the infant during the few few months of life, when they are most at risk, prior to developing their own active protection through infant immunisation," said Helen.

For those mothers who do not receive the vaccine in pregnancy or who deliver preterm infants, their babies are at highest risk of severe infection.

This also raises questions about alternative strategies such as whether the immunisation could be given earlier - at birth. Helen's group recently investigated this as part of a large national study, the largest study of its kind in the world. Further research is required to better understand the immunisation strategies that will provide the best overall protection for our most vulnerable babies.

The last whooping cough epidemic occurred in Australia in 2010, where more than 34,000 cases were notified nationally.

"Australia has not experienced a whooping cough epidemic of that size since, but we are well overdue for another one."

"I am also interested in looking at strategies for improving uptake in pregnant women so our most vulnerable are protected when the next epidemic hits," said Helen.



60% of Australian women are overweight or obese. This is a major concern as type 2 diabetes is projected to be the leading cause of disease burden in Australia by 2023.

established very early in life. Associate Professor Rebecca Robker leads the Ovarian Cell Biology group and has studied the ovary for many years. Her understanding of the ovary's importance for women's health led her to look at the effect of maternal obesity on egg development.

"When examining the oocytes of obese mice we noticed there was a reduced level of mitochondrial activity. This was an important discovery as all of the mitochondria in the subsequent offspring must be generated from those in the egg," said Rebecca.

Mitochondria are energy-producing 'organelles' within living cells. They are essential for the normal functioning of our body tissues, and Rebecca has shown that obesity leads to an endoplasmic reticulum stress response in ovarian cells that causes damage to the mitochondria.

"The reduced levels would affect an offspring's metabolism, potentially predisposing them to obesity later in life. In support of this, we found that the offspring conceived from the eggs of obese mothers were heavier," explained Rebecca.

Once Rebecca and Postdoctoral Researcher Dr Linda Wu uncovered the type of stress involved, they were the first to test whether candidate drugs could protect the eggs and improve embryo development.

"These compounds were highly successful in preventing the stress response – they restored egg quality, embryo development and mitochondrial DNA levels to those equivalent of a healthy mother," said Linda.

Rebecca and Linda's research has been undertaken largely in mice, however, they believe similar mechanisms are at play in humans. Through restoring egg quality, offspring from obese women will be less susceptible to obesity later in life.

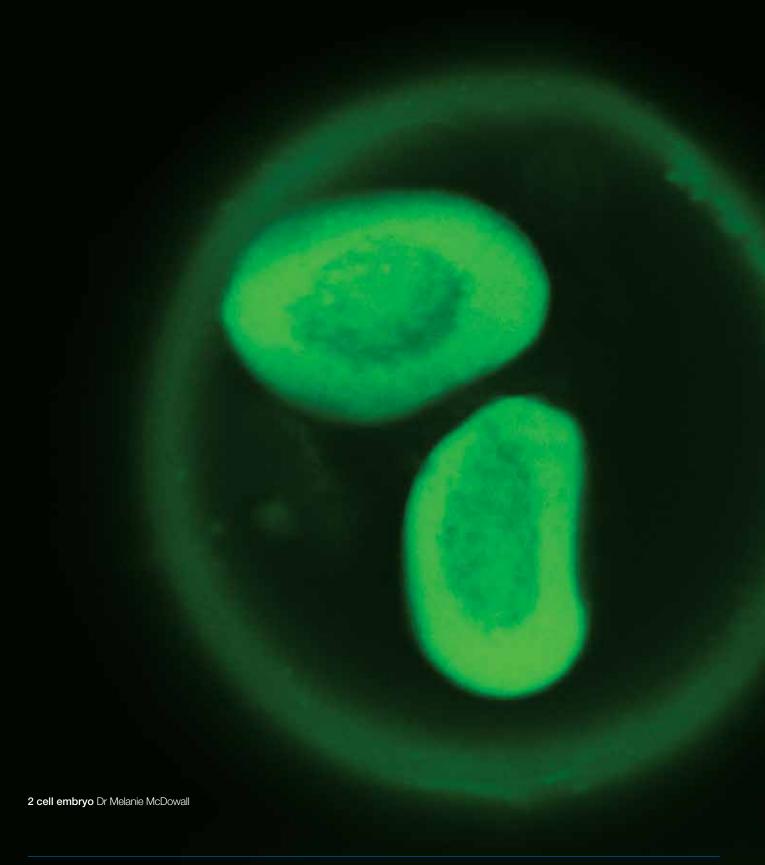
"Although this research offers relief for obese women struggling to conceive and who are concerned for their children's longterm health, we believe it highlights that a woman's nutritional state prior to getting pregnant matters greatly."

"Women are urged to eat healthy diets to optimise their chances for a healthy conception and to prevent multi-generational disease risk passing onto their children."

While this research sends an important message to would-be mothers, it is important to note that nutritional cues are also passed on through sperm from the father.

"The next piece of the puzzle is understanding how the male and female cues interact in programing the offspring not just for obesity, but a range of metabolic conditions," said Rebecca.

Research Highlights



2014 Discovery highlights

Excellence in Research for Australia

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 (DIISR).

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.

The most recent ERA results were released in 2012. The Robinson Research Institute, through the School of Paediatrics and Reproductive Health, performed in the highest level in both the 2012 and the earlier 2010 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:

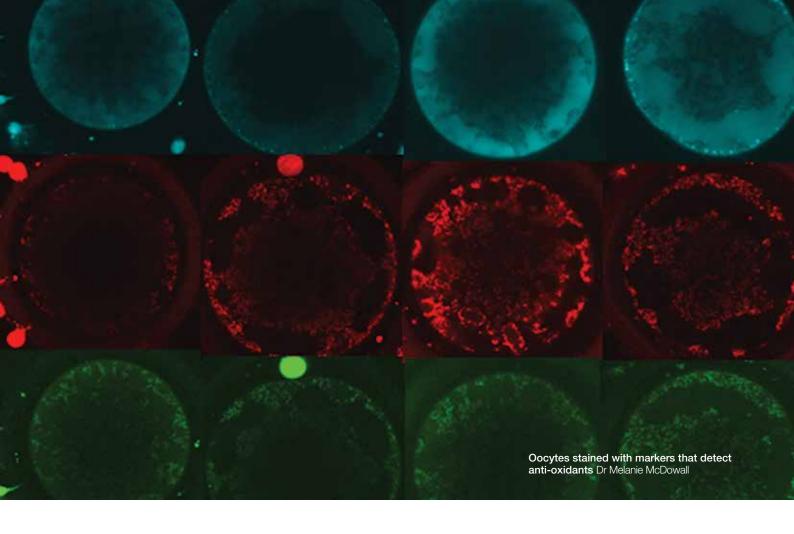
Research in 2014 resulted in:

- Understanding that the contribution of genetic mutations to cerebral palsy is higher than previously believed. Alastair MacLennan and colleagues advanced the field by finding common mutations amongst cases of cerebral palsy.
- > Identification of a novel gene implicated in intellectual disability with epilepsy. Lachlan Jolly and Jozef Gecz discovered a link with the USP9X gene, coding for ubiquitin specific protease.
- > Identification of the role for a receptor called CRIg implicated in diabetes, arthritis and inflammatory bowel disease. Tony Ferrante and colleagues found CRIg to be a key gateway through which inflammatory mediators work to promote or resolve inflammation and tissue damage.

- > A potential intervention to reverse the impact of obesity in pregnancy on the offspring. Rebecca Robker and Linda Wu demonstrated that mitochondrial loss in offspring results from obesity in pregnancy, and they were able to reverse these changes during the final stages of oocyte development.
- > Mapping of more than 1,000 genes that are differentially expressed in the oviduct and regulated by the steroid hormone progesterone. Lisa Akison and Rebecca Robker's research is important in understanding how progesterone establishes an optimal environment for early embryo development.
- > Discovery that hemoglobin is present in the ovary, particularly granulosa and cumulus cells, as well as the oocyte. Hannah Brown and Jeremy Thompson are investigating why this gas-binding protein appears in these cells, and how this contributes to healthy ovarian function.
- > Evidence revealing that pregnant women who eat a diet high in fat and sugar are 50% more likely to deliver preterm. Jessica Grieger and Vicki Clifton believe that dietary changes prior to pregnancy and during pregnancy will prevent many preterm deliveries.
- > Discovery of 12 isoforms of the glucocorticoid receptor in the human placenta. Zarqa Saif and Vicki Clifton are now exploring how these isoforms enable placental cells to refine their response to environmental stressors.
- > Utilising x-rays to measure the depth of the airway surface liquid to assess the state of hydration on the airway surfaces of cystic fibrosis patients.

 David Parsons, Martin Donnelley and collaborators at the Japanese Spring-8 x-ray synchrotron developed this non-invasive technique.
- > Pioneering the use of genome editing (CRISPR/CAS9) technology to rapidly generate genetically modified mouse strains for biomedical research. Paul Thomas and colleagues have produced over 15 mutant strains that are providing new insight into diseases such as epilepsy and intellectual disability.

- > Demonstration that dietary sodium affects vascular health in children with type 1 diabetes. Jennifer Couper, Chad Andersen and Alexia Pena's discovery has implications for diet management in affected children.
- > Finding that gastric emptying is more rapid in children with type 1 diabetes. Shiree Perano and Jennifer Couper found gastric emptying affects these childrens' ability to control blood glucose levels after meals.
- > Demonstration that patterns of cytokines in the mammary gland vary over different stages of the menstrual cycle. Pallave Dasari and Wendy Ingman's finding of inflammatory cytokines at ovulation advances understanding of how the biology underpinning breast cancer risk, and may lead to new preventative strategies.
- > New data showing that oxygen utilisation accurately identifies those preterm infants at increased risk of significant brain injury. Michael Stark believes this novel approach will lead to improved neuro-protection through early identification of infants requiring interventions.
- > Discovery that male factors present in seminal fluid have a major impact on the phenotype of offspring programming obesity and metabolic dysfunction in males when disrupted. John Bromfield, John Schjenken and Sarah Robertson discovered that male seminal fluid effects are mediated in part through the regulation of cytokines in the female reproductive tract.
- > An invitation to Sarah Robertson,
 Rebecca Robker and Michelle Lane
 from Science to explain how information
 transmitted through female and male
 gametes at the time of conception can
 have life-long effects on offspring health.
- > Finding that healthy female embryos at mid-gestation display hallmarks of intrauterine growth restriction consistent with differences in fetal biometry at birth. Stefan Hiendleder believes this could explain sex-specific differences in postnatal health outcomes.



- > Demonstration of the interface between the maternal endocrine system and the developing oocyte. Darryl Russell uncovered a specific family of proteins regulated by maternal hormones, which control the development and ovulation of the oocyte.
- > Discovery that follicular cells of women with diminished ovarian reserve have altered metabolic function, deacteylation and desuccinylation. Michelle Lane, Leanne Pacella and Deidre Zander-Fox demonstrated the molecular nature of the ovulated oocyte is different in these women and it appears to have a reduction in mitochondrial function.
- New studies showing how the hyaluronan (HA) inhibiter, 4-methylubelliferone (4-MU) significantly inhibits the growth of ovarian cancer cells. Martin Oehler and Carmela Ricciardelli believe reducing HA production is a promising strategy to improve ovarian cancer survival.
- > Identification of new genetic pathways in follicular development. Ray Rodgers and colleagues discovered that granulosa cells change dramatically and thecal cells barely change during follicle development, and small follicles vary considerably in their gene expression profiles, but large or atretic follicles are much less variable.

- > Discovery of a method of engaging the tumour necrosis factor (TNF) receptor to give a more selective signal to cells and reduce the side effects of potential therapies. Tony Ferrante and colleagues believe these findings may mediate the effects of therapeutics that result in lung damage in children.
- > Demonstration that a six-month structured lifestyle intervention program in subfertile women with a BMI ≥ 29kg/m2 is successful. Ben Mol and Meike Mutsaers' multicenter randomised controlled trial showed that 45% of ongoing pregnancies were achieved spontaneously in the intervention group, versus 28% in the control group.
- > Improvements in IVF success through more effective quality embryo selection.

 Melanie McDowall is researching how autofluorescence signals of metabolism can be used as a diagnostic for embryo health, without damaging the embryo.
- > Discovery that the trace element selenium protects the egg from oxygen radicals in the late stages of follicular development. This advance by Ray Rodgers and colleagues is pertinent information for people living in areas with low levels of selenium in the soil and food.

- > Evidence proving that healthy eating and increased physical activity during pregnancy improves outcomes for babies at birth. Jodie Dodd and colleagues' LIMIT trial (the world's biggest study of its kind) resulted in fewer babies born over 4kg, decreased chance of respiratory distress syndrome and reduced length of stay in hospital.
- > Improved understanding of risk factors leading to severe whooping cough.
 Helen Marshall showed that infants who were less than 2 months of age, presented with a fever, were born preterm and had a concurrent infection were more likely to develop severe whooping cough.
- > Interventions to prevent or ameliorate risks of pregnancy complications. Claire Roberts and Gus Dekker have developed a test that uses a combination of genetic biomarkers and clinical and lifestyle factors to predict risks in early pregnancy for future complications including preeclampsia, preterm birth, growth restriction and gestational diabetes.

Funding highlights

In 2014 the Robinson Research Institute attracted funding from major bodies to support our research. Highlights are listed below.

NHMRC

Project Grants commencing in 2014:

\$763,953 to Professor Jozef Gecz

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

\$755,660 to Associate Professor Michael Ridding

Characterising post stroke neuroplasticity in humans? Identifying a critical window for rehabilitation

\$755,934 to Professor Jodie Dodd

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

\$576,174 to Associate Professor Cheryl Shoubridge

Investigating the role of mutations in the ARX homeobox transcription factor contributing to intellectual disability

\$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 Associate Professor Rebecca Robker

The obesity prone oocyte-causes, consequences, treatments

Centres for Research Excellence awarded in 2014:

\$2.5 million to Professor Jennifer Couper

Professor Jennifer Couper (CIA), Professor Jodie Dodd and Dr Lynne Giles awarded a CRE for the Protection of Pancreatic Beta Cells.

\$2.5 million to Professor Helena Teede

Professor Helena Teede (Monash University CIA) together with RRI members Professors Robert Norman, Michael Davies and Ray Rodgers and Drs Lisa Moran and Alice Rumbold awarded a CRE for evaluation, management and health care needs of Polycystic Ovary Syndrome and related health implications.

Project grants awarded in 2014:

\$585,276 to Professor Sarah Robertson

Inflammatory cytokines as causal agents in peri-conception programming of offspring health

\$397,077 to Dr Michelle Lane

Metabolic and molecular basis of embryo signaling

ARC

Associate Professor Jeremy Thompson is a Chief Investigator on an application led by Professor Tanya Monro; Director of the Institute for Photonics and Advanced Sensing. They were awarded \$23,000,000 by the ARC to establish a Centre of Excellence for Nanoscale BioPhotonics – commencing in 2014.

The ARC awarded Professor Paul Thomas \$390,000 for the project commencing in 2014: Genetic control of spermatogenesis - defining the role of SOX3 in spermatogonial progenitor cells.

Alzheimer's Australia

Dr Mitchell Goldsworthy was awarded \$50,000 for his project: Combined TMS-EEG for early diagnosis of Alzheimer's disease.

Australian Pork Limited

Associate Professor Mark Nottle was awarded \$191,000 for his project: Development of thyroid biomarker for use in pre-pubertal gifts to select for embryo survival.

Cerebral Palsy Alliance Research Foundation

Professor Caroline Crowther and colleagues were awarded \$250,000 for their project commencing in 2014: Working to improve the survival and good health for babies born preterm: The Wish project follow up study.

Channel 7 Children's Research Foundation

RRI members were awarded 16 project grants commencing in 2014/2015 totaling more than \$965,000 from the Channel 7 Children's Research Foundation. This includes \$58,600 to Dr Nicolette Hodyl for: Regulating inflammation in the preterm neonate: the contribution of microRNAs.

Juvenile Diabetes Research Foundation

Professor Jennifer Couper was awarded \$7.8 million for the Environmental Determinants of Islet Autoimmunity study.

Ovarian Cancer Research Foundation

Professor Martin Oehler was awarded \$338,000 for two projects: Autoantibody biomarkers for ovarian cancer detection and Biospecimen collection and processing, maintenance of databases, and provision of samples for the OCRF tissue bank.

Women's and Children's Hospital Foundation

RRI members were awarded 9 project grants commencing in 2014/2015 totaling \$599,157. This included \$75,000 to Professor Tony Ferrante for: Vitamin D and innate immunity in the neonate.

Professor Jennifer Couper

In October, the Hon Tony Abbott announced the creation of the \$2.5 million Centre of Research Excellence in the Protection of Pancreatic Beta Cells.

Led by Professor Jennifer Couper, this CRE brings together an expert team of clinicians and researchers from across Australia to investigate:

- > What causes the immune system to attack pancreatic beta cells?
- > Why do certain genes put some people at greater risk of developing type 1 diabetes?
- > Where could we possibly intervene to prevent or reduce beta cell destruction?
- > How can we preserve beta cell function in people already diagnosed with type 1 diabetes?



Fellowships and Awards

ARC

ARC Future Fellow

Associate Professor Megan Warin (awarded 2014)

NHMRC

Commencing in 2014

Early Career Fellowship

Dr Rosalie Grivell and Dr Luke Grzeskowiak

Awarded in 2014

Senior Research Fellowship

Associate Professor Jeremy Thompson

Senior Practitioner Fellowship

Professor Jodie Dodd and Professor Ben Mol

Career Development Fellowship

Associate Professor Helen Marshall

Early Career Fellowship

Ms Philippa Middleton

CJ Martin Biomedical

Early Career Research Fellowship

Dr Alison Care

Peter Doherty Biomedical Early Career Research Fellowship

Dr Prabha Andraweera, Dr Nicole McPherson and Dr Ann-Maree Vallence

Other Fellowships (awarded 2014)

Barbara Kidman Women's FellowshipDr Adriana Parrella

Cerebral Palsy Foundation Fellow

Dr Clare van Eyck

Lloyd Cox Fellowship

Professor David Kennaway, Dr Julia Pitcher, Associate Professor Michael Ridding and Associate Professor Darryl Russell

Robinson Research Institute Fellowship

Dr Hannah Brown

Women's and Children's Hospital Friend's Fellowship

Ms Jane Tuckerman

Awards and Prizes

Australian Society for Medical Research (ASMR)

Ms Chantelle McIntyre awarded the Best Presentation at the ASMR Annual Scientific Meeting

Australian Society for Clinical Immunology and Allergy

Dr Jovanka King awarded the Best Clinical Round Presentation

Australian Society for Immunology

Mr Hanan Wahid awarded the Graham Jackson Memorial Mucosal Immunology Prize

Endocrine Society of Australia

Dr Lisa Moran awarded the Ken Wynne Post-Doctoral Research Award

Healthy Development Adelaide (HDA)

Ms Bing Wang awarded the HDA PhD Scholarship and Dr John Schjenken awarded a HDA Travel Grant

International Conference of Spermatology

Dr Nicole McPherson awarded the Best Scientific Talk

International Society for Animal Genetics

Mr Ruidong Xiang awarded a Travel Grant

National Public Health Association of Australia

Ms Bing Wang awarded the Early Career Public Health Award in Immunisation

Perinatal Society of Australia and New Zealand

Dr Kathryn Martinello awarded the Early Career Researcher Travel Award

Safework SA

Ms Renae Fernandez awarded the Augusta Zadow Scholarship

Skeptic Society

Emeritus Professor Alastair MacLennan awarded Co-Skeptic of the Year

Society for Reproductive Biology

Professor Robert Norman awarded Life Membership

Dr Melanie McDowall awarded the Meat and Livestock Australia New Scientist Award

Society for the Study of Reproduction

Dr John Schjenken awarded the International Best Abstract Award and the Larry Ewing Memorial Trainee Travel Grant

Society of Obstetric Medicine of Australia and New Zealand

Dr Luke Grzeskowiak awarded the Andrew Phippard Memorial Award for Best Oral Scientific Presentation and Research, and a Travel Grant

Texas A&M University

Professor Sarah Robertson awarded the Raymond O. Berry Award

The University of Adelaide

Professor Vivienne Moore awarded HDR

Supervisor of the Year

Dr Lynne Giles awarded an Academic Leadership Award

Professor Jozef Gecz and Dr Lachlan Jolly jointly awarded the Most Outstanding Paper in the School

Ms Macarena Gonzalez awarded the Outstanding Postgraduate Student Award

Professor Claire Roberts awarded the Excellence in Higher Degree by Research Supervision

Dr Adrian Kaczmarek awarded the Florey Postgraduate Research Poster Prize Mr Victor Chen, Ms Shanshan Han and Ms Noor Lokman awarded the Deans Commendations for Doctoral Thesis Excellence

Ms Siew Wong awarded DR Stranks Postgraduate Travelling Fellowship

Ms Harshavardini Padmanabhan awarded the 3 Minute Thesis Award

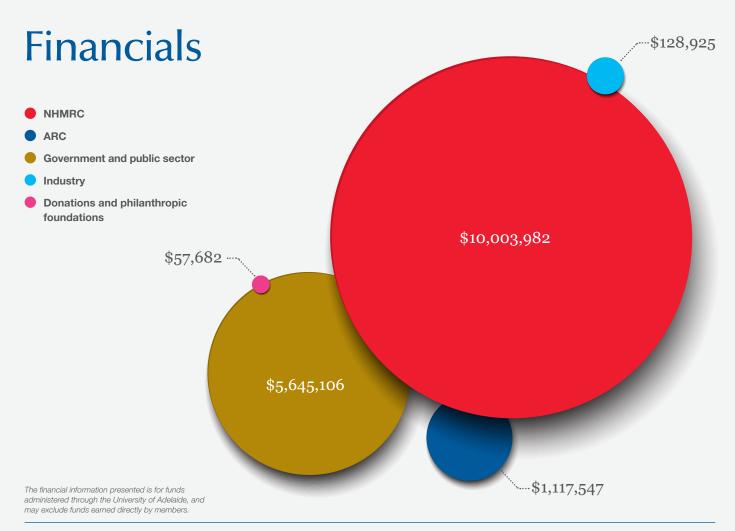
Ms Ella Green awarded the Derrick Rowley Prize for Honours in Microbiology and Immunology

Women's and Children's Health Network

Dr Amy Keir awarded the Young Investigator of the Year and the New Investigator Award

Dr Jovanka King awarded the Registrar as Trainer of the Year Award

World Congress for Reproductive Biology
Dr Hannah Brown awarded a Travel Grant





At least 1 in 6 Australian couples experience infertility and now 4% of children are conceived by IVF. However, only 17% of IVF cycles are successful and result in a live birth.

To select the best embryos for transfer following IVF, morphology is thought to be the best indicator - that is, quality is judged by appearance. However, differences between blastomeres within embryos are not always seen using morphology, which partially explains why the best quality embryos can be hard to identify.

Dr Melanie McDowall, a Senior Post-Doctoral Scientist in the Early Development Research Group is taking a new approach to embryo selection. Using autofluorescence, a technique that utilises a cell's natural emission of fluorescent light under UV illumination, embryos can be examined under a microscope, imaged and returned to the culture undisturbed. The resulting images highlight differences in blastomeres, and poor quality embryos are easily identified.

"The exciting thing about autofluorescence is that it is non-invasive, takes five minutes, uses technology which currently exists in most labs, and embryos continue to grow with no negative effects on development."

"Using this simple technique would limit the number of poor quality embryos used in IVF - leading to an increase in the number of successful pregnancies," said Melanie.

Using autofluroescence, Melanie compared embryos exposed to two different concentration levels of oxygen. Once an egg is fertilised and enters the oviduct the oxygen concentration decreases to 7%. She found that culturing embryos at 7% led to more successfully developed embryos than culturing at the atmospheric oxygen level of 20%, and this was reflected in a change in autofluorescence.

"When we culture embryos we try to provide conditions similar to those occurring naturally in the body. Through autofluroescence techniques, we found significantly fewer differences between blastomeres in embryos cultured at 7% oxygen than we did in stressed embryos cultured at 20% oxygen."

"You simply cannot pick up these differences using traditional morphology techniques," said Melanie.

Melanie is currently collaborating with researchers at Macquarie University and the ARC Centre of Excellence for Nanoscale BioPhotonics using a technique known as non-labeling hyperspectral analysis. This technique also uses autofluroescence to examine the embryo but it is more powerful and can measure at least 8 different molecules, showing patterns of increased heterogeneity in stressed embryos.

Melanie's work has significant implications for the IVF industry. IVF is currently very expensive and with such low rates of successful pregnancies, techniques that select high quality embryos cost effectively will be beneficial for both clinics and patients.

"In the future I believe this technique will be widely used in human reproduction and may also provide the ability to identify an incorrect number of chromosomes in an embryo - this currently cannot be tested without embryo biopsy."

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 hospitals ensure our scientists and clinicians are integrated within South Australia's medical practice, play a role in shaping effective health policy and have access to clinical material as appropriate.

Jean Hailes

The Institute collaborates with Jean Hailes through the National Alliance on Polycystic Ovarian Syndrome (PCOS). This unique initiative brings together multidisciplinary clinicians, women with PCOS, researchers and government representatives, and has developed 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 Institute for Photonics and Advanced Sensing (IPAS) were successful in receiving a \$23,000,000 ARC Centre of Excellence for Nanoscale BioPhotonics grant, headquartered at the University of Adelaide. Institute research leader Associate Professor Jeremy Thompson is a group leader on thisproject and collaborates with IPAS to develop new technologies to advance reproductive health research and practice.

Fertility clinics

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



Women's and Children's Health Research Alliance

Through the WACHRA Alliance, the Institute builds allegiance 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 site. This alliance seeks to foster research excellence in the area of women's and children's health in South Australia, translate research findings into policy, practice and delivery, establish a highly visible focus for funding, ensure sufficient research infrastructure needs are met, and communicate the benefits of health investment to the wider community.

Healthy Development Adelaide

The Institute is a major founding partner of Healthy Development Adelaide (HDA). HDA promotes, facilitates and enables multidisciplinary research that advances the understanding of healthy development, and the physical, psychological and social health of infants, children and adolescents.

Established in 2004 as an initiative of the University of Adelaide, HDA plays a key role in South Australia linking research, service delivery and policy development, and is currently led by Institute research leaders Professor Claire Roberts and Professor Michael Sawyer.

In 2014, 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 the University of Adelaide.

HDA runs a suite of events each year to create opportunities for communication, networking and multidisciplinary research collaborations, and ran 9 events in 2014. Additionally HDA supports the next generation of researchers and offered 5 top-up PhD scholarships funded by the Channel 7 Children's Research Foundation and 8 travel grants to outstanding PhD Candidates in 2014.

Your Fertility

Your Fertility works to address the gap in community knowledge and understanding about modifiable factors that affect fertility. By sharing the latest scientific and medical 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 (VARTA), Jean Hailes for Women's Health and Andrology Australia, Your Fertility targets its messages to Australian women and men aged 25-35 years old. As a partner, the Robinson Research Institute made important contributions to the program and its major activities, including:

Fertility Week 2014 (1-7 September)

Fertility Week is a national campaign promoting fertility awareness, and is a major focus of the Your Fertility program. Fertility Week 2014 focused on raising awareness of the fertile window of the menstrual cycle and how to time sex to achieve pregnancy. The theme sought to address poor public understanding of this issue as many women are not aware of the best time for conception or may over-estimate their knowledge.

Annual Meeting

Researchers from the Institute met with VARTA representatives to explore potential collaboration to promote and translate emerging research into public education resources and web content for Your Fertility. Professor Sarah Robertson accepted an invitation to be the guest presenter for

VARTA's annual Louis Waller lecture, which will take place in 2015 during Fertility Week.

South Australian Health and Medical Research Institute (SAHMRI)

The Robinson Research Institute connects with SAHMRI to develop collaborative partnerships in research relevant to the Healthy Mothers, Babies and Children research theme.

Presentations and speaker invitations

In 2014 Robinson Research Institute members were invited to deliver more than 140 presentations. Of these more than 55 were international invitations.



University and Institute Collaborations

The Robinson Research Institute collaborates with national and international universities and research institutes including but not limited to:

Institution	Country
ANZAC Research Institute	Australia
Baylor College of Medicine	USA
Benaroya Research Institute	USA
Birmingham Women's Hospital	UK
Bristol University	UK
Charles Darwin Institute	Australia
CSIRO	Australia
ETH Zurich	Switzerland
Flinders University	Australia
Garvan Institute of Medical Research	Australia
Goethe University	Germany
Harvard Pilgrim Health Care	USA
Howard Florey Institute	Australia
Hudson Institute of Medical Research	Australia
Indiana University	USA
Japan Synchrotron Radiation Research Institute	Japan
King's College London	UK
LIMES Bonn	Germany
March of Dimes	USA
McGill University	Canada
Medical Research Council	UK
Monash University	Australia
MRC National Institute for Medical Research	UK
Mount Sinai Hospital	Canada
National Institutes of Health	USA
Oregon National Primate Research Center	USA
Oxford University	UK
Peking University	China

Institution	Country
Prince Henrys Institute for Medical Research	Australia
Royal Children's Hospital Melbourne	Australia
Shanghai Jiao Tong University	China
Telethon Institute for Child's Health Research	Australia
The University of Auckland	New Zealand
The University of Edinburgh	UK
The University of Newcastle	Australia
The University of Nottingham	UK
The University of South Australia	Australia
The University of Western Australia	Australia
QIMR Berghofer Medical Research Institute	Australia
University of California, San Francisco	USA
University of Cambridge	UK
University College Cork	Ireland
University College London	UK
University of Lausanne	Switzerland
University of North Carolina at Chapel Hill	USA
University of Pennsylvania	USA
University of Reading	UK
University of Sassari	Italy
University of Southampton	UK
University of Westminster	UK
Utrecht University	Netherlands
Victoria University	Australia
Vanderbilt University	USA
Vrjie Universiteit Brussell	Belgium
Walter and Eliza Hall Institute of Medical Research	Australia

International Visitor Spotlight



Professor Richard A Anderson United Kingdom

Professor Richard A Anderson is the Elsie Inalis Professor of Clinical Reproductive Science, and Head

of Section, Obstetrics and Gynaecology at the MRC Centre for Reproductive Health at Queen's Medical Research Institute. University of Edinburgh.

Richard and Professor Ray Rodgers began collaborating on ovarian development in 2009 – with Richard focusing on germline cells in humans and Ray on the hormoneproducing cells and other areas in a bovine model.

At the time of meeting, Ray had been unsuccessfully looking for expression of gene linked to polycystic ovary syndrome in the adult ovary. Ray turned his attention to perturbed fetal development that could lead to PCOS in later life and first investigated this in the bovine model and then in humans with Richard. With Richard's parallel studies in humans, they found a gene that was expressed at a critical stage of ovary development. As a result, Richard contributed with Ray's leadership, to a major review in leading journal, Endocrine Reviews. Richard visited the Institute in 2014 to continue this research collaboration.



Dr Min Jin China

Dr Min Jin is Chief of the Center for Reproductive Medicine at the 2nd Affiliated Hospital, Zhejiang University.

Min is an expert in assisted reproductive technology, polycystic ovary syndrome and reproductive immunology research - with overlapping research interests with Professors Sarah Robertson and Rob Norman, Min learnt about the Institute's research when Rob visited China in 2012. She then read about our work in reproductive immunology publications online, and made contact to arrange a 12 month visit to the Institute. During Min's time in Adelaide she achieved a substantial amount, developing new flow cytometry protocols for the assessment of immune cells in reproductive disorders.

During Min's latest trip to the Institute, she commenced a new clinical study to evaluate how the oral contraceptive pill affects the phenotype of T regs in women's peripheral blood. Following this study, Sarah visited Dr Jin in China to advance the collaboration, and together they are now evaluating immune cells in Asian women to establish a new study in China. This productive visit has resulted in a new ongoing collaboration between the RRI and Zhejiang University, and both partners look forward to working together in the future.



Professor Neil Johnson New Zealand

Professor Neil Johnson is the President Elect of the World Endometriosis Society, Medical

Director of Fertility Plus in Auckland, and Honorary Academic with the University of Auckland and the University of Adelaide.

Around 1 in 10 women suffer from endometriosis and currently the only accurate way to diagnose this painful and crippling condition is through an invasive laparoscopy procedure. Neil's mission is to change this and is collaborating with RRI members Drs Louise Hull and Vicki Nisenblat who are conducting systematic reviews to develop low invasive diagnostic techniques for endometriosis including imaging and biomarkers of urine, blood and endometrium samples.

In addition, Neil is collaborating with Professors Ben Mol and Rob Norman and Dr Paul Duggan, with a goal of establishing multi-centre research in endometriosis. Large scale collaborative trials across Australia and internationally will be the most reliable way to unearth new information and develop effective interventions.



Clinical translation

The Robinson Research Institute's research changes policy and practice, leading to improved patient treatments and better community health.

Global Obstetrics Network (GONet)

In 2010, Professor Ben Mol co-initiated the Global Obstetric Network, which he leads as Chair. The primary goal of this network is to facilitate a worldwide collaborative approach to clinical trials and observational studies in the field of maternal-fetal medicine and obstetrics.

During the last five years GONet has developed or completed 10 individual patient data meta-analyses from merged large data sets of randomised studies, defined uniform and relevant endpoints for clinical trials in preterm birth, and facilitated the development of clinical guidelines.

GONet has been invited to present its philosophy for collaborative research at the annual general meeting of the Global Coalition to Advance Preterm Birth Research, a coalition of the main funders for preterm birth research around the world.

Preterm Birth International Collaborative (PREBIC)

The Preterm Birth International Collaborative is a multinational collaboration of clinicians and research scientists. The collaboration aims to improve pregnancy and birth outcomes, thereby optimising infant health and long-term development.

Professor Ben Mol is a member of PREBIC, and has played an instrumental role in the scientific meetings and workshops. These workshops provide an opportunity for members to meet and discuss the latest developments in preterm birth research, identify knowledge gaps, and plan future projects.

World Health Organisation Taskforce

Associate Professor Helen Marshall was appointed to the World Health Organisation Taskforce to: Evaluate influenza to inform vaccine impact and economic modeling, particularly in relation to maternal influenza immunisation.



While this taskforce seeks to inform maternal influenza vaccination programs globally, it has a particular focus on low resource settings, and evaluates the evidence of the burden of influenza, and the safety and effectiveness of influenza vaccines in pregnant women.

Additionally, the taskforce will review the evidence of the impact of influenza on the developing fetus, including the potential for congenital abnormalities from influenza infection in early pregnancy. The taskforce will develop guidelines to inform decision-making for the introduction of influenza vaccine programs in low resource countries.

NHMRC Embryo Research Licensing Committee

Professor Robert Norman AO has been a member of the NHMRC Embryo Research Licensing Committee for the past six years. This committee is involved in regulating human embryo research and embryonic stem cell development from laboratories throughout Australia.

The Committee meets every three months to discuss research proposals in the areas of embryonic stem cell research, human embryo culture and training for procedures such as pre-implantation genetic diagnosis biopsies.

Additionally the committee is heavily involved in discussion regarding mitochondrial transfer, development of embryonic stem cell lines for particular diseases and research into their origins and treatment, and authorisation of the use of embryos for development of new culture techniques and equipment.

Perinatal Practice and Guidelines

Professor Jodie Dodd is actively involved in translating research findings into improved clinical practice and health policy. Through her role as Chair of the South Australian Maternal and Neonatal Clinical Network and Chair of the SA Maternal and Perinatal Mortality Committee, she regularly contributes to the development of statewide perinatal practice guidelines and policy documents, which promote evidence-based

health care within hospitals and the wider perinatal community.

Her research findings have improved clinical practice in South Australia with several states developing subsequent guidelines based on the South Australian model. Additionally her findings have been incorporated into the United Kingdom's guidelines relating to the management of women with twin pregnancies.

Expert Panel to the NHMRC

The Australian Research Centre for Health of Women and Babies (ARCH) 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 continued to develop the national evidence-based antenatal care guidelines - which have now been released.





A corridor discussion between colleagues led to a deeper understanding of sex differences in utero.

Males and females follow different growth strategies

Over several years, Professor Stefan Hiendleder has investigated the epigenetic and non-mendelian genetic factors in bovine fetuses at mid-gestation. While discussing his findings with colleague Dr Karen Kind, they realised that since males and females have very different body proportions, different growth trajectories must occur in utero.

Once he classified his data by sex, new insights were revealed. Stefan showed that female fetuses display Intrauterine Growth Restriction (IUGR)-like features, even when offspring go on to be delivered within the normal birth weight range.

"We found that females had lower fetal and placental weights, smaller umbilical cord vessel diameters and a lower fetus to placenta weight ratio than males at mid gestation. Commonly used clinical indicators of IUGR such as weight ratios of the brain to liver, brain to fetus and heart to fetus were significantly higher in females."

"Additionally, lower amounts of insulin-like growth factor 2 (IGF2) gene transcript in the female brain and heart, and lower levels of circulating IGF2 and total IGF binding proteins are consistent with the hypothesis of sex-specific restriction of nutrient supply," explained Stefan.

Stefan who leads the Epigenetics and Genetics Group, believes these findings help to explain the sex-specific differences observed in major non-communicable diseases.

"There are many examples of diseases affecting males and females differently - adolescent boys have higher systolic blood pressure than girls, more males die from cardiovascular disease before the age of fifty than females, while the risk for fatal coronary heart disease associated with type 2 diabetes is higher in females than in males.

"There is increasing evidence that sex-specific differences for these diseases stem from factors and exposures in early life, and what we've discovered provides new insight and a new way to consider this research," said Stefan.

Stefan then approached Professor Claire Roberts who leads the Placental Development Group, to work together with PhD candidate Consuelo Estrella to explore more deeply the significance of his findings.

"We know that the placenta and umbilical cord display strong sexual dimorphism in normal pregnancies. This may affect nutrient and oxygen supply through the fetoplacental circulation and contribute to sex-specific growth and development," explained Stefan.

While Stefan's research utilised bovine fetuses, he believes similar principles would operate in humans.

"We used the bovine as the best fit model as it is outbred and carries a single fetus, with gestation length, relative fetal growth curve and maturity at birth similar to humans. As such we would expect similarities between this model and humans," said Stefan.

The next steps for Stefan's research will include detailed genome-wide molecular profiling of key tissues to identify mechanisms and drivers of this sex-specific fetal growth.

Commercial development

Advancement in fertility, pregnancy and child health is enabled by successful partnerships with the private sector to develop and deliver new technologies, treatments and therapies. Innovative research discoveries made by Robinson Research Institute members are being developed with commercial partners to transform medical practice and the health of our community.

22 Robinson Research Institute



In 2014 the Institute worked with a variety of industry partners to generate over \$1 million in contract research, consulting income and royalty income.

The Institute is also actively engaged in research translation to improve clinical practice through non-commercial pathways. Several Research Leaders are involved in setting policy and changing clinical practise through various translational activities.

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. Professor Sarah Robertson, who spent more than 20 years working on cytokine regulation of embryo development, leads the science behind the technology. The key to its success is the technology's ability to closely mimic the natural environment of the uterus and support early embryo growth and firm implantation.

The work has entered a new phase with new trials to evaluate a second-generation formulation. A blastocyst culture medium containing GM-CSF, marketed as BlastGen® is currently in trial in partnership with Fertility SA and other international partners. BlastGen® is due to be released to the international market in 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, a quality assurance test for media and other products used in IVF. A variety of national and international companies and reproductive medicine clinics 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.

Production and supply of antibodies

Professor David Kennaway partners with Buhlmann Laboratories, to supply and use antibodies that form the active agents in assays to detect the hormone melatonin. The antibodies are incorporated into kits sold by Buhlmann to measure melatonin for laboratory and clinical applications in Australia and around the world.

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 Dickenson now licenses this biomarker for sale on the international market. The antibody is being tested for diagnostic utility in a number of diseases including type1 diabetes IBD and infertility, and is a new tool to advance research into regulatory T lymphocytes in laboratories around the world.

Cell Therapy Manufacturing

In 2014 a new \$63 million CRC for Cell Therapy Manufacturing was jointly established with the University of South Australia, with Associate Professor Simon Barry leading the T cell therapy programme. This CRC aims to develop novel cell manufacturing devices and protocols aimed at increasing the availability and reducing the cost of cell therapy.

Collaboration with Cook Medical

Several Institute Research Leaders enjoy a strong relationship with Cook Medical LLC - a privately owned medical device company based in Bloomington Indiana, USA. Cook produce more than 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 as a consultant, and supported several research projects which focus on the development of assisted reproductive technologies, especially in collaboration with The University of New South Wales and Vrije Universiteit Brussel (Belgium).

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 Sensing Technologies and Advanced Reproduction Research lab, which is a joint project between the Robinson Research Institute and the Institute for Photonics and Advanced Sensing.

New patents

Continuing a strong culture of translation, Robinson Research Institute members filed several new patent applications and are progressing commercialisation in the areas of IVF, mastitis technology, swallowing disorders and plasma biomarkers for ovarian cancer.



Community and Sector Engagement

Mr Tony Zappia MP Visits the Robinson Research Institute

In April, the Institute welcomed Mr Tony Zappia, MP for the Labor Party, to the Medical School precinct to showcase and share information about the Institute's key areas of research.

The Institute's research agenda and the importance and advantages of investing in the early stages of life and development was discussed. This highlighted the imperative to invest in research that improves not only the long-term intergenerational health of families, but also the economic impact to the community.

Mr Zappia toured the Medical School facilities and laboratories. He met with key Research Leaders and Clinicians and learned about the Institute's leading research in reproduction, pregnancy and child health.

New Frontiers for a Healthy Start to Life workshop

In May the Institute initiated The New Frontiers for a Healthy Start to Life workshop, to encourage collaborations between established and emerging researchers, within the Institute and with interstate colleagues.

This two-day conference focusing on fertility, pregnancy and child health was held at Serafino McLaren Vale and attended by 20 researchers from Monash University, The University of Melbourne, Prince Henry's Institute, The University of Newcastle and the Robinson Research Institute. Due to the events success and positive feedback, this workshop is scheduled to again run in 2015.

Current Controversies in Gestational Diabetes conference

In May the Institute hosted the Current Controversies in Gestational Diabetes conference, and was pleased to welcome Professor Chittaranjan Yajink (Director of the Diabetes Unit, KEM Hospital Pune, India) as the main discussant during the day.



L to R: Dr Suzette Coat, Dr Luke Grzeskowiak, Prof Claire Roberts, Sam Buckberry and Prof Jodie Dodd at the RRI Symposium

The conference covered diabetes care from all angles including prevention, diagnosis, management, follow-up and fetal impact, and was attended by more than 40 people from a range of disciplines and locations (local, interstate and international).

Introduction to writing a Cochrane Review workshop

In May the Institute hosted the Australasian Cochrane Centre's annual Introduction to writing a Cochrane Review workshop, facilitated by Miranda Cumpston and Kelly Allen from the Australasian Cochrane Centre in Melbourne.

Over 30 local and interstate review authors who are commencing Cochrane systematic reviews attended the three-day workshop. A mixture of presentations and hands-on sessions provided authors an overview of the methods required to write protocols and provided them with the tools to begin.

The Cochrane Collaboration is a global, independent network of health professionals, researchers, patient advocates and others, responding to the challenge of making the vast amounts of evidence generated through research useful for informing decisions about health.

Work Experience Students

The Institute supported two year-10 work experience student placements in June. Each student spent time with multiple research teams at the Medical School and Norwich sites to get a taste of the scope of work being undertaken across the Institute. These students participated in basic laboratory work under the supervision of post-docs and senior researchers, and gained an understanding of the extensive work that happens behind-the-scenes with medical and clinical research.

Research Tuesdays: Less gain, less pain?

In its ninth year, the Research Tuesdays lecture series shares the breadth and depth of the University of Adelaide's research with the community.

Professor Jodie Dodd, Head of the Institute's Health of Pregnant Mothers and Babies Group, was selected to present in July on the topic: Less gain, less pain? How limiting gestational weight gain is affecting pregnancy outcomes for obese mothers and their babies.









Held in the University's Bragg's Lecture Theatre and attended by more than 100 people, Jodie discussed the implications of being overweight or obese during pregnancy and the results of her recent clinical trial.

Inaugural INSPIRE Series luncheon

Initiated in 2014, the INSPIRE Series provides the opportunity for the Institute's early career researchers and PhD students to hear from and engage with the Institute's Emeritus Faculty.

Held in August, this luncheon was hosted by Professor Robert Norman AO and guest speaker Emeritus Professor Jeffrey Robinson CBE. E/Prof Robinson shared insights and provided advice from his impressive and comprehensive research career.

The luncheon was successful and highly valued by all who attended. The Institute plans to host a similar event in 2015 for a new group of members.

Food Allergies in Early Life

In September, the Institute co-hosted the Food Allergies in Early Life seminar with SAHRMI, FOODplus, Women's and Children's Health Research Institute and Healthy Development Adelaide.

This event provided the opportunity for the public to hear from some of Australia's finest practitioners and researchers in food allergy development, and answered the following questions:

- > Does the food pregnant women eat play a role in allergy development?
- > Will my child outgrow his/her food allergy?
- > What is the difference between food allergy and intolerance?

Lloyd Cox Memorial Lecture

In October, the Institute hosted the inaugural *Lloyd Cox Memorial Lecture*. This new lecture series to be held annually, features international research and policy leaders, tackling grand health challenges in pregnancy and child health.

The Institute was delighted to welcome Professor Jane E Harding, Deputy Vice Chancellor, University of Auckland to present the inaugural lecture on the topic: Health for now or for life? Dilemmas and trade-offs in caring for mothers and babies.

This lecture series plays tribute to Professor Lloyd Cox who was appointed as the foundation professor of The University of Adelaide's Obstetrics and Gynaecology Department in 1958. He strongly believed in close collaboration between scientists and clinical practitioners and this culture continues today within the Robinson Research Institute. Professor Cox established obstetrics and gynaecology as a science-based department and was instrumental in bringing infertility as a medical issue to the attention of mainstream medicine.

- Attendees from the Current Controversies in Gestational Diabetes conference
- E/Prof Alastair MacLennan AO, Prof Bob Seamark, Prof Rob Norman AO, E/Prof Brian Setchell, Prof Grant Sutherland AC, A/Prof Ossie Petrucco and E/Prof Jeffrey Robinson CBE at the INSPIRE series luncheon
- 3. Laura Spencer, Shanshan Han, Prof Jane E Harding, Emily Bain and Mairead Hooper at the Lloyd Cox Memorial Lecture
- A/Prof Peter Richmond, A/Prof Helen Marshall, Dr Tom Snelling, Maureen Watson, Prof Maria Makrides and A/Prof Ann Koehler at the SA Vaccinology update

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SA Vaccinology Update

The Institute teamed up with SA Health, the Women's and Children's Hospital and SAHMRI, to host the inaugural SA Vaccinology conference in October. The sold out event was opened by the Hon Jack Snelling MP, Minister for Health and featured a range of local, interstate and internationally recognised speakers on maternal and childhood immunisation.

This forum provided the opportunity for GPs, practice nurses, midwives, obstetricians and other health practitioners to come together to progress the research agenda for vaccine research and practice in South Australia. Feedback received from the 100+ guests was very positive and a similar event is scheduled for 2015.



Research Symposium

The 2014 annual Robinson Research Institute Symposium was held at the National Wine Centre in November. The full day program provided the opportunity for members to network and learn more about the great research being undertaken across the Institute's four themes.

This event saw a record number of attendees and poster submissions, and included a full program with 16 research presentations, 51 poster presentations and a Q&A with key research leaders facilitated by Dr Paul Willis (Director of RiAus).

The day concluded with an awards presentation, and networking over wine and canapés. Congratulations to A/Prof Jeremy Thompson, who received the 2014 Director's Award. Other award recipients included:

- > Dr Noor Alia Lokman Best Early Career Researcher Poster
- Harshavardini Padmanabhan Joint Best Student Poster
- > Daniel Pederick Joint Best Student Poster
- > Consuelo Amor S. Estrella People's Choice Poster
- > Dexter Chan 2014 Jeffrey Robinson Honours Scholarship
- > Ella Green 2014 Robinson Research Institute Honours Scholarship

Sponsorship

To support our members and to increase brand awareness, the Robinson Research Institute sponsored three events in 2014.

Society for Reproductive Biology

The Institute was proud to again support the Society for Reproductive Biology (SRB) by sponsoring the SRB Robinson Research Institute Mid-Career Award, awarded after national competition to Institute member Associate Professor Rebecca Robker in 2014.

The award was presented at the Annual Scientific Meeting of the Endocrine Society of Australia and the Society for Reproductive Biology at the Melbourne 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 2014 was the 9th year of our partnership. The Institute will again sponsor this award in 2015 and 2016.

ASMR Annual Scientific Meeting

For the first time, the Institute sponsored the ASMR Annual Scientific Meeting by providing the prize for the Best Presentation in the Field of Reproduction, Pregnancy or Child Health, awarded to Institute member Dr Prabha Andraweera.

Held in June at the Adelaide Convention Centre, this event provides the opportunity for early-career researchers and higher degree by research students to network, practice their presentation skills and share their research with their peers.

The Australian Society for Medical Research (ASMR) is the peak professional society representing Australian health and medical research.

Young Investigator Award

In 2014, the Institute was proud to be a major sponsor of the Young Investigator Award, awarded to Institute member Dr Amy Keir. Run by the Women's and Children's Hospital Foundation, these awards recognise and promote outstanding research undertaken by South Australia's young researchers in the area of women's and children's health. The prize is judged on the basis of quality of science, and ability to communicate using language that is readily understood by the public.

Science Stories

Science Stories profiles the Institute's early career researchers and PhD students, and provides a behind-the-scences look at their research. To read the full stories visit the Institute's website.



Is chronic pain a symptom of the brain? **Dr Ann-Maree Vallence**

Dr Ann-waree vallence

Two people experience the same injury. Both receive identical treatment and rehabilitation programs – so naturally, we would expect to see similar results. Unfortunately this is not always the

case. Six months later one patient has fully recovered, while the other develops a chronic pain condition. What caused the transition to chronic pain and why did it happen to one patient and not the other? Dr Ann-Maree Vallence, a Postdoctoral Fellow in the Neuromotor Plasticity and Development Group, is undertaking studies to understand how changes in the brain may be contributing to the development of chronic pain.



A new approach to improve IVF success.

Dr Melanie McDowall

At least 1 in 6 Australian couples experience infertility and now 4% of children are conceived by IVF – and this number is on the rise. Age is the largest cause of infertility and increasingly women are having

children later in life, and turning to IVF. However, IVF is not a magic solution that works for all women. Only 17% of IVF cycles are successful and result in a live birth. Why is the success rate so low? This is a complicated question and the full answer is not clear. However, Dr Melanie McDowall, a Senior Postdoctoral Fellow in the Early Development Research Group has focused her research on increasing IVF success and hopes to gain clinical acceptance for her new and uncomplicated approach.



Fit for a gene – how sexbiased gene expression contributes to fetal growth.

Sam Buckberry

It is well known that there are sex differences in fetal growth in utero. Males on average are larger than females at birth – demonstrating that males grow faster in utero. However,

this difference in fetal growth has other consequences. Several studies have shown that the sex of the fetus can also influence the risk of pregnancy complications such as preeclampsia and growth restriction. So how does the male development strategy differ from females, what role does the placenta play and why are males at greater risk? Sam Buckberry, a PhD candidate in the Placental Development Group, has conducted extensive genetic analyses to understand how sex-biased gene expression may contribute to sex-specific fetal development strategies in utero and what that could mean for predicting the risk of developing a pregnancy complication.



Is shift work harming your baby?

Dr Tamara Varcoe

Approximately 16% of the working population in Australia are shift workers, with females accounting for almost half – 48%. Shift workers are at greater risk of developing a range of health problems including

increased weight gain, diabetes, cardiovascular disease and even breast cancer. However, working shifts during pregnancy may also negatively affect the developing baby. Dr Tamara Varcoe, an Early Career Fellow in the Sleep Disorders Group, is focusing her research on understanding the effects of prenatal shift work exposure on not only the mother during her pregnancy, but also on the fetus in utero, and whether there are consequences for those babies as they grow and develop into adults.



The Robinson Research Institute continues to make a strong impact in the media. In 2014, the Institute disseminated 22 media releases, reaching more than 4.5 billion people, with online, press and television increasing substantially from 2013.

The Institute actively publicises its research outcomes in the media to better inform the community about fertility, pregnancy and child health issues. The Institute will continue to engage the media in 2015 to share its discoveries, and increasingly it will utilise social media for communication and conversations between researchers and the community.

Follow the Robinson Research Institute

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youtube.com/user/RobinsonInstitute

Media Circulation		
Internet	4,538,765,300	
Television	11,010,000	
Radio	1,825,300	
Press	679,790	





Approximately 50% of women have a BMI of 25+ in early pregnancy, which can lead to a host of pregnancy complications for both themselves and their baby.

Results of the world's largest pregnancy study of its kind have shown that a lifestyle intervention to improve diet quality and increase physical activity is associated with significant improvements in outcomes for babies.

Pregnant women with a BMI of 25+ were invited to participate in the LIMIT trial during their first antenatal visit to the Women's and Children's Hospital, Lyell McEwin Hospital or Flinders Medical Centre. Women were randomly allocated to receive either a comprehensive lifestyle intervention or standard antenatal care.

Women allocated to the intervention group were provided with healthy eating recommendations - to reduce intake of processed foods and saturated fat, and increase consumption of fruits and vegetables. Additionally, they were encouraged to increase walking and incidental activity and to set simple and realistic goals such as swapping white bread to wholemeal bread, or getting off the bus one stop earlier.

Study leaders Professor Jodie Dodd and Dr Rosalie Grivell designed the intervention to be achievable within the current antenatal care model so recommendations could be implemented.

"We understand how difficult it can be for women to change their diet and increase movement during pregnancy - particularly if they led a sedentary life prior to their participation in the trial."

"We provided women with advice that encouraged modest changes and we were surprised to see such significant health outcomes for their babies," said Jodie. The intervention group were 18% less likely to give birth to a large baby weighing 4kg or more, had a 53% reduction of moderate to severe respiratory distress syndrome in their babies, and length of hospital stay was reduced, compared with infants born to women receiving standard antenatal care.

"We were surprised to see that there wasn't a significant difference in weight gain between the two groups."

"The differences in outcomes for babies was significant resulting from simple, practical and achievable lifestyle changes," said Rosalie.

In parallel to their LIMIT trial, Jodie and Rosalie ran an economic evaluation to analyse the cost of the intervention. They found the additional cost of \$320 per woman to receive the lifestyle intervention was offset by the reduction in hospital costs.

"We hope that our comprehensive lifestyle intervention will be rolled out across hospitals in Australia and enhance current antenatal care provided to pregnant women."

"This easy-to-implement program not only improves outcomes for babies, but is cost-neutral - it's a no brainer," said Jodie.





Professor Bill Breed

Comparative Biology Reproduction of Mammals

Comparative morphology and evolution of gamete form and their interaction with Australian mammals

Australia has a unique mammalian fauna that includes both southern Gondwanan origin - the marsupials, and northern Asian origin the native rodents. Our work focuses on the morphology and evolution of their gametes, sperm and eggs, and their interaction at fertilisation. By comparing reproductive biology of different species, we can find common strategies and unique differences that provide insight on the evolution of reproductive biology more broadly. Our group passionately believes in the conservation of Australia's native fauna and much of our recent research has focused on identifying diseases with the long-term aim of minimising their adverse effects on the populations of these species.

During 2014 we focused on the adverse environmental effects of high temperatures on testis function, quality of sperm production, and the pathology of several diseases, especially those in koalas and wombats.

Our work on gamete interactions at the time of fertilisation in an old endemic rodent species was published together with a broad study on the co-evolution of rodent sperm and egg coats. Additionally, we published a study on the plasma biochemistry of koalas with and without oxalate nephrosis, and a preliminary investigation of the effects of sarcoptic mange on hairy-nosed wombats.

Group Members

Research Leader: Bill Breed

Senior Lecturer: Eleanor Peirce

PhD Candidates: Liberty Olds, Karleah Trengove and Harsha Wechalekar

Research Assistant: Chris Leigh

Honours Students: Alison Pullen and Hanna

Maclennan



Professor Frank Grützner

Comparative Genome Biology

Seeking to understand how genetic and epigenetic mechanisms contribute to human diseases through comparisons with other mammalian species

The comparison of genes, genomes and epigenetic mechanisms in different species has provided many fundamental insights into how genes function in humans, how they evolved, and how they contribute to diseases. Studying genes in species distantly related to humans has also helped the development of novel drugs including treatment for type 2 diabetes.

The Comparative Genome Biology 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, accompanied by massive loss or change

of genes involved in digestion. Studying monotremes provides the opportunity to identify the role of key genes involved in stomach function and metabolism in humans, and may lead to the identification of new therapeutic targets for metabolic diseases such as diabetes.

In 2014 we continued to investigate the role of genes in the piRNA pathway in the ovary and ovarian cancer. We also began new research to investigate if the interaction of genes in the nucleus changes in ovarian cancer when compared to normal cells. We finished our analysis of the histology of the monotreme pancreas and continued our work on GLP-1 mediated Insulin release. Additionally, our long-term collaboration with Professor Kaessmann culminated in two Nature publications, which provided fundamental insights into the evolution of non-coding RNAs and Y-chromosomes in mammals.

Group Members

Research Leader: Frank Grützner

Visiting Research Fellow: Dan Kortschak

Lecturer: Tasman Daish

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

Honours Student: Cyan Sylvester

External Collaborators: Peter Donnelly (Oxford University), Briony Forbes (Flinders University), Henrik Kaessman (University of Lausanne) and James Turner (Medical Research Council London)



Associate Professor Leonie Heilbronn

Obesity and Metabolism

Understanding and overcoming the metabolic risks of IVF

Globally, the number of children and adults conceived by in vitro fertilisaton (IVF) totals more than five million. Accumulating evidence suggests that IVF children have altered health profiles compared to their non-IVF peers, including increased fatness, raised blood pressure, increased fasting blood glucose and triglycerides, and lower flow mediated blood vessel dilation.

The Obesity and Metabolism Group aims to uncover new data on the long-term health consequences of IVF, and drive research towards best IVF practice. They recently showed that adults conceived by IVF displayed significantly lower insulin sensitivity compared to matched control adults. These changes may be associated with an increased risk of type 2 diabetes in later life. Currently we are unsure whether these differences are due to IVF or the result of genetics, socio-economic status, or parenting differences. The group aims to uncover if metabolic changes are associated

with the process of controlled ovarian stimulation used to collect eggs for IVF. In 2014 the group observed gender specific consequences of fertility treatments in offspring of mice. They showed that male mice conceived by IVF displayed impaired glucose tolerance and insulin resistance in the liver when they were lean and obese. The ovarian stimulated mice did not show a phenotype compared to naturally conceived mice, suggesting it is the process of IVF - not the hormone treatments - that may increase type 2 diabetes risk. In contrast, IVF females displayed no phenotype but both IVF and ovarian stimulated mice were more susceptible to the metabolic consequences of obesity, and were at increased risk of developing type 2 diabetes. This work emphasises the continued necessity to improve the technical practice of IVF, in order to strive for best possible health outcomes for IVF children.

Group Members

Research Leader: Leonie Heilbronn

Postdoctoral Researcher: Amy Ryan

Research Assistants: Briohny Bartlett and Nicole Isaacs

PhD Candidates: Thomas Butler, Miaoxin

Chen and Bo Liu

RRI Collaborators: Rob Norman and Rebecca

Robker

External Collaborators: Gary Wittert (University of Adelaide), Siobhan Banks (University of South Australia), Alison Coates (University of South Australia), Michelle Keske (Menzies), Dorit Samocha-Bonet (Garvan Institute), Charmaine Tam (University of Sydney), Manny Noakes (CSIRO) and Grant Brinkworth (CSIRO)



Associate Professor Louise Hull

Endometriosis

To identify diagnostic tools and therapies for endometriosis and translate them into clinical practice

Endometriosis affects 10% of women causing pelvic pain and infertility. Surgery is required for diagnosis and medical therapies treat symptoms rather than the cause of the disease. Diagnostic improvements and the development of a broader range of therapies with fewer side effects is vital to help women with this debilitating condition.

The Endometriosis Group have identified and evaluated microRNAs as a blood based diagnostic for endometriosis. They have also undertaken Cochrane Reviews of diagnostic methods for endometriosis.

Mouse models of endometriosis have been established to evaluate how different environmental factors contribute to the disease. The group have found that seminal plasma may contribute to the endometriotic disease process, while specific cytokins such as $TGF\beta$ regulate the progression of lesion growth on endometriotic lesion development. Additionally, the group established a bio bank of endometriosis tissues and have been engaged in undertaking Phase III and IV trials for pharmaceutical companies aiming to improve treatment options for women.

Group Members

Research Leader: Louise Hull

Research Fellows: Jonathan McGuane and

Vicki Nisenblat

NHMRC Early Career Fellow: Wang Zhao

PhD Student: Zahied Johan

Honours Student: Katherine Watson

Summer Student: Gabriel Kuo

RRI Collaborators: Wendy Ingman, Rob

Norman and Sarah Robertson





Associate Professor Wendy Ingman

Breast Biology and Cancer

Exploring how the immune system in the breast affects susceptibility to cancer and mastitis

Breast cancer is the most common type of cancer in Australian women, affecting 1 in 8 before the age of 85. While breast cancer treatment has improved, little progress has been made in reducing the incidence of this disease. Understanding the unique biology of this tissue will shed light on why the breast is particularly susceptible to cancer.

Lactation mastitis is a debilitating inflammatory disease of the breast that affects 1 in 4 breastfeeding women. The disease causes localised pain, and is frequently accompanied by the rapid onset of systemic symptoms including fever, muscle aches, chills and fatigue. In some cases, mastitis leads to breast abscess, which must be surgically drained, and in severe disease there may be permanent disfiguration of

the breast. Low milk supply frequently accompanies these symptoms and leads to many women ceasing breastfeeding.

The Breast Biology and Cancer Group is based at the Basil Hetzel Institute, and group members work with breast and plastic surgeons at The Queen Elizabeth Hospital to understand how hormones affect the biological function of breast tissue. We made substantial progress in the development of a new tissue bank to support breast cancer prevention research, and we now have the laboratory protocols in place to collect and store living breast cells from women undergoing surgery. These cells will be used to investigate the biological pathways that affect cancer risk. Additionally, we developed a new mouse model of mastitis, which is

a significant improvement on the previous models, and provides some exciting new opportunities to explore inflammation in the mammary gland.

Group Members

Research Leader: Wendy Ingman

Postdoctoral Researchers: Pallave Dasari, Danielle Glynn and Eleanor Need

Research Nurse: Kathryn Mildren

Research Officer: Leigh Hodson

PhD Candidates: Siti Noordin and Sally Sun

Masters Student: Vahid Atashgaran
Honours Student: Maddison Archer

Research Assistant: Harshani Pedige

RRI Collaborator: Sarah Robertson



Dr Michelle Lane

Gamete and Embryo Biology

Understanding the impact of environmental insults to gametes on the developmental trajectory of the embryo, and how this influences disease development

Obesity in reproductive aged men and women has increased exponentially in the last three decades, with more than 50% of women and men now overweight or obese when their children are conceived. Male and female obesity is associated with impaired fertility, and an increased risk of metabolic dysfunction in offspring - both parents contribute to this. In our animal models, male obesity impairs sperm function, reduces pregnancy rates, increases miscarriage and impairs the reproductive and metabolic health of two generations, affecting male and female offspring differently. We have shown that obesity results in alterations to the epigenetic composition of sperm, thus identifying a previously underestimated contribution of male health at conception on the health of pregnancy and offspring.

The Gamete and Embryo Biology Group is focused on uncovering how paternal health cues are passed to the next generation, and determining the extent to which non-genetic transmission is modifiable through lifestyle and diet interventions. We also seek to understand whether the molecular changes in animal models we have observed also exist in humans.

In 2014 our group demonstrated that diet and exercise interventions in obese males improved metabolic composition, the molecular nature of the sperm, and resulted in improvements to the health of the offspring. We further determined that oxidative stress appears to be a major causative agent in paternal transmission. In our studies on mitochondria, we demonstrated that in vitro treatment of aged oocytes with a mitochondrial stimulant improved embryo quality and increased pregnancy rates.

Group Members

Research Leader: Michelle Lane

Research Fellow: Tod Fullston

Research Assistants: Wan Xian Kang, Lauren Sandemann and Marni Spillane

PhD Candidates: Nicole McPherson, Leanne Pacella and Helena Shehadeh

Honours Student: Edwina Blue

Affiliate members: Deirdre Zander-Fox

RRI Collaborators: Julie Owens and Rebecca

Robker

External Collaborators: John Aitken (University of Newcastle), Rob McLachlan (PHMRI), Moira O'Bryan (Monash University) and Gary Wittert (University of Adelaide)



Professor Ben Mol

Evidence Based Women's Health Care

Evaluation of the effectiveness of health care for women and implementation of best practice

Much medical practice around the world is conducted without evidence that interventions are beneficial to the patient and will not cause harm. Many such interventions are commonplace and have been conducted for years (some for many decades) with little to no questioning as to the effectiveness of treatments.

The Evidence Based Women's Health Care Group is challenging current practice and believes all medical interventions in reproductive health care require an underlying evidence base demonstrating treatments are expected to do more good than harm.

The group aims to develop evidence on the effectiveness of all medical interventions in this area, preferably through large collaborations in randomised clinical trials, to provide insight on the available evidence tailored to the individual patient for both patients and doctors. To achieve this, international collaboration through

coordination of research agendas for clinical and basic research, and the establishment of guidelines is essential. The group aims to involve young people, create large datasets and initiate international collaboration.

During 2014 Ben co-initiated the PROMPT initiative (prospective meta-analysis in pessary trials), which brought together 30 researchers, commencing 15 pessary trials around the world. Additionally, planning commenced for future meta-analysis and international presentations. This study is positioned within the global obstetric network GONet.

Looking ahead Ben aims to grow GONet, and is arranging several events to further establish international collaboration. These include meetings at SMFM and ESHRE, hosting international researchers in Australia, and integrating the Australian/New Zealand's perinatal trial network IMPACT in these activities.

Group Members

Research Leader: Ben Mol

Research Fellows: Luke Grzeskowiak, Astrud Tuck and Tamara Varcoe

RRI Collaborators: Caroline Crowther, Michael Davies, Jodie Dodd, Gus Dekker, Bill Hague, Louise Hull, John Lynch, Michelle Lane, Helen Marshall, Vivienne Moore, Rob Norman, Martin Oehler, Julie Owens, Claire Roberts, Sarah Robertson, Michael Stark and Jeremy Thompson

External Collaborators: Siladitya Bhattacharya (University of Aberdeen), Arri Coomarasamy (University of Birmingham), Tony Duan (Shanghai Tongji University), Bill Grobham (Northwestern University), Justus Hofmeyr (University of Witwatersrand), Rodolfo Pacagnella (University of Campinas), Shakila Thangaratinam (Blizard Institute), Homan Tuong (Vietnam National University) and Xiaoke Wu (Heilongjiang University of Chinese Medicine)



Professor Rob Norman AO

Reproductive Endocrine and Medicine

Improving outcomes in IVF, Polycystic Ovary Syndrome and related conditions

Approximately 1 in 10 couples will experience infertility and more than 1 in 10 women suffer from Polycystic Ovary Syndrome (PCOS), which is the most common condition of female reproduction. Many interventions to improve fertility involve manipulating reproductive hormones through drugs and techniques such as IVF.

The Reproductive Endocrine and Medicine Group seeks to understand the mechanisms underlying reproductive disorders and the role hormones play. We are increasing our understanding of the impact of various factors including obesity, stress, lifestyle and genetic factors on reproductive outcomes.

In 2014 we were successful in obtaining an NHMRC National Centre for Research Excellence (CRE) in PCOS in collaboration with Professor Helena Teede from Monash University. The CRE will continue to increase our contributions to PCOS, and will place Australia at the forefront of delivery on healthy outcomes for patients with this condition.

Together with Professor Ben Mol we evaluated the outcomes of several hundred patients who received ovulation induction at the local fertility clinic, Fertility SA. This demonstrated that ovulation induction can be highly successful and IVF is rarely required for these patients.

In 2015 we intend to grow the CRE to include new diagnostic methods, improved ultrasounds, and a better understanding of menstrual cyclicity. We will continue our work on the effect of obesity on reproduction, particularly the egg, early pregnancy and long-term consequences, and will continue to look at dietary interventions for PCOS.

Additionally, we aim to grow the strong relationships we have established with overseas groups in Europe, USA and Asia, particularly China.

Group Members

Research Leader: Rob Norman

Clinical Researcher: Helen Alvino

RRI Collaborators: Michael Davies, Leonie Heilbronn, Louise Hull, Neil Johnson, Ben Mol, Lisa Moran, Rebecca Robker and Ray Rodgers

External Collaborators: Bart Fauser (University of Utrecht), David Handelsman (ANZAC Institute), Roger Hart (University of Western Australia), Nick Maclon (University of Southampton), Tanya Monro (University of South Australia) and Helena Teede (Monash University)





Associate Professor Mark Nottle

Reproductive Biotechnology

Development of organ, tissue and cell replacement therapies

There is a global shortage of human organ, tissue and cell donors to treat life threatening childhood and adult conditions. 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 group seeks to develop new biotechnologies to address the challenge of tissue transplantation. In particular, they are developing the pig as a large animal model for human stem cell research. In 2014 the group demonstrated that porcine embryonic stem cells have the ability to differentiate to multiple cell types, including insulinproducing cells that may have utility as a new therapy for diabetes. The group aims to continue this research to characterise the clinical value of these and other cell types in a pig model.

Group Members

Research Leader: Mark Nottle
Research Fellow: Ivan Vassilev

Research Manager: Leanne Srpek

Research Assistants: Emmy Bouwman and Stephen McIlfatrick

RRI Collaborators: Toby Coates, Stefan Hiendleder, Michelle Lane, David Parsons and Paul Thomas

External Collaborators: Peter Cowan (St Vincents Hospital), Emmanule Cozzie (University of Padau), Wayne Hawthorne (Westmead Millennium Institute), Nam Kim (Chungbuk University), Andrew Lew (WEHI), Philip O'Connell (Westmead Millennium Institute), Simon Robson (Harvard Medical School) and John Paul Soulillou (Universite de Nantes)





Professor Martin Oehler and Dr Carmela Ricciardelli

Reproductive Cancer

Identification of novel biomarkers and therapeutic targets for ovarian cancer

Ovarian cancer is a devastating disease and the leading cause of death from gynaecological malignancies. It affects approximately 1 in 90 women in Australia and over 70% of patients present with advanced disease. Despite improvements in surgery and new developments in chemotherapy, ovarian cancer mortality rates have not changed dramatically 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 seeks to understand the mechanisms involved in ovarian cancer spread, resistance to chemotherapy and the identification of novel biomarkers for detection.

In 2014 our research focused on further understanding the role of the sugar molecule, hyaluronan (HA) in chemo-resistance. We characterised the function and expression of an enzyme transketolase (TKT) involved in sugar metabolism in ovarian cancer cells. Additionally, we established an ex vivo tissue explant model to assess drug responses in human ovarian cancer tissues.

In 2015 we will determine whether a protein regulated by ovarian cancer-peritoneal interactions can be used as a diagnostic marker for serous ovarian cancer in independent cohorts. We will also assess whether hyaluronan inhibitors are effective at reversing chemo-resistance using established ovarian cancer cell lines and primary cells derived from ovarian cancer patients.

Group Members

Research Leaders: Martin Oehler and Carmela Ricciardelli

Research Assistants: Anita Oehler, Carmen Pyragius and Izza Tan

Postdoctoral Researcher: Noor Lokman

Honours Students: Noor Hammodi and Emily Hawkins

RRI Collaborator: Frank Grutzner, Ray Rodgers and Darryl Russell

External Collaborators: David Callen (University of Adelaide), Peter Hoffmann (University of Adelaide), Andrew Ruszkiewicz (SA Pathology), Andrew Stephens (Prince Henry's Institute) and Florian Weiland (University of Adelaide)



Professor Sarah Robertson

Reproductive Immunology

Understanding how cells and cytokines of the immune system contribute to regulation of the reproductive process from conception to birth

In pregnancy, the female immune system recognises the fetus as foreign and requires an active state of immunological tolerance to be established to allow implantation and development of the fetus. Many of the reproductive and pregnancy disorders including unexplained infertility, recurrent miscarriage, preeclampsia and preterm birth - have their origins in immune and inflammatory disturbances that cause the placenta to not develop properly. This leaves the placenta vulnerable to immune attack and inflammatory injury that impairs fetal growth.

The Reproductive Immunology Group explores the mechanisms through which the female immune system becomes activated to confer tolerance before embryo implantation. In particular, we focus on events at conception that elicit a sequence of events to stimulate generation of cells called regulatory T cells (Treg cells). Treg cells are anti-inflammatory and pro-tolerance and

are crucial for robust placental development and pregnancy success.

In 2014 we made substantial progress in understanding how several factors integrate to influence the quality of immune adaptation for pregnancy. The cytokine IL10 was identified as crucial for generating competent Treg cells. Importantly, we discovered that the hormone progesterone interacts with cytokines to confer functional stability and prevent potentially destructive Th1 and Th17 cells from becoming activated. Seminal fluid initiates this process, and our experiments implicate several microRNAs induced in female tissues by male sperm signaling to be a key factor driving Treg cell differentiation at conception. Work in our laboratory showed the crucial importance of TLR4 signaling in the pathway through which both infectious and sterile inflammatory insults converge to overcome tolerance and accelerate the timing of birth.

Group Members

Research Leader: Sarah Robertson

Research Fellow: Kerrilyn Diener

RRI Research Fellow: Hannah Brown

Senior Postdoctoral Researchers: Lachlan Moldenhauer and David Sharkey

Postdoctoral Researchers: Peck Yin Chin and John Schjenken

PhD Candidates: Hanan Wahid and

Bihong Zhang

Research Officer: Camilla Dorian

Honours Students: Dexter Chan and Ella Green

Affiliate Member: Maria Makrides

RRI Collaborators: Louise Hull, Simon Barry, Wendy Ingman, Rebecca Robker and Jeremy Thompson

External Collaborators: Mark Hutchinson (University of Adelaide), David Olson (University of Alberta), Kenner Rice (NIH Washington) and Alison Quayle (Louisiana State University)



Associate Professor Rebecca Robker

Ovarian Cell Biology

Identifying cellular mechanisms driving ovulation and embryo development

Ovarian function is central to many aspects of women's health. In addition to producing essential hormones, the ovary nurtures oocytes, providing the building blocks they need to form an embryo. Uncovering the molecular mechanisms that control ovarian processes is essential for understanding the very basics of female fertility in all mammalian

The Ovarian Cell Biology Group aims to uncover new knowledge of ovarian biology and how processes go awry in various infertility disorders. In Australia, obesity rates are amongst the highest in the world, and obesity is associated with female subfertility, altered embryo growth and elevated risk of obesity in offspring. We are investigating how excess fat within the oocyte impairs its ability

to form an embryo and how to reverse the detrimental effects. In mice we have shown that female obesity leads to mitochondrial damage in oocytes, which persists into the tissues of offspring. Most importantly, we have discovered a class of compounds that when administered to obese mice, prevents the mitochondrial changes in oocytes and offspring tissues.

We are also investigating the basic biology of the oviduct to understand how it nurtures embryos and influences their healthy development. If transport of the fertilised oocyte does not progress normally, ectopic pregnancy can result. Using microarray analysis of oviducts from mice lacking the progesterone receptor we were able to identify and characterise the expression of

progesterone target genes that are likely to sustain and transport the embryo during the first few days of life.

Group Members

Research Leader: Rebecca Robker

Postdoctoral Researcher: Linda Wu

PhD Candidates: Miaoxin 'Victor' Chen, Macarena Gonzalez and Siew Wong

RRI Collaborators: Leonie Heilbronn, Michelle Lane, Robert Norman, Sarah Robertson, Darryl Russell and Jeremy Thompson

External Collaborators: Michael Barry (Fertility SA), John Carroll (Monash University), Mark Febbraio (Baker IDI Heart & Diabetes Institute) Jon Hennebold (Oregon National Primate Research Center) and Justin St John (MIMR-PHI)





Professor Ray Rodgers

Ovarian Developmental Biology

Understanding the role of the ovary in fertility and endocrine function

Reproductive health significantly impacts a woman's wellbeing throughout her life, irrespective of her choice to have children. In addition to producing eggs, the ovary's hormones govern cyclical changes regulating somatic and psychological health at puberty, across the menstrual cycle, during the establishment and maintenance of pregnancy, and in parturition, lactation and menopause.

The Ovarian Developmental Biology Group studies the basic cellular biology of the ovary to understand and prevent diseases of the ovary. Throughout life the ovary continually changes its cellular structures as follicles and corpora lutea grow and regress within it. There are many opportunities for processes to go wrong which can lead to common disorders including hormone imbalances,

infertility, polycystic ovary syndrome, premature menopause and ovarian cancers. In 2014 we undertook transcriptome profiling (>18,000 genes) of different follicular cells during their development both in vivo and in vitro. This broad-brush approach identified new genetic pathways and hitherto unknown behaviours of cells, which is important for future research in understanding the development and function of the ovary.

Additionally, we examined ovaries at the Australian Synchrotron. We are now able to identify which cells in the ovary accumulate trace elements such as selenium, zinc, copper and iron. With this understanding, we can formulate new hypotheses and identify the function of these trace elements in the ovary and for fertility.

Group Members

Research Leader: Ray Rodgers

Postdoctoral Researcher: Katja Hummitzch

Research Assistants: Wendy Bonner, Nicholas Hatzirodos and Yvonne Miels

PhD Candidates: Mel Ceko, Katrina Copping

and Monica Hartanti

Honours Student: Nicole Bastian

RRI Collaborators: Michelle Lane, Sarah Robertson and Darryl Russell

External Collaborators: Richard Anderson (University of Edinburgh), Ross Bathgate (Howard Florey Institute), Hugh Harris (University of Adelaide), Phil Knight (University of Reading), Lisa Martin (Monash University), Viv Perry (University of Nottingham) Dieter Reinhardt (McGill University) and Dagmar Wilhelm (Monash University)



Associate Professor Darryl Russell

Ovarian and Reproductive Cancer

Defining the molecular mechanisms of hormone control of ovarian folluculogenesis

Ovarian follicles coordinate input from the maternal system and oocyte secreted factors to guide oocyte maturation. This interaction impacts the endocrine health of women and ultimately the lifelong health of offspring.

The Ovarian and Reproductive Cancer Group is focused on understanding the unified mechanisms by which hormone signals and tissue structure determine the health and function of ovaries. The group seeks to harness this knowledge to improve reproductive health and advance treatments for infertility and cancer.

We aim to:

- > Understand the fundamental mechanisms by which hormones and tissue morphogenesis control ovarian function
- > Harness this knowledge to improve reproductive health and advance treatments that directly address the

- causes of infertility and endocrine dysfunction
- > Apply our experience in hormone controlled morphogenic processes to understand the mechanisms of reproductive organ cancer incidence and metastasis

In 2014, we published a number of studies that characterised novel aspects of the molecular control of oocyte development and ovarian function. We demonstrated that a range of environment and lifestyle stressors influence ovarian somatic cell function and in turn impact oocyte and embryo health. The mechanisms by which stressed oocytes signal to somatic cells and the response intended to prevent damage, which can lead to infertility or poor fetal developmental outcomes, continue to be investigated. These stress response mechanisms are important in the initiation and progression of cancers of reproductive organs.

Group Members

Research Leader: Darryl Russell

Senior Research Associate: Jill Muhling

Postdoctoral Researchers: Lisa Akison and Kylie Dunning

PhD Candidates: Adrian Kaczmarek and Izza Tan

Research Officer: Laura Watson

RRI Collaborators: Frank Grutzner, Michelle Lane, Carmela Ricciardelli, Claire Roberts, Sarah Robertson, Rebecca Robker, Ray Rodgers and Jeremy Thompson

External Collaborators: Robert Gilchrist (UNSW), Juan Carlos Rodriguez-Manzaneque (Genyo, University of Granada) and John Sandy (Rush University)





Professor Paul Thomas

Neural Development

Generation and analysis of mouse models for epilepsy and intellectual disability

Neurological disorders are amongst the most common condition in children. The Neural Development Group seeks to uncover the genetic causes of neurological disorders with a particular interest in epilepsy and intellectual disability, which affect approximately 3% of the population.

Using mouse models and stem cells, the group aims to understand the disease mechanisms that underpin these debilitating conditions. Using CRISPR/CAS9 genome editing, the group has established novel 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 2015 the group will continue to expand their expertise in genome editing, and will analyse existing mouse models of epilepsy and intellectual disability to investigate disease mechanisms and explore new therapies.

Group Members

Research Leader: Paul Thomas

Research Fellow: James Hughes

Research Assistants: Sandie Piltz and Melissa

PhD Candidates: Dale McAnich and Ella

Thomsor

Masters Student: Louise Robertson

Honours Students: Daniel Pederick and Ruby



Associate Professor Jeremy Thompson

Early Development

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

Accompanying fertilisation are dynamic molecular and biochemical processes that significantly impact subsequent embryonic and fetal development, as well as adult health. The newly fertilised egg is extremely sensitive to the microenvironment within the maternal reproductive tract, and this is reflected in the resetting of its epigenetic code. If the metabolic microenvironment surrounding the oocyte and embryo is altered as a result of IVF, diet or 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 on the earliest stages of embryo development. Our multi-disciplinary collaborative team utilise multi-disciplinary approaches to answer questions on the nano-scale. Our major focus is to explain how environmental stress impacts early

development, to develop new tools to measure the changes, and to successfully develop interventions to reduce the impact.

Our involvement with the ARC Centre of Excellence for Nanoscale Biophotonics saw the development and use of new and novel technologies and techniques designed to better understand the nano-scale implications of perturbed embryo development. With the application of new fluorophores, we are mapping the metabolic heterogeneity between individual blastomeres of embryos, revealing that whole embryo metabolic analysis often masks the variability between individual blastomeres. Continued efforts in defining histone modifications within oocyte and early embryo chromatin has revealed major perturbations associated with not only hyperglycemic conditions but also standard conditions encountered during the IVF process. This raises questions about the long term effects of IVF on the health of children that must be addressed.

Group Members

Research Leader: Jeremy Thompson

Postdoctoral Researchers: Hannah Brown and Melanie McDowall

Laboratory Manager: Lesley Ritter

Research Assistants: Annie Whitty and

Melissa White

PhD Student: Ryan Rose

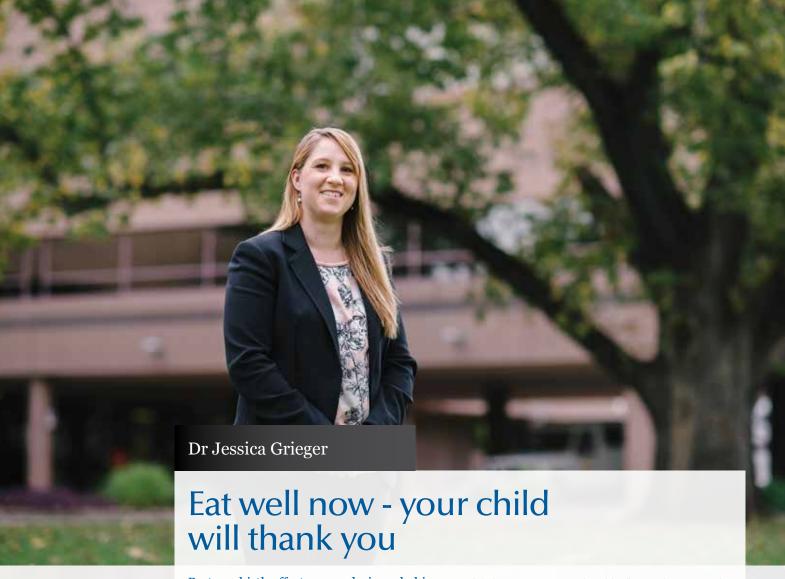
Technical Officer: Anwar Fatohi

Manager, IVF Vet Solutions: Marie Anastasi

Visiting Researcher: Nelida Rodrigues-Osorio

RRI Collaborators: Michelle Lane, Sarah Robertson, Rebecca Robker and Darryl Russell

External Collaborators: Andrew Abell (University of Adelaide), Michael Barry (Fertility SA), Jose Buratini (Universidade Estadual Paulista), Pablo Cetica (University of Buenos Aires), Gabriel Davit (University of Buenos Aires), Michel DeVos (Vrije Universiteit Brussel), David Gardner (University of Melbourne), Rob Gilchrist (University of New South Wales), David Mottershead (Mottasis Review), Ryan Rose (Fertility SA), Johan Smitz (Vrije Universiteit Brussel) and Yvonne Stokes (University of Adelaide)



Preterm birth affects around 1 in 10 babies and is a leading cause of infant disability and death – understanding the contributing factors is crucial to prevent early labour.

It is well understood that maternal nutrition during pregnancy can significantly affect fetal growth, development and birth weight. Postdoctoral Research Fellow Dr Jessica Grieger built upon this knowledge, and for the first time evaluated the pre-conception diet of more than 300 South Australian women to better understand the association between maternal nutrition and perinatal outcomes.

Jessica found that women who eat a poor diet in the year before they become pregnant are around 50% more likely to deliver their baby preterm than those who follow a healthy diet.

"In our study, women who ate protein-rich foods including lean meats, fish and chicken, as well as fruit, whole grains and vegetables, had significantly lower risk of preterm birth."

"On the other hand, women who consumed mainly discretionary foods, such as takeaway, potato chips, cakes, biscuits, and other foods high in saturated fat and sugar were more likely to have babies born preterm," Jessica explained.

This is an important discovery as diet is a modifiable factor that can be changed relatively easily and can potentially reduce the risk of preterm birth.

If women understand the impact diet has on the health of their baby they may be motivated to change their eating habits prior to conceiving as well as during pregnancy.

"It is important to note that this dietary change needs to be a wholefood approach. It has been shown that supplementation is not useful in preventing preterm birth." said Jessica.

Dietary intervention is often difficult pre-pregnancy, as around 50% of pregnancies are unplanned.

However, Jessica hopes to continue her research by developing a dietary intervention study, to look at the benefits of switching to a healthy diet for protecting against preterm birth, low birth weight and pre-eclampsia.

"Unlike other risk factors for preterm delivery such as genetics and age, diet is a modifiable risk factor. It is never too late to make a positive change. We hope our work will help promote a healthy diet before and during pregnancy. This will help to reduce the number of neonatal deaths and improve the overall health of children," Jessica says.



Associate Professor Vicki Clifton

Pregnancy and Development

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

Pregnancy complications may arise from pre-existing diseases that affect the health of the mother and the development of her baby. Asthma for example, is highly prevalent in Australian women and associated with poor outcomes for babies including preterm delivery, stillbirth and growth restriction. These poor outcomes can be minimised if asthma is managed effectively during pregnancy.

The Pregnancy and Development Group take a multi-layered approach to understanding asthma during pregnancy and its impact on mother and baby. We examine clinical issues associated with improving health service, health education and communication, and asthma management, as well as understanding the mechanisms that affect fetal development and long-term health of the children of mothers with asthma.

Our group recruits pregnant women at their first antenatal visit and follows them

throughout gestation and post partum to determine the events that contribute to the health of their child. We look at maternal diet, asthma control, health knowledge, literacy and communication. In the children we examine cardiovascular health, growth, neurodevelopment and immune development, and link outcomes to in-utero events. From these studies we have demonstrated that poor diet increases the risk of preterm delivery.

In 2014 we uncovered 12 isoforms of the glucocorticoid receptor in the human placenta. This discovery paves the way for a greater understanding of how glucocorticoids may affect fetal growth and development. Additionally we developed a phone app for early pregnancy to determine how to best communicate with women and provide important health information to them at crucial time points in pregnancy.

Group Members

Research Leader: Vicki Clifton

Emeritus Member: Basil Hetzel

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

Senior Postdoctoral Researcher: Dianne Rodger

Research Nurse: Kate Roberts-Thompson

Research Midwives: Julia Dalton and Karen Rivers

Honorary Titleholder: Nayana Parange

PhD Candidates: Natalie Aboustate, Maureen Busuttil, Isabella Rose-Meredith, Julie Tucker, Amy Wooldridge, Ian Wright, Chow Yan and Nurul Zainal

Administrative Assistant: Kelly Fulton

RRI Collaborators: Gus Dekker, Kathy Gatford, Stefan Hiendleder, Karen Kind, Julie Owens, Claire Roberts and Cheryl Shoubridge

External Collaborators: Anil Roy (Royal Adelaide Hospital) and Brian Smith (Basil Hetzel Institute)





Professor Caroline Crowther and Ms Philippa Middleton

Health of Women and Babies

Improving the health of women and babies

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 a diverse research program that encompasses care from preconception through pregnancy and childbirth, infancy and later life using systematic review, individual participant data meta-analyses, randomised trial, cohort studies, qualitative and quantitative research methodologies.

In 2014 the Health of Women and Babies Group continued to conduct major NHMRC funded randomised clinical trials that evaluated care

> 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

during pregnancy and childbirth. Amongst

these were:

- > IDEAL Investigation of dietary advice for women with borderline gestational diabetes
- > MAGENTA Magnesium Sulphate at 30 to 40 weeks gestational age: neuroprotection trial
- > 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
- > My Baby's Movements Trial Maternal awareness of fetal movements to prevent stillbirth

We completed the evaluation of the South Australian Family Birthing Program and made strong recommendations for its continuation and further development.

Group Members

Research Leaders: Caroline Crowther and Philippa Middleton

Research Fellows: Emily Bain and Shanshan Han

Research Officers: Melissa Ewens, Daniela Gagliardi, Michaela Jarrett and Ellen Lyrtztis

Senior Clinical Trials Manager: Pat Ashwood

Research Manager: Tanya Bubner

Administrative and Data Assistants: Mary Paleologos, Caroline Holst and Kaye Robinson

PhD Candidates: Angela Brown, Emer Heatley and Zohra Lassi

Honours Student: Laura Spencer

Data Management Team: Vincent Ball, Sasha Zhang, and Tran son Thach





Professor Jodie Dodd

Health of Pregnant Mothers and Babies

Improving health outcomes for pregnant women and their babies

Good nutrition and physical activity are important for women of reproductive age, particularly during pregnancy. The risk of pregnancy complications, including high blood pressure, preeclampsia, gestational diabetes and caesarean birth increases with maternal BMI, and may be improved through optimal nutrition and exercise.

The Health of Pregnant Mothers and Babies Group investigate the effect of diet and lifestyle interventions during pregnancy on pregnancy complications and infant health outcomes. Optimal nutrition and exercise during pregnancy may reduce the risk of poor infant health including high birth weight, nursery admissions, as well as an increased lifetime risk of subsequent obesity and cardiovascular disease.

In 2014 the findings of the LIMIT randomised controlled trial were published, involving 2,212 pregnant women who were overweight or obese. Women who received dietary and lifestyle advice made significant

improvements to both their diet and physical activity patterns. Additionally, their babies were less likely to be born with a birth weight above 4kg. Ongoing follow-up of the children continues.

Group Members

Research Leader: Jodie Dodd

Emeritus Professor: Jeffrey Robinson

Research Manager: Andrea Deussen

Clinical Researchers: Rosalie Grivell, Andy

McPhee and Cecelia O'Brien

Statistician: Lisa Yelland

Postdoctoral Researcher: Lisa Moran

Research Coordinators: Angela Newman and

Courtney Cramp

Research Dietitians: Courtney Cramp and Stephanie Zrim

Research Assistants: Lauren Cates, Tiffany Cornish, Ashlee Fairclough, Louise Fraser, Caroline Holst, Lavern Kannieappan, Anita Lo, Ellen Lyrtzis, Caroline Sheppard, Gosia Smezja, Fleur Spronk and Sui Zhixian

Research Midwife: Meredith Kelsey

Senior Scientist: Anne MacPherson

Research Officer: Thach Tran

Data Managers: Vincent Ball and Sasha Zhang

PhD Candidate: Tulika Sundernathan

Masters Students: Rachel Earl and Sarah Cash Administrative Assistant: Jacqueline Smith

RRI Collaborator: Julie Owens

External Collaborators: Matt Gillman (Harvard Pilgrim Health Care), Mark Kilby (Birmingham Women's Hospital), John Kingdom (Mt Sinai Hospital), Debbie Lawlor (Bristol University), Lucilla Poston (King's College London), Greg Ryan (Mt Sinai Hospital), Shakila Thangaratinam (QMUL) and Rory Windrum (Mt Sinai Hospital)



Professor Bill Hague

Obstetric Medicine

Improving outcomes for pregnant women with medical complications

Over 10% of pregnant women experience medical complications. Complications may predate pregnancy, or develop during or after pregnancy, with some cases threatening the lives of both mother and baby. While early identification and appropriate therapy is vital, the research base for some therapeutic decisions is limited with insufficient evidence to support interventions.

The Obstetric Medicine Group seek to develop and evaluate interventions for two major medical disorders of pregnancy; gestational diabetes and preeclampsia.

In 2014 our group contributed to a major international trial comparing tight with less tight blood pressure control in pregnant women. The trial showed benefit for women in the prevention of severe hypertension with no adverse effect on the fetus. Additionally, results were published from a large international randomised trial of anticoagulant treatment in the prevention of pregnancy complications in women with a thrombotic tendency - showing no benefit of treatment over standard care.

In 2015 we will establish two trials; to compare pregnancy and health economic outcomes in women diagnosed with gestational diabetes using new World Health Organization criteria, and to treat women with the pregnancy liver disease, obstetric cholestasis.

Group Members

Research Leader: Bill Hague

Clinical Researcher: Suzette Coat

PhD Candidate: Mansi Dass Singh





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

Prenatal growth trajectory and birth weight are strongly associated with developmental capacity and health throughout life. We now know that prenatal growth and weight at birth are determined not only by nucleotide sequence of genes, but also by epigenetic mechanisms, such as imprinting, which regulate gene expression and phenotype at a higher level. Additionally, 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.

The Epigenetics and Genetics Group focuses on dissection of the complex molecular genetic architecture of prenatal growth trajectory and birth weight. We uncover novel epigenetic and genetic effects on prenatal growth and their interactions with environmental factors. This allows us to identify risk factors and to develop intervention strategies for optimal outcomes at birth.

In 2014, we used an animal model to determine the effects of parental genomes, fetal sex, and non-genetic maternal factors on placental and fetal phenotype at mid-gestation. We identified for the first time specific contributions of the maternal and paternal genome to placental, fetal and umbilical cord characteristics. Surprisingly, we found that while placental phenotype (nutrient source) is predominantly controlled by the maternal genome, umbilical cord phenotype (nutrient flow) is predominantly controlled by the paternal genome. This provides further evidence for and refines the conflict of interest or "tug of

war" hypothesis for the evolution of maternal and paternal imprinting. Additionally, we demonstrated that abundance of the imprinted maternally expressed miRNA harbouring long non-coding RNA H19 is correlated with placental and fetal phenotype.

Group Members

Research Leader: Stefan Hiendleder

PhD Candidates: Consuelo Estrella, Ali Javadmanesh, Entesar Shuaib and Ruidong Xiang

Research Manager: Dana Thomsen

RRI Collaborators: Vicki Clifton, Kathryn Gatford, Karen Kind, Julie Owens and Claire Roberts

External Collaborators: Axel Janke (Goethe University), Sergio Ledda (University of Sassari), Eckhard Wolf (LMU and Gene Center Munich) and Susanne Ulbrich (ETH Zurich)





Professor Claire Roberts and Professor Gus Dekker

Placental Development

Understanding placental development and maternal adaptation to pregnancy,

and developing screening tools to identify women at risk for 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. Currently no reliable clinical assessments are 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.

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.

Ongoing projects include:

- > Predicting risk for pregnancy complications
- > The role of Vitamin D in the placenta and pregnancy success
- > Epigenetic programming of placental and fetal development
- > Placental invasion and the blood supply to the placenta
- > The Influence of fetal sex on the placental transcriptome

We have developed algorithms that predict a woman's risk for pregnancy complications using a combination of clinical, biochemical and genetic markers. Our next step is to validate these algorithms in an independent cohort. If validated successfully, these algorithms may be used in antenatal clinics during the first trimester of pregnancy.

Group Members

Research Leaders: Claire Roberts and Gus Dekker

Research Fellow: Tina Bianco-Miotto

Postdoctoral Researchers: Prabha Andrawera, Amanda Highet and Sean O'Leary

Research Assistant: Dylan McCullough

PhD Candidates: Sam Buckberry, Sultana Khoda, Jessica Laurence, Shalem Leemaqz, Dee McCormack and Rebecca Wilson

Honours Students: Ben Mayne and Zimin Zhuang

External Collaborators: Louise Kenny (University College Cork) and Lesley McCowan (The University of Auckland)



25% of first pregnancies in Australia are affected by one of the four major complications – which can lead to a range of life-long health issues (or even death) for both mother and baby.

The four most common pregnancy complications are preeclampsia, preterm birth, intrauterine growth restriction and gestational diabetes. For first time mothers there is no way of knowing the risk of developing these potentially life-threatening conditions.

Professors Claire Roberts and Gus Dekker who jointly lead the Placental Development Group recognised the necessity for early screening and prevention. They have spent the last 10 years running the 'SCOPE' study, collecting and analysing data and biological samples from pregnant women at the Lyell McEwin Hospital. With Shalem Leemagz, a statistician and PhD scholar in the group, the world's first screening test to predict a woman's risk for developing one or more of the above pregnancy complications has been designed.

"Gus, Shalem and I have developed algorithms that combine subtle variations in DNA sequences in genes involved in placental development with clinical, socioeconomic, lifestyle and family history data that can predict a woman's risk for having a pregnancy complication," said Claire.

This new screening test could be administered in early pregnancy and would allow clinicians to initiate treatments for women at risk earlier, helping to reduce the severity of, or to prevent, the complications.

"If it is identified in early pregnancy that a woman is at risk of preeclampsia for example, low dose aspirin before 16 weeks gestation could delay the onset or prevent it completely," explains Claire.

Claire and Gus anticipate this screening test would be simple to integrate into practice. Currently women are screened for Down syndrome at 12 weeks gestation with a blood test. At this appointment additional blood could be taken by clinicians and run through the

"Down syndrome occurs in 1 in 700 pregnancies, while the four main pregnancy complications occur in 1 in 4 pregnancies - we anticipate there will be great interest in amalgamating this test into current practice from both a health and an economic perspective," said Claire.

The algorithms have been developed in over 3,200 pregnant women in Australia and New Zealand to best predict each woman's risk of complications.

These complications can lead to a range of health issues for the resulting babies, some which can alter their health for life.

"Health issues originating in pregnancy range from childhood obesity, mild learning and behavioural problems, to severe disabilities such as cerebral palsy, intellectual handicap and blindness or even death."

"Additionally, when the pregnancy is compromised, both mother and baby are at higher risk of developing adult onset diseases, including cardiovascular disease and type 2 diabetes," said Gus.

The next step is to test women right across Australia and commercialise the algorithms so they can be offered to pregnant women by clinicians all over the world.

"Our hope is that this relatively simple screening test will be offered to pregnant women in all countries - resulting in improved pregnancies and healthier babies for all women," said Claire.







Professor Michael Davies and Professor Vivienne Moore

Life Course and Intergenerational Health (LIGHT)

Uncovering how inequalities in the health of women and children arise though

integrated social and biological pathways, and identifying opportunities for change

Early life is the foundation for future health and life potential. Growth and development of the child, both before birth and after, are intimately linked to the health and well being of the mother. The mother's health reflects her current environment and social circumstances, policies and structures in place in society, and her health inheritance from previous generations.

The LIGHT Group aims to understand the interplay of social and biological factors that influence health over the life course. Our research aims to uncover:

- > How chronic diseases are transmitted through generations, and effective interventions
- Developmental origins of congenital malformations, reproductive disorders, type 2 diabetes and cardiovascular disease

- > Social determinants of health
- > The political and gendered implications of the above findings

In 2014, we published research demonstrating variable poorer perinatal outcomes for babies conceived through different infertility treatments compared to naturally conceived babies. We continued our investigations into child growth, showing that body size of the mother prior to pregnancy is the strongest predictor of accelerated growth in children before 3.5 years. We also demonstrated that a mother's body size before pregnancy is positively associated with insulin resistance in children at 9-10 years, irrespective of whether the mother had gestational diabetes and independent of the current body size of the child, suggesting genetic and/or developmental programming origins.

Group Members

Research Leaders: Michael Davies and Vivienne Moore

Research Fellow: Alice Rumbold

Senior Postdoctoral Researcher: Wendy March, Melissa Whitrow and Tanya Zivkovic

Statisticians: Chris Davies, Suzanne Edwards and Kristyn Willson

Academics: Lynne Giles and Megan Warin

CIS Facility Coordinator: Stephanie Champion

Research Coordinator: Kendall Smith

PhD Candidates: Renae Fernandez

and Renae Kirkham



Professor David Kennaway

Circadian Physiology

The impact of disruption of circadian rhythms on physiological processes

Shift work increases the risk of developing a range of chronic disorders including heart disease, diabetes and obesity. These effects occur independently to confounding factors such as socioeconomic status and smoking, and the risk increases with the number of years of exposure. Approximately 370,000 Australian women of reproductive age (20-44 years) work at night either permanently or on rotating shift rosters of varying types. The resulting altered sleep and meal times, together with altered light exposure, disrupts many physiological systems and rhythms. There is emerging evidence that not only do women who work shifts experience poorer fertility, but pregnant women working shifts are at increased risk of spontaneous abortion, preterm birth and low birth weight.

Additionally, our animal studies have shown that disrupting circadian rhythms during the prenatal period may program metabolic disease in the subsequent offspring as they grow into adulthood.

During 2014 the Circadian Physiology Group continued studies on the physiological changes that occur when animals are subjected to simulated shift work. In addition young adults living in a specially built apartment were studied before and after 4 simulated 12-hour night shifts.

These studies have demonstrated that mismatching the timing of sleep opportunity and food availability adversely affects glucose metabolism and insulin sensitivity in both animal and human models. In the case

of the human trial, our preliminary evidence indicates that as few as 4 consecutive 12 hour night shifts induces insulin resistance even when there is no sleep deprivation.

Group Members

Research Leader: David Kennaway

Research Fellows: Michael Boden and Tamara Varcoe

Research Officers: Leewen Rattanatray and Mark Salkeld

External Collaborators: Glenn McConell (Victoria University), Amanda Page (University of Adelaide) and Shantha Rajaratnam (Monash University)



Emeritus Professor Alastair MacLennan AO

Cerebral Palsy

Discovery of the genetic causes of cerebral palsy

Cerebral palsy is a neurodevelopmental disorder affecting posture and movement control for 1 in every 400 children. This disability greatly affects quality of life for those affected and their families. Its prevalence has not changed during the past 50 years and costs Australia billions of dollars per year.

The Australian Collaborative Cerebral Palsy Research Group is investigating the contribution of genetic variants (mutations) to cerebral palsy susceptibility and the possible interaction of environmental triggers during pregnancy.

During 2014 our unique cerebral palsy family DNA biobank increased substantially with recruitment in SA, NSW and Qld. Using exome sequencing we have shown a much higher rate of mutations that are

plausible causes of cerebral palsy than the 1-2% previously described in the literature. Results were presented at the American Genetics Society Annual congress and has now been published in Molecular Psychiatry. Detailed in silico and animal function studies have commenced to explore the underlying pathways by focussing on high priority cerebral palsy candidate genes.

We have a second large cohort of cerebral palsy families ready for exome sequencing and gene function. Further exome sequencing, identification of contributing copy number variations and whole exome sequencing are likely to increase the discovery of genetic variants contributing to cerebral palsy which may allow early diagnosis and genetic interventions.

Group Members

Research Leader: Alastair MacLennan

Genetic Scientist: Mark Corbett PhD Candidate: Gai McMichael

Statistician: Stephen Bent

Research Officers: Clare Van Eyk and Kelly

Harper

Project Officer: Jessica Broadbent

Research Assistant: Joshua Woenig

Administrative Assistant: Corrine Reynolds

RRI Collaborator: Jozef Gecz

External Collaborators: Mathew Bainbridge (Baylor College), Daniel Geschwind (UCSF), Richard Gibbs (Baylor College), Eric Hoffman (National Institute of Health) and Michael Kruer (Souix Falls)





Professor Julie Owens and Dr Kathryn Gatford

Early Origins of Health and Disease

Testing interventions to improve long-term outcomes after perinatal exposures

The early environment - before and shortly after birth - influences an individual's risk of developing major non-communicable diseases, including diabetes, cardiovascular disease, impaired neurological function and allergy. As an example, over 18% of the risk for Type 2 diabetes can be explained by poor growth in early life. Importantly, the effects of adverse prenatal exposures are not always permanent or irreversible.

The Early Origins of Health and Disease Group seeks to optimise development of the infant through improving maternal health during pregnancy, or reversing adverse consequences of problems during pregnancy. This includes mechanistic studies to understand how exposures affect long-term outcomes, with the aim of developing new interventions and improving current practices.

In 2014, we examined the outcomes from experimental models testing

metabolic, neurological and immunological consequences of restricted placental function, supply to the infant before birth, and three intervention strategies. We demonstrated for the first time that restricted growth before birth protects against susceptibility to allergy. We aim to identify the pathways responsible and potential new approaches to protect infants and children against allergy development. Additionally, we developed new ways to characterise learning outcomes in our experimental models of pregnancy complications, and are developing a new focus on exercise as an intervention for progeny who grew poorly before birth. In collaboration, we contributed to the assessment of effects of antenatal lifestyle advice in overweight and obese women, and improved understanding of how an overweight father impairs the metabolic and reproductive health of his child.

Group Members

Research Leaders: Julie Owens and Kathryn Gatford

Emeritus Professor: Jeffrey Robinson

PhD Candidates: Vincent Chu. Patricia Grant. Himawan Harryanto, Dane Horton, Damien Hunter, Wee-Ching Kong, Ezani Mohamed Jamil, Hong Liu, Saidatul Mohammad, Siti Sulaiman, Tulika Sundernathan and Amy Wooldridae

Honours Student: Manpreet Kaur

RRI Collaborators: Vicki Clifton, Jodie Dodd, Stefan Hiendleder, Karen Kind, Julia Pitcher and Claire Roberts

External collaborators: Robert Bischof (Monash University), Jane Black (Monash University), Debbie Lawlor (Bristol University), Glenn McConell (Victoria University), Margaret Morris (University of New South Wales), Tim Moss (Hudson Institute of Medical Research), Beverly Muhlhausler (University of Adelaide), Caroline Relton (Newcastle University), and Rebecca Simmons (University of Pennsylvania)





Professor Lyle Palmer

Genetic Epidemiology

Investigating the epidemiology and genetic epidemiology of the origins of health and disease

The burden of disease in pregnancy, birth and childhood is increasing, both clinically and economically. In order to disentangle the complex genetic and environmental determinants of key phenotypes in early life and childhood, large-scale and comprehensive cohort resources are required.

The Genetic Epidemiology Group aims to understand the genetic and environmental determinants of complex disorders such as preterm birth, preeclampsia, growth in utero, and development over childhood (ie growth,

lung function and blood pressure trajectory). Our focus is on applying multidisciplinary approaches using combined statistical, epidemiological, genetic, molecular, informatic and clinical disciplines to better understand and treat important diseases. In 2014, Lyle's focus was to initiate and lead the Adelaide Family Health Studies. This project seeks to integrate existing world-class research resources in SA with new infrastructure. A leadership and protocol development group has been established,

and a successful stakeholder workshop was held to develop scope and strategy.

In 2015 Lyle will further develop the Adelaide Family Health Studies through collaborating

Family Health Studies through collaborating with RRI genetic research experts and developing key enabling informatic, statistical and biospecimen banking resources.

Group Members

Research Leader: Lyle Palmer





Associate Professor Michael Ridding and Dr Julia Pitcher

Neuromotor Plasticity and Development (NeuroPAD)

Investigating how early life events affect the development of the human brain and its ability to learn and remember, and to recover from injury or illness

Experiences throughout life constantly shape and rewire the brain. This occurs through changing the strength of existing neural connections and developing new ones, and is known as neuroplasticity. Neuroplasticity underlies our ability to learn and remember new skills, to forget information, and also to recover from injuries to the brain. While this ability is life-long, the brain is at its most plastic in fetal life and early childhood. This facilitates the rapid learning of our early development, but it also makes the brain more vulnerable to adverse experiences and injury in early life. During this time the brain is less able to adapt appropriately to experiences and recover from injury in later life.

The NeuroPAD team aims to understand how experiences and injuries alter human brain motor and cognitive function

throughout the lifespan, and to develop effective therapies and interventions to ameliorate the negative consequences.

In 2014, NeuroPAD began two significant 3-year projects, both funded by grants from NHMRC. Michael is leading an international multi-centre trial to determine the optimal time to commence rehabilitation after patients suffer a stroke. This trial includes developing and optimising new non-invasive brain stimulation techniques for rehabilitation. Julia is leading a large cohort study investigating how altered stress hormone responsiveness and epigenetic changes in various neurological genes influences the learning and memory difficulties common in children and adolescents born preterm. This includes testing a number of brain training and noninvasive brain stimulation interventions.

Group Members

Research Leaders: Michael Ridding and Julia Pitcher

Postdoctoral Researchers: Richard Harris, Brenton Hordacre, Luke Schneider and Ann-Maree Vallence

Research Fellows: Nicolette Hodyl and Mitchell Goldsworthy

Clinical Researchers: Nicholas Smith and Michael Stark

Research Nurses: Louise Goodchild and Ros Lontis

PhD Candidates: Rebecca Collins and Sam Darvishi

Honours Students: Bianca Piantedosi and Robert Sadler

External Collaborators: Angela Clow (University of Westminster) and John Rothwell (University College London)





Associate Professor Michael Stark

Neonatal Medicine

Ensuring life-long health for newborns born preterm

Events, illnesses and treatments in the newborn period can have a profound and long-term effect on growth, development and life-long health. Integrating clinical and basic science research projects is critical to advancing our understanding of the major morbidities that complicate preterm birth, and to form the basis of novel interventions to improve outcomes for babies born too soon.

The Neonatal Medicine Group aims to integrate basic and clinical research to inform best practice in the care of preterm newborns. In 2014, the group focused on four main themes: neonatal nutrition, oxygen physiology with a particular focus on the mechanisms that underlie neonatal brain injury, transfusion medicine, and optimising neurodevelopmental outcome following preterm birth.

Research highlights in 2014 include:

- > Completion of a study on early neonatal brain injury and cerebral oxygen kinetics
- Commencement of a randomised control trial of washed red blood cell transfusion in very preterm neonates to prevent significant neonatal morbidity
- Adoption of the Reggio Emeilia philosophy within the NICU
- On-going world leading research into neonatal nutrition for the Future Foods for Australians CRE

In 2015 we aim to consolidate the research themes with a particular focus on neurodevelopmental outcomes for infants born preterm, new projects focusing on the immune basis of bronchopulmonary dysplasia, and new international collaborative

projects focusing on evidence-based transfusion practice in the neonatal population.

Group Members

Research Leader: Michael Stark

Clinical Partners: Chad Andersen, Ross Haslam and Andrew McPhee

Research Fellow: Nicolette Hodyl
PhD Candidate: Natalie Aboustate

Senior Neonatal Fellow: Kathryn Martinello

Postdoctoral Researcher: Vicki Xafis
Consultant Neonatologist: Amy Keir





A cross-disciplinary research project led to the identification of the trace element selenium in the bovine ovary.

team identified 5 elements in the bovine ovary, including selenium, which is highly concentrated in the ovarian follicles.

"Selenium is an essential trace element found in protein-rich foods like red meat, seafood and nuts. It is important for many biological functions, such as immune response and thyroid hormone production, and acts as an antioxidant, helping to detoxify damaging chemicals in the body."

"Our findings are important, because they show that selenium and selenoproteins (ie GPX1) are at elevated levels in large, healthy ovarian follicles," said Melanie.

The team found that gene expression of GPX1 was significantly higher - in some cases double - in oocytes that yielded a

"We suspect GPX1 plays a critical role as an antioxidant during the late stages of follicle development, helping to lead to a healthy environment for the egg," said Hugh.

Selenium deficiency is not usually a problem in Western diets, although people who avoid certain food groups or eat food

mainly grown on selenium-deficient soils

society, with one in six couples in Australia being infertile. Further research is needed to better understand how selenium levels could be optimised, helping to improve a

so it isn't just a case of taking multiple supplements," explained Ray.

This collaborative project resulted from the researchers' recognition that oxidative stress and its alleviation would be important in tissue remodeling processes and in protecting the DNA of eggs from oxidative damage. They suspected these processes would likely involve trace element biology in the ovary.

The team then set out to identify parts of the ovary where particular elements were concentrated at certain times during development and regression of ovarian follicles, and to begin to understand what biochemical processes were responsible for observed concentration of trace elements in the ovary.

With selenium they were able to identify the selenoprotein involved and how this was related to human oocyte quality by collaborating with Associate Professor Darryl Russell and Dr Michelle Lane.

The next steps in this research are to identify how selenium is concentrated in the follicle, to identify when and where oxidative stress occurs, and to identify the causes of this stress.



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 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 affecting many children, such as type 1 diabetes and irritable bowel syndrome, as well as cancer and other diseases.

The Molecular Immunology Group seeks to characterise human Tregs under normal conditions, with a view to understand what goes wrong with these cells in immunological disorders. Using state of the art molecular biology, the group investigates all the genes involved in immune function in Tregs, and aims to understand how key genes are

regulated in a coordinated way to control normal function.

The group is developing a Treg cell therapy that could be administered to patients to reset or redirect the immune system to prevent autoimmune disease or transplant rejection. In order to understand how mutations alter immune tolerance we developed a new technology that is able to map interactions at long distances that form as a result of DNA looping. This will allow for the first time the identification of the gene targets of point mutations associated with disease, by mapping them to the regions of the genome that they interact with. This strategy allows us to then ask if the target gene expression is altered by the mutation. The group aims to test this approach in patients with type 1 diabetes, to map how gene mutations lead to disease.

Group Members

Research Leader: Simon Barry

Research Fellows: Cheryl Brown and Timothy Sadlon

Research Assistants: Arunesh Mohandas and Batjargal Gundsambuu

PhD Candidates: Kristen Malatesta, Steve Pederson and John Walsh

Honours Candidate: Vincent Wong

RRI Collaborators: Jennifer Couper, Wendy Ingman, Sarah Robertson and Darryl Russell

External Collaborators: Marc Beyer (LIMES Bonn), Dan Campbell (Benaroya Research Institute), Thomas Duhen (Benaroya Research Institute), Greg Goodall (Centre for Cancer Biology), Randall Grose (SAHMRI), Giovanna Lombardi (King's College London), Kellie MacDonald (QIMR), Joachim Schultze (LIMES Bonn), Raymond Steptoe (Diamantia Institute) Tim Tree (King's College London) and Kathryn Wood (Oxford University)



Professor Toby Coates

Transplantation

Treatment of Type 1 diabetes with replacement beta cells

Type-1 diabetes is a major cause of morbidity and mortality in children and adult Australians. It is caused by autoimmune destruction of the pancreatic beta cells, the only insulin secreting cell type in the body.

The Transplantation Group performs clinical islet cell transplantation as a part of South Australia's only Nationally Funded Centre for Islet Cell Transplantation. In the laboratory we investigate new sources of insulin-secreting tissue for transplantation as well as novel ways to protect transplanted pancreatic beta cells from destruction by the immune system. In collaboration with A/Prof Mark Nottle, our group generated insulin-secreting tissue from porcine embryonic stem cells. This is

a potentially exciting infinite source of beta cells for transplantation and the treatment

of type-1 diabetes. Porcine insulin was the mainstay of insulin therapy for many years in the clinic, and these cells are a model for developing cell transplantation techniques. The group also continued to work on novel ways to alter the immune system and protect pancreatic beta cells by exploring the IGF-II pathway and transducing pancreatic beta cells with programmed death ligand-2 (PDL-2). This is a naturally occurring T cell death ligand, which deletes both allo-reactive and auto-reactive T cells (that cause destruction of the insulin secreting beta cells at the start of type-1 diabetes). In the longer term, this novel strategy may result in improved treatments for this prevalent autoimmune condition.

Group Members

Research Leader: Toby Coates

Senior Scientists: Christopher Drogemuller, Chris Hope, Svjetlana Kireta, Jodie Nitschke and Danielle Penko

Senior Postdoctoral Researchers: Claudine Bonder, Shane Grey and Plinio Hurtado

Clinical Researchers: Rob Carroll, Shilpa Jesudason and Chen Peh

Postdoctoral Researchers: Claire Jessup and Darling Rojas-Canales

Technical Officer: Julie Johnston

PhD Candidates: Mariea Bosco, Ernesto Hurtado Perez, Bron Lett and Kisha Sivanathan

Masters Student: Fredrick Chia

Honours Students: Alexander fuss, Peter Rose and Sebastian Stead

RRI Collaborator: Mark Nottle





Professor Jennifer Couper

Diabetes

Preventing type 1 diabetes and its complications

The incidence of type 1 diabetes in childhood has increased worldwide, doubling in Australia over the last 20 years. This suggests the modern changing environment plays a role in its development. 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:

- > Environmental exposures that drive the disease
- > Immune regulatory function
- > The protection of blood vessel health in children and adolescents

In 2014, a national cohort study from pregnancy to determine how the modern environment drives the development of type

1 diabetes (ENDIA) expanded into a Centre of Research Excellence with national and international collaborations. Additionally, a randomised controlled trial to assess the efficacy of metformin in preserving vascular health in type 1 diabetes was completed, as was a study to help blood glucose control after meals in children with cystic fibrosis and type 1 diabetes.

In 2015 we plan to continue our ENDIA study with national and US collaborators, follow up older children at risk of type 1 diabetes, conduct intervention trials, and look at the treatment of cystic fibrosis related diabetes. Additionally, our group is the Australian centre measuring vascular images for an international trial to prevent diabetes complications in adolescents.

Group Members

Research Leader: Jennifer Couper

Research Fellow: Jessica Philips

Clinical Partner: Alexia Pena

Sonographer: Roger Gent

Research Coordinator: Megan Penno

Research Nurses: Sarah Beresford and Meredith Krieg

PhD Candidates: Jemma Anderson and Shiree Perano

Masters Student: Myf Geyer

(WEHI)

RRI Collaborators: Simon Barry, Jodie Dodd and Lynne Giles

External Collaborators: Fergus Cameron (Royal Children's Hospital Melbourne), Peter Colman (RMH and University of Melbourne), Maria Craig (University of Sydney), Liz Davis (Telethon Institute), David Dunger (University of Cambridge), Jo Forbes (University of Queensland), Kim Donaghue (University of Sydney), Len Harrison (WEHI), Michael Horowitz (Royal Adelaide Hospital), Tim Jones (Telethon Institute), Tony Papenfuss (WEHI), Jo Petrosino (Baylor College of Medicine), Bill Rawlinson (University of New South Wales), Chris Raynar (Royal Adelaide Hospital), Richard Sinnott (University of Melbourne) and John Wentworth





Professor Antonio Ferrante

Developmental & Genetic Immunology

Molecular and cellular approaches to identify pathways responsible for chronic inflammatory diseases in childhood and treatment development

Children afflicted with autoimmune and allergic inflammatory diseases experience life-long pain and disability. Current anti-inflammatory treatments affect the ability of the immune system to combat infection, which is greatly concerning for young children. Major efforts are underway to understand the key pathways that initiate and maintain inflammatory conditions, to improve diagnosis and management of patients.

The Developmental and Genetic Immunology Group aims to identify novel pathways connecting cytokines, receptors and intracellular signalling molecules that are important in the pathology of inflammatory diseases, and to identify biomarkers for diseases such as allergy, arthritis, diabetes and inflammatory bowel disease.

In 2014 we focused on how cytokines regulate a newly identified complement receptor called CRIg. This is a unique complement receptor expressed selectively

on subpopulations of macrophages, a cell type which plays a major role in inflammation and disease development. Our work is the first to identify the cytokine patterns which up or down-regulate CRIg expression on macrophages. We also described the various spliced forms of CRIg expressed and the functional consequences of cytokine-altered CRIg on the macrophages' antimicrobial activity versus cytokine production. Tumor necrosis factor, central to the development of these inflammatory conditions, decreases expression of CRIg in macrophages. This is consistent with suppressing tumor necrosis factor promoting inflammation, and a converse role for CRIg in inflammation.

Our next steps will be examining whether anti-cytokine therapy works through modulation of CRIg expression on macrophages and whether novel approaches (e.g. neutraceuticals or pharmaceuticals) can be taken to modulate CRIg, thereby providing a new approach to treating inflammatory diseases.

Group Members

Research Leader: Antonio Ferrante

Senior Scientists: Charles Hii and Nick

Gorgani

Scientists: Alex Quach, Bernadette Boog, Clare Mee and Yongqin Li

Immunopathologist: Tatjana Banovic

Paediatric Immunologist: Jovanka King

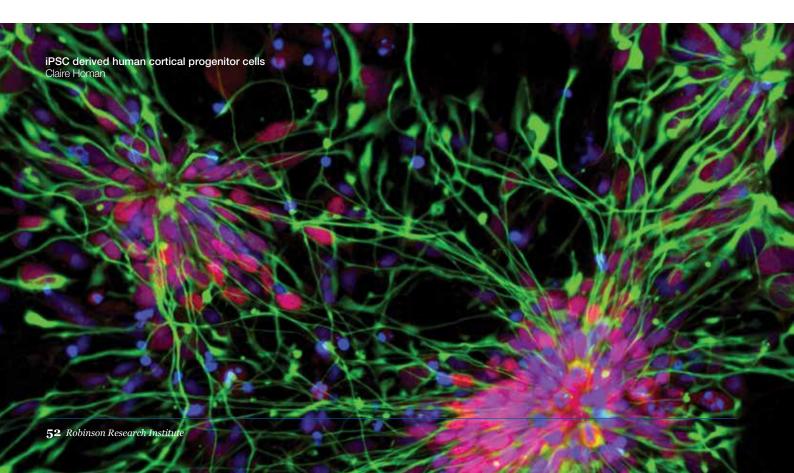
PhD Candidates: Usma Munawara, Cheung Szevan and Marwah Basin Khlah

Honours Students: David Shields, Hannah Sullivan and Nahan Huvnh

Trainees: Saif Alsaif, Anh-Hong Nguyen and Fiona Norris

RRI Collaborators: Jennifer Couper and Declan Kennedy

External Collaborators: Catherine Abbott (Flinders University), Paul Anderson (University of South Australia), Peter Hofmann (University of Adelaide), Suresh Mahaligam (Griffith University), Howard Morris (University of South Australia) and Susan Prescott (University of Western Australia)







Professor Jozef Gecz

Neurogenetics

Investigation of the genetics and biology of human neurological disorders

Intellectual disability, epilepsy, autism and cerebral palsy are among the most frequent developmental disabilities, together affecting 4% of children. Over the last decade major advances have been made in the understanding of the genetic architecture of these disorders with thousands of novel genes and tens of thousands of mutations identified. Translating genetic variation to the understanding of the biology, cell and molecular pathways involved in these disorders is crucial for improved diagnosis, management and treatment of these conditions.

The Neurogenetics Group seeks to identify and interpret novel genetic variations associated with paediatric neurological disorders, intellectual disability, epilepsy, autism and cerebral palsy.

During 2014 we identified and characterised genetic mutations in multiple novel genes. One example is USP9X - ubiquitin specific protease - that is implicated in intellectual disabilities, epilepsy and multiple cancers. Additionally, using systematic whole exome sequencing of 200 singleton cases with cerebral palsy and their parents, we revealed (in collaboration with the Cerebral Palsy Group) that at least 14% of cerebral palsy is very likely genetically derived. This is a major advance in the understanding of the causes of cerebral palsy, as until now, perinatal complications were the most cited explanation. We have also been involved in a major international study of high-resolution genetic investigations of 33,000 patients with intellectual disability or autism, from which numerous novel and candidate diseaseassociated genes have been identified.

Next we aim to translate genetic variation and molecular pathways involved for better precision medicine for children and families with intellectual disability, epilepsy, autism and cerebral palsy.

Group Members

Research Leader: Jozef Gecz

Senior Scientists: Lachlan Jolly

Research Officer: Mark Corbett, Duyan Pham and Raman Sharma,

Clinical Researcher: Bregje van Bon

Research Assistants: Renee Carroll, Alison Gardner, Marie Shaw, Annie Sun and Josh Woenig

PhD Candidates: Claire Homan and Stanley Tan

RRI Collaborators: The Cerebral Palsy Group -Alastair MacLennan, Gai McMichael, Clare van Eyk, Eric Haan, et al.



Associate Professor Michael Gold

Allergy and Vaccine Safety

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

Prevention and management of food allergy and allergic disease

In westernised and developed countries there is an evolving epidemic of allergic disease that primarily affects children under 5 years of age. 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 to understand the role of exposure in the development of tolerance to egg.

During 2014 multiple trials were progressed looking at early versus late introduction of egg into an infant's diet, the possible therapeutic benefits of heat-treated egg, and fish oil supplementation in pregnancy.

Once completed, these studies will provide evidence based feeding guidelines for Australian infants and mothers.

Development of new ways to monitor the safety of vaccines

When a new vaccine or seasonal flu 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.

In 2014, two studies continued: Vaccine Assessment using Linked Data and Stimulated Telephone Assisted Rapid Safety Surveillance. Results from both studies will significantly advance how we evaluate vaccines in Australia.

Group Members

Research Leader: Michael Gold

Postdoctoral Researcher: Gabriella Lincoln

Research Nurses: Christine Health and Mary Walker

PhD Candidate: Katherine Duszynski, Karen Best, Merryn Netting and Adrianna Parella

Co-Investigators: Annette Braunack-Mayer, Nigel Stocks, Nicole Pratt, Maria Makrides, Debbie Palmer and Imme Pentila

RRI Collaborators: John Lynch and Helen Marshall



Professor Jon Jureidini

Critical and Ethical Mental Health

Critical appraisal and meta-research to promote safer, more effective and more ethical research and practice in mental health

Misinformation about mental health and mental disorders in children and adults misleads health professionals, the media, the public, and governments, jeopardising the rational allocation of billions of dollars of taxpayers' money every year.

The Critical and Ethical Mental Health research group conducts research (particularly critical appraisal and metaresearch), teaching, and advocacy in mental health, to promote safer, more effective, and more ethical research, policy and practice in mental health.

During 2014 we focused on citation distortion/misrepresentation, the RIAT (restoring invisible and abandoned trials) project in which we re-analysed an infamous study of antidepressants in children, and we looked at social determinants of mental health and ethical issues related to the protection of participants in clinical trials.

Our next steps are to critically review participant protection in psychiatric/mental health trials, mortality associated with mental disorders, and early intervention in mental health. We also aim to delve into citation

content misrepresentation and conflict of interest in the health arena.

Group Members

Research Leader: Jon Jureidini Research Fellow: Anne Tonkin

Postdoctoral Researcher: Melissa Raven



Professor Declan Kennedy

Sleep Disorders

Understanding morbidity associated with sleep disordered breathing and the effect on neurocognition and vascular function

Sleep disordered breathing affects between 3-10% of children, and even relatively mild condition has significant daytime effects on neurocognitive domains and behaviour. During the last three years we evaluated the effect of sleep disordered breathing and found vascular function is different in those children who snore vs do not snore. We are currently looking more closely at vascular function to ascertain whether the vessel changes we found are related to the severity of the child's condition.

The Sleep Disorders Group seeks to delineate the effect of sleep disordered breathing on children's health and develop testing to identify children who need treatment - such as adenotonsillectomy. During 2014 our group had two main objectives:

- > To assess neurocognition and behaviour in young children awaiting adenotonsillectomy (postoperative evaluation to be completed in 2015)
- > To assess vascular function and inflammatory markers in children with sleep disordered breathing.

Our group collaborates with SAMHRI, The University of Adelaide's Engineering Department, and The University of South Australia's Neurovascular Research Unit.

Group Members

Research Leader: Declan Kennedy

Head of School: Kurt Lushington

Director Pulmonary Medicine: James Martin

Principal Scientist: Yvonne Pamula





Associate Professor Helen Marshall

Vaccines and Infectious Diseases

Optimising protection for babies, children and pregnant women against serious infectious diseases through improved immunisation strategies

Infections such as whooping cough, meningococcal disease and influenza still cause death and disability in young infants. During the last whooping cough epidemic ten babies died, with most of these babies under 4 months of age. One in ten children who are diagnosed with meningococcal disease will die from the infection and a further 40% will develop a long-term disability.

The Vaccines and Infectious Disease Group aims to improve protection and outcomes for children from serious infections, and monitor community acceptance of immunisations. Immunising pregnant women is becoming increasingly important and has a dual benefit; protection for the mother against serious infections and protection for her newborn. Pregnant women who develop influenza during pregnancy have double the risk of fetal death, whereas women who are immunised against influenza during pregnancy provide protection for their newborn in the first months of life.

Our research into one of the most serious and life-threatening infections, meningococcal disease, identified that children who present with a high fever and are diagnosed with both meningitis and septicemia or were born preterm are more likely to have long-term complications including disability. With our interstate collaborators we have embarked on the largest study in the world, assessing the safety and effectiveness of immunising newborn babies in the first week of life to provide better protection against whooping cough infection.

In 2015 we will lead a national study to further examine the long term effects of meningococcal disease such as deafness and neurological problems.

Group Members

Research Leader: Helen Marshall

Clinical Researchers: Sue Evans, Suja Mathew and Trinh Tran

Postdoctoral Researchers: Joanne Collins and Adriana Parrella

Research Manager: Michelle Clarke

Research Scientists: Susan Lee and Jane

Tidswell

Research Nurses: Christine Heath, Verity Hill,

Mark McMillan, Jane Tuckerman, Mary Walker and Kristen Zyhajo

PhD Candidate: Bing Wang

Masters Student: Lexa Shrestha

RRI Collaborators: Simon Barry, Gus Dekker, Jodie Dodd, Mike Gold, John Lynch, Andy McPhee and Ben Mol

External Collaborators: Ross Andrews (Charles Darwin University), Hossein Afzali (University of Adelaide), Annette Braunack-Mayer (University of Adelaide), Jim Buttery (University of Melbourne), Katherine Edwards (Vanderbilt University), Stephen Lambert (Queensland Children's Medical Research Institute), Kristine McCartney (University of Sydney), Peter McIntyre (University of Sydney), Terry Nolan (University of Melbourne), Andy Pollard (University of Oxford), Julie Ratcliffe (Flinders University), Peter Richmond (University of Western Australia), Matthew Snape (University of Oxford), Rebecca Tooher (University of Adelaide), Steve Wesselingh (SAHMRI), Nicholas Wood (University of Sydney) and Gregory Zimet (Indiana University)



Associate Professor David Parsons

Cystic Fibrosis

Development of gene therapy for the prevention and treatment of cystic fibrosis airway disease

Cystic fibrosis 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.

The Cystic Fibrosis Group aims to develop an effective genetic therapy for the prevention and treatment of cystic fibrosis airway disease. Research activities are focused on achieving effective lentiviral CFTR vector gene delivery, transduction of airway stem cells in situ to enable extended gene expression, and development of rapid and accurate outcome measures for assessment of airway disease and the effects of novel therapeutics.

During 2014 the group demonstrated that CFTR gene transfer improved survival in mice and that their techniques could also be successfully applied in ferret airways. Using synchrotron x-ray imaging in mice, the group can now non-invasively measure the depth of the airway surface fluid that controls airway health in cystic fibrosis. PhD projects examined stem cell populations in CF and normal mice, and how the gene vector can be delivered by aerosolisation. Honours projects examined how airway pre-treatment influences lung gene transduction in mice, and the effectiveness of the group's viral gene vector compared to other vector systems.

In 2015 the group will continue to advance their work into clinically suitable protocols and agents. Related novel genetic treatments using stem cells are also being explored, and x-ray imaging techniques are continuing to be developed.

Group Members

Research Leader: David Parsons

Postdoctoral Researchers: Patricia Cmielewski and Martin Donnelley

PhD Candidates: Nigel Farrow, Ryan Green, Chantelle McIntyre and Harsha Padmanabhan

Honours Student: Sharnna Devereux and Fiona Craig

Research Coordinator: Bernadette Boog and Corrine Reynolds

RRI Collaborators: Simon Barry, Mark Nottle and Paul Thomas

External Collaborators: Ivan Bertoncello (Melbourne University), Ric Boucher (University of North Carolina), Andreas Fouras (Monash University), Albert Juhasz (University of South Australia), Tim Kuchel (SAHMRI), Ivan Lee (University of South Australia), Maria Limberis (University of Pennsylvania), Jonathan McQualter (University of Melbourne), Kaye Morgan (Monash University), Karen Siu (Monash University), Euan Smith (University of South Australia), Karen Siu (Monash University), Kentaro Uesugi (JSDTI), Naoto Yagi (JASRI) and Roger Yazbek (Flinders University)







Professor Michael Sawyer

Research and Evaluation

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

Optimal physical and mental health is important for strong and resilient communities. Unfortunately, many mothers and children experience sub-optimal health and wellbeing - for example, 13% of new mothers experience significant symptoms of depression, while at any single point in time 14% of children and adolescents experience mental health problems. What is concerning is the repeated finding that only a minority of those experiencing 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 children 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 the community. The effectiveness of these interventions is assessed in clinical trials, conducted as part of routine service delivery in the community child health service.

In 2014 Michael and colleagues trialled the eMums program, a new intervention that combines the skills of community nurses and the Internet to reach large numbers of mothers. The effectiveness of this intervention is being evaluated through a

pragmatic preference randomised controlled trial conducted within the community child health service in South Australia. Follow-up assessments will conclude in 2015 and will compare this program with current standard practice in the child health service. The results of the evaluation will refine the eMums program for future use.

Group Members

Research Leader: Michael Sawyer

PhD Candidates: Amy Kaim and Sara Pfeiffer

Research Assistants: Olivia Carger, Christine Mpundu-Kaambwa, Jacqueline Peters and Christy Reece

Project Officer: Jennifer Clark



Associate Professor Cheryl Shoubridge

Molecular Neurogenetics

Investigating molecular mechanisms and impact of mutations in genes causing X-linked intellectual disability, to assess molecular targets for therapeutic intervention

Approximately 1 in 50 people worldwide suffer from intellectual disability, and the cost to Australia is estimated at \$14 billion annually. Intellectual disability is described as significantly impaired cognitive functioning, coupled with a deficit in adaptive behaviour with onset before the age of 18. In many cases, therapies to prevent or ameliorate the consequences of these genetic disorders are not yet available.

The Molecular Neurogenetics group seeks to uncover the genetic causes of intellectual disabilities and seizures, with the aim of developing effective therapies to improve the quality of life for patients and their families.

In 2014 we continued to identify novel genetic causes that contribute to intellectual disability and seizures. We identified submicroscopic changes to the structure of the X-chromosome in those affected by delays to language and autistic spectrum disorder. Using mice with the intellectual disability gene on the X-chromosome we uncovered developmental deficits at the cellular level due to mutations in this gene. Using next generation approaches we established the impact of these mutations on the transcriptome of the developing brain, and uncovered evidence of the components of the pathways implicated in disruption to cognitive abilities and seizures.

During 2015 we will continue to build on the progress we have made through mouse modeling and will establish the behavioural and seizure phenotype of these animals as a baseline for treatment regimes.

Group Members

Research Leader: Cheryl Shoubridge

Postdoctoral Researcher: Kristie Lee

PhD Candidate: Tessa Mattiske

Research Officer: Susan Hinze

Research Assistant: Ching Moey

RRI Collaborators: Jozef Gecz

External Collaborators: Gaelle Friocourt (INSERM), Nigel Jones (University of Melbourne), Jeffrey Noebels (Baylor College of Medicine) and Terance O'Brien (University of Melbourne)

Fostering Research Excellence

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

Core Facilities

The Institute's core facilities enhance research capability, to deliver more efficient. and cost effective research.

Adelaide Research Assay Facility (ARAF)

Led by Professor David Kennaway



The Adelaide Research Assay Facility provides specialised, highthroughput and highsensitivity assays of physiologically important analytes for academic

researchers and commercial customers Australia-wide.

ARAF provide services and consultation for specialised measurements of analytes in human or animal biological fluids or cell culture / tissue extracts. These cover broad research areas including but not limited to endocrinology, neuroscience, physiology, immunology, pathology and cancer.

In 2015 the facility aims to test and validate a number of new reproduction and endocrine related assays and add them to the 'library' of validated assays.

Bioinformatics Facility

Led by Dr Stephen Bent



Bioinformatics enhances the Institute's capability in systems biology approaches to basic science and clinical research investigating human and animal reproduction and

development. Strategies to design and analyse transcriptome, deep-sequencing, genome and proteome data sets are a powerful approach to generating fundamental knowledge on systems and processes in biology and disease.

Bioinformatic methods allow researchers to follow a complementary path in their research that promotes exploratory analysis and hypothesis generation, as well as focused analysis of previously identified targets of interest. This can provide stronger and more clinically applicable results from a research program, and yield publication, funding, and patent outcome improvement.

Biostatistics Facility Led by Dr Nancy Briggs



The Biostatistics Facility provides expert advice in research design, statistical analysis and presentation of data. This service complements researcher expertise

through the provision of effective statistical analysis that delivers clear and precise answers to their questions.

In 2015, biostatistics will continue to be afforded to research leaders to improve the likelihood of securing future NHMRC grants and to provide general research design advice for continuing and new research projects.

Cohort and Intergenerational Studies Facility (CIS)

Led by Professor Julie Owens



The Cohort and Intergenerational Studies Facility underpins the strategic utilisation of unique Adelaide aenerated longitudinal studies - both cohorts and randomised controlled trials - established before or at birth, or in childhood. CIS and its resources enhance collaborations, support novel interrogations of accrued data and enable pooling of studies. This will advance research to address complex challenges in reproductive and paediatric health, now and into the future.

CIS aims to align, maintain and enhance cohorts, databases and related resources, stimulate research that addresses prioritised complex challenges in reproductive and paediatric health, and increase participation in national and international consortia. This will lead to increased publications in high quality journals and international invitations to present findings, thereby ensuring wide dissemination of findings to an international audience.

Gene Silencing and Expression Facility (GSEx)

Led by Dr Jill Muhling



The Gene Silencing and Expression Facility provides gene manipulation services to Australian researchers in a fully equipped PC2 laboratory. The facility offers custom

production of lentiviral, AAV and retroviral vectors, and stock viruses for purchase by the microlitre. In addition, customers can access CRISPR, non-viral vector and other cell and molecular biology services.

In 2014, GSEx produced over 50 viral vectors, of which approximately half were custom requests. These viruses have been used to infect immortal cell lines and primary cell cultures. GSEx demonstrated the effectiveness of both lentivirus and AAV in mouse cumulus oocyte complexes and cancer cell lines in rodents and humans. Additionally, the facility

demonstrated robust reporter expression following human T-cell infection.

SA Genome Editing Facility (SAGE) Led by Professor Paul Thomas



The SA Genome
Editing Facility uses
cutting edge genome
editing technology to
generate mutant mice
for a wide range of
applications. Utilising
new CRISPR/CAS9
system technology,

the facility offers a number of services including generation of custom knock out, point mutation and tagged alleles.

SAGE's services are highly accessible offering a significantly reduced cost and fast turnaround compared to traditional ES cell methods - providing researchers an edge when applying for grants and publishing in high impact journals.

After commencing operations in August 2014, three mutant lines were produced with another eleven projects underway. In 2015 SAGE aims to grow its understanding

of CRISPR/CAS9 technology and expand the services on offer to include production of conditional alleles.

Investing in People and Building Capacity

RRI delivers a suite of programs and scholarships to develop research and build skills and expertise in members. In 2014 more than \$1 million in funding was awarded to groups and individuals within the Institute. Investment in research capacity and outcomes includes the following:

Investment for Success

This program aims to increase the Institute's NHMRC funding by developing highly competitive project grant applications into more competitive applications for the 2015 round submission.

Investment serves to enable proof-ofconcept studies, experiments or analysis, to ensure rapid publication of a pivotal paper or increase scientific quality, significance and innovation.

2014 recipients:

- > Associate Professor Simon Barry
- > Associate Professor Leonie Heilbronn
- > Dr Nicolette Hodyl
- > Associate Professor Wendy Ingman
- > Dr Michelle Lane
- > Emeritus Professor Alastair MacLennan
- > Associate Professor Helen Marshall
- > Associate Professor David Parsons
- > Dr Carmela Ricciardelli
- > Associate Professor Rebecca Robker



Jeffrey Robinson Honours Scholarship

Dexter Chan

In 2014, the Institute awarded the Jeffrey Robinson Honours Scholarship to Dexter Chan.

During his undergraduate degree at the University of Adelaide, Dexter undertook a placement in Professor Sarah Robertson's lab as part of his genetics course. This placement sparked his research interest and he subsequently joined Sarah's group the following year as an honours student, undertaking the project *The role of miR146a in the peri-conception period of early pregnancy*.

Dexter looked at whether miR146a has an effect on cytokine production during early conception, and if pregnancy outcome is affected by miR146a deficiency. Cytokines produced in the peri-conception period are key for a number of events including implantation and the establishment of immune tolerance of the mother towards the fetus.

Dexter's work throughout his honours year has further deepened his interest in the field and he will commence his PhD under the supervision of Prof Sarah Robertson and Dr John Schjenken in 2015.

"I really enjoyed my honours year. I worked with so many researchers at different levels of their careers and made some great friends through sharing the office with the other students."

"It was a very different experience to my undergraduate degree and I was inspired by the incredible research being undertaken, both in my group and in other areas of the Institute."

Dexter was both humbled and grateful for the opportunity to be the Jeffrey Robinson Honours Scholar in 2014.

"It wasn't until my supervisors notified me of the opportunity that I even considered it. The scholarship provided me an advantage as it paid for my living



expenses and removed the need to work part time - I was able to spend more time on my research and refine my skills."

"I'm looking forward to commencing my PhD and continuing to be a part of the amazing and potentially life-saving research that's being undertaken at the Institute", said Dexter.

Dr Nicolette Hodyl and Dr Jessica Grieger

This fellowship funds the salary of 'Emerging Star' early career researchers. It aims to support career development to enable competitiveness for NHMRC Career Development Fellowship or similar.

In 2014 the fellowship was awarded to Dr Nicolette Hodyl (left) and Dr Jessica Grieger, who will commence in 2015.





High Impact Paper Funding

Publishing in high impact journals is a leading factor in research success and career development. This program provides financial support to enable the publication of research findings in prestigious journals that attract an international audience. This provides heightened credibility and esteem to our research achievements.

In 2014 five members received funding for their high impact publications.

Innovation Seed Funding

This pilot program supports early and mid-career researchers to collaborate across research groups and themes and to explore novel research questions. Its goal is to refine and progress these concepts towards competitive, fundable research that addresses significant knowledge gaps.

This program supported eight projects in 2014, bringing together 24 researchers. The following highlights the story and progress of one of the funded projects:

Collaborate to **Publication Success**

Major funding bodies increasingly value collaboration and co-publication. The Institute initiated this program in 2014 to assist researchers to co-author research publications and increase publication output.

In 2014 Maria Gardiner from Thinkwell facilitated a series of workshops with leaders from the Fertility and Conception theme to progress joint publication ventures.

Innovation Seed Funding Recipient Story

Dr Prabha Andraweera

Dr Prabha Andraweera from the Placental Development Group teamed up with Drs Hannah Brown, Tina Bianco-Miotto and Stephen Bent to initiate the project Identifying molecular pathways in the placenta implicated in the link between preeclampsia and later life coronary artery disease.

This project investigates genetic and epigenetic changes in the placenta that may be implicated in the link between preeclampsia and coronary artery disease (CAD). Preeclampsia is a pregnancy specific disorder and a leading cause of maternal and infant morbidity and mortality, occurring in 2-8% of pregnancies and accounting for up to 15% of maternal deaths. There is increasing evidence that the harmful effects of preeclampsia on a woman's health may not be restricted to the duration of pregnancy, but it could represent an important risk factor for future cardiovascular events.

The placenta plays a vital role in pregnancy and is also a programming agent for later life CAD. However, very little progress has so far been made in identifying the molecular



processes in the human placenta that could be implicated in the link between preeclampsia and later life CAD.

The group is seeking to uncover whether:

- 1. Similar genes are implicated in the risk for preeclampsia and CAD
- 2. Epigenetics changes in the placenta may have a role in both preeclampsia and later life CAD

This research project builds on Prabha's PhD on the topic of Angiogenesis regulating gene polymorphisms in adverse pregnancy outcomes. Hannah and Tina have expertise in molecular genetics and epigenetics, and Stephen will identify transcription factors that may regulate differentially expressed genes. Together they are well placed to achieve their goals.

Visiting Speakers

The Visiting Speakers Program supports external research leaders to visit the Institute, and aims to encourage collaboration between Institutions, and provide insight and new perspectives on our research priorities.

In 2014 the following visitors were supported

- > Professor Jeremy Grimshaw, University of Ottawa, Canada. RRI Host: Philippa Middleton
- > Professor Stanley Ulijaszek, Institute for Social and Cultural Anthropology, Oxford, UK. RRI Host: Dr Megan Warin
- > Professor Bart Fauser, University of Utrecht, The Netherlands. RRI Host: Professor Rob Norman
- > Dr Kara Britt, Peter MacCallum Cancer Centre, Melbourne. RRI Host: Associate Professor Wendy Ingman
- > Professor Patrick Bossuyt, Academic Medical Center, University of Amsterdam. RRI Host: Professor Ben Mol
- > Professor Chittaranjan Yajnik, Diabetes Unit, King Edward Memorial Hospital, India. RRI Host: Professor Bill Hague
- > Professor Helena Teede, Monash University, Melbourne. RRI Host: Dr Lisa Moran
- > Professor Geoffrey W. Tregear, Howard Florey Institute, Melbourne. RRI Host: Professor Ray Rodgers

- > Professor John E. J. Rasko AO, Sydney Medical School, University of Sydney. RRI Hosts: Dr Hannah Brown and Professor Jozef Gecz
- > Professor Laura Bennet, The University of Auckland, NZ. RRI Host: Dr Julia Pitcher
- > Louise Johnson and Karin Hammarberg, Victoria Assisted Reproductive Treatment Authority, Sydney. RRI Hosts: Professors Ray Rodgers and Darryl Russell
- > Professor Chris O'Neill, University of Sydney. RRI Hosts: Dr Hannah Brown and Associate Professor Jeremy Thompson
- > Professor David Gardner, Department of Zoology, University of Melbourne. RRI Hosts: Dr Hannah Brown and Associate Professor Jeremy Thompson
- > Dr Anita Kozyrsky, University of Alberta, USA. RRI Host: Associate Professor Vicki Clifton

Exchange Program

The Exchange Program seeks to build collaborations with interstate and international researchers and to expand the international profile of the Institute - with the aim of increasing research capacity and facilitating access to international funding, databases and expertise.

In 2014 six visits were supported, building links with research groups from Denmark, the UK, and the USA.

Visitors to the Robinson Research Institute

- > Professor David M. Olson, Department of Obstetrics and Gynecology, University of Alberta, USA. RRI Host: Professor Sarah Robertson
- > Professor Tessa Roseboom, Academic Medical Center, University of Amsterdam, Denmark. RRI Host: Professor Ben Mol

Hosts to Robinson Research Institute Members

- > Professor Rebecca Simmons, Center for Research, Reproduction and Women's Health, University of Pennsylvania, USA. RRI Visitor: Dr Kathy Gatford
- Dr Lars Henning Pedersen, Department of Clinical Medicine – Obstetrics and Gynaecology, Aarhus University, Denmark. RRI Visitor: Dr Luke Grzeskowiak
- > Professor Lucilla Poston, Division of Women's Health, King's College London, UK, RRI Visitor: Professor Jodie Dodd
- > Professor Angela Clow, Psychophysiology and Stress Research Group, University of Westminster, UK. RRI Visitor: Dr Nicolette Hodyl.

Travel Story



Dr John Schjenken

Dr John Schjenken from the Reproductive Immunology Group attended the 2014 Society for the Study of Reproduction conference in Michigan, USA.

What was a highlight of the conference?

I was fortunate to receive the International Best Abstract Award from the Australia New Zealand region for my presentation: Novel immune mechanisms for seminal fluid action through the TLR4 signalling pathway.

Did you meet any researchers or collaborators of significance?

I was introduced to Dr Stephen Krawetz, who is a world-leading expert in RNA transcripts in sperm and his publications have been highly influential in my field. We discussed new methods for extracting RNA from sperm and my research - which is seeking to understand how sperm

transcripts, particularly miRNA may interact with the uterine epithelium to influence the female immune response to coitus. Dr Krawetz showed strong interest both in our work and exploring a future collaboration.

How has the experience supported you?

I learnt about the latest research from my peers, presented my work and received feedback, which is instrumental in my career development. Additionally, networking with researchers from around the world who are working in the field of reproductive immunology has broadened my scientific network

Travel Grants

Supporting early career researchers to travel so they can present and share their research findings at national and international conferences and meetings is essential for career development and building a strong track record.

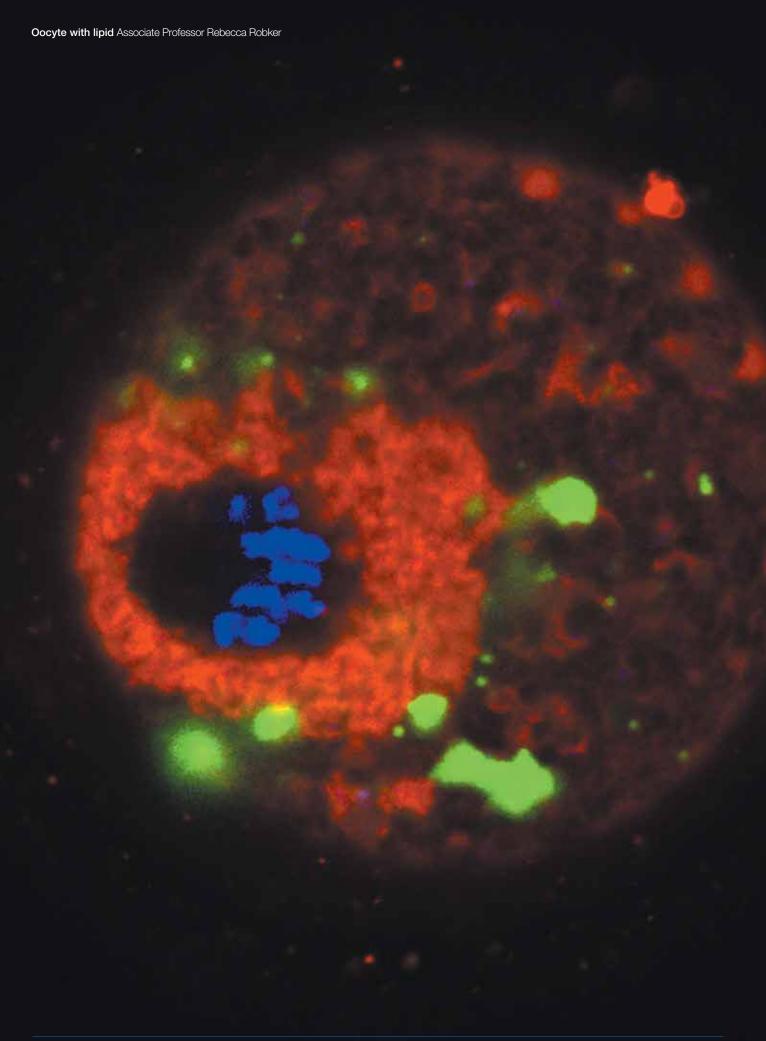
Attendance at key conferences enables networking with peers, and the opportunity to develop future collaborations.

In 2014 this jointly funded program with the School of Paediatrics and Reproductive Health, allocated \$70,000 to 54 research staff and students who visited 27 conferences. Researchers are encouraged to submit a brief story about their travel – above is what Dr John Schjenken had to say about his experience.

Media Training

9 institute members attended a one-day media skills course run by Science in Public. Participants received professional insights and guidance from highly experienced and talented television, radio and print journalists. The challenging and practical day included 1-on-1 media practice with the experts who provided constructive feedback and coaching.

"The opportunity to speak directly with and practice our skills on journalists was invaluable. I'll be putting into practice what I learnt." Dr Megan Warin, 2014 participant.



Robinson Research Foundation

The Robinson Research Foundation supports the life-giving research of the Institute and aims to:

- > Raise vital funds to seed new areas of innovative research, support the development of the next generation of researchers, and fund special enabling equipment
- > Raise public awareness of the clinical and policy benefits of the work of the Institute in order to enhance the uptake of research findings

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

In 2014 two major engagement events were held:

Friends and Benefactors Event

Hosted by the University of Adelaide's Engagement Branch, this event provided the opportunity for University alumni and benefactors to gain an insight into specific areas of research in need of funding.

Held in March, the event introduced the concept of 'Healthy Children for Life' with a specific focus on preterm birth. Guests were provided insight and expertise from Institute members Professor Sarah Robertson, Philippa Middleton and Laura Spencer. Thank you to all guests for attending and your ongoing support.

Excellence in Research Dinner - Macquarie Private Wealth

Hosted by Macquarie Private Wealth, the *Excellence in Research Series* provides insight into the research from each of the University of Adelaide's five research Institutes. The Robinson Research Institute featured in September's event – with Associate Professor Michael Stark presenting on the topic *Born Too Soon: Building better health outcomes*.

Once again, funds raised on the evening were generously matched by Macquarie Private Wealth and will be directed towards ongoing research efforts into preterm birth. We thank both our supporters for their donations and for Macquarie Private Wealth for not only hosting this wonderful event but for matching donations raised.



Robinson Research Foundation Committee 2014

Neil Howells (Chair)
Joanna Close
Paul Griffin
Alf Ianniello
E/Prof Colin Matthews
Ian Nightingale
Dr Dyann Smith



A message from the Chair

Each year I learn more about the vital research conducted by the Robinson Research Institute. Its Research Leaders and Members are world class in their field and all hold an unwavering passion and dedication to addressing major health issues in fertility, pregnancy and child health in our community. They are truly inspiring and particularly so, in light of the challenging funding environment in which they operate.

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

The Foundation has a role in fostering opportunities to raise awareness and funds that will in turn be used to support new and ongoing research. This is essential to ensure our discoveries can continue to 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 Committee for their support and commitment to the Institute throughout 2014. This year the work of the committee has moved closer to working in greater partnership with the University's Engagement Branch and we look forward to further embedding the new strategy in 2015.

To our supporters and donors – on behalf of the Foundation Committee, Research Members and Staff of the Institute – thank you all so very much for your generous and ongoing support.

I look forward to your continued engagement and encourage you to help us spread the word about the life changing research that happens here at the Robinson Research Institute.

Neil Howells

Chair Robinson Research Foundation

Member list

Thank you to all of the Institute's members who have contributed to another successful year. 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.

Members

Aboustate, Natalie Akison, Lisa Anastasi, Marie Andersen, Chad Anderson, Jemma Andraweera, Prabha Archer, Maddison Ashwood, Pat Atashgaran, Vahid Bain, Emily Ball, Vincent Banovic, Tatjana Barry, Simon Bartlett, Briohny Basin Khalah. Marwah Bastian, Nicole Beaumont, Greg Beresford, Sarah Best, Karen Bianco-Miotto, Tina Blue, Edwina Boden, Michael Bonder, Claudine Bonner, Wendy Boog, Bernadette Bosco, Mariea Bouwman, Emmy Braunack-Mayer, Annette

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This list aims to be as comprehensive as possible and any omissions are unintentional.

Shuaib, Entesar

Piltz, Sandie

Pitcher, Julia

Publications

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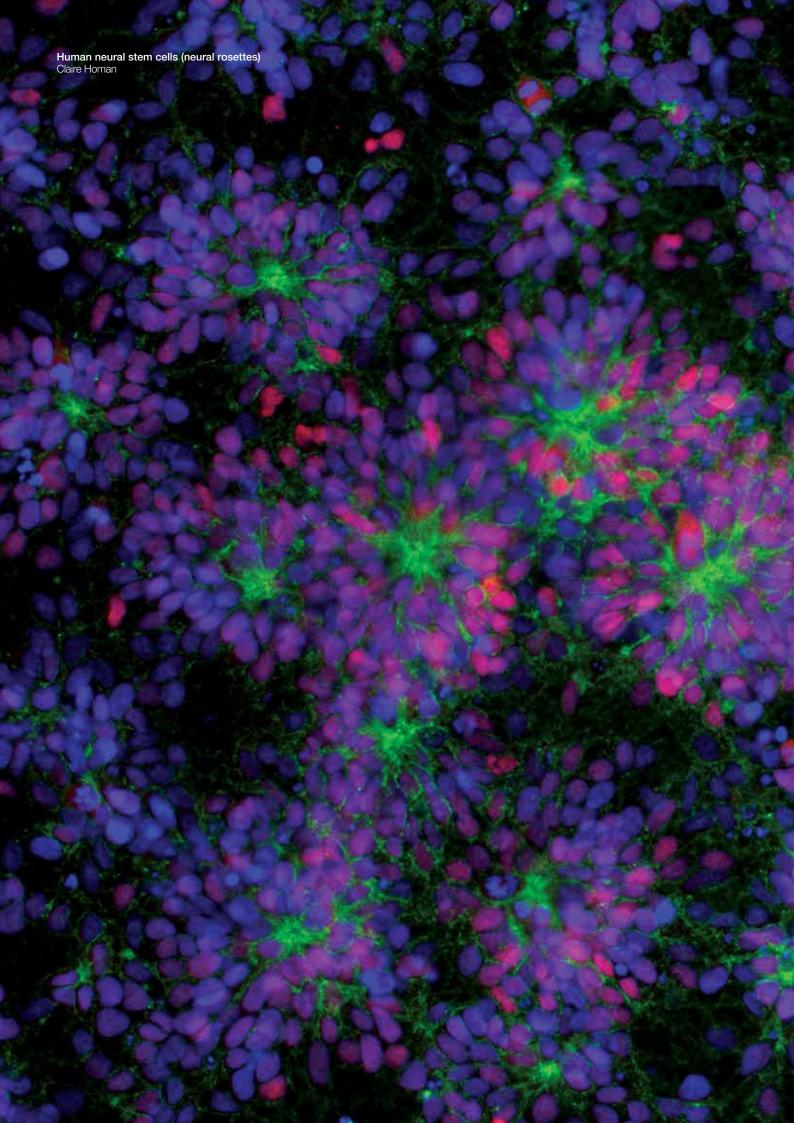
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