

# ANNUAL REPORT 2018

**Robinson Research Institute** 



EARLY NURTURING, LEARNING **EXPERIENCES AND PHYSICAL HEALTH** FROM AGES ZERO TO FIVE GREATLY **IMPACT SUCCESS OR FAILURE IN SOCIETY. THE MOST ECONOMICALLY EFFICIENT TIME TO DEVELOP SKILLS AND** SOCIAL ABILITIES IS IN THE VERY EARLY YEARS WHEN DEVELOPMENTAL SUPPORT **IS MOST EFFECTIVE.** 

THE HECKMAN CURVE

WE BELIEVE IT'S POSSIBLE TO INTERRUPT THE CYCLE OF VULNERABILITY BY **ADDRESSING THE RISK FACTORS FOR BOTH MOM AND BABY. BILL AND MELINDA GATES FOUNDATION** 

CHILDREN REPRESENT THE FUTURE, AND **ENSURING THEIR HEALTHY GROWTH AND DEVELOPMENT OUGHT TO BE A PRIME CONCERN OF ALL SOCIETIES.** WORLD HEALTH ORGANIZATION

### Starting at conception, the earliest stages of life set the trajectory of development and life course health for all individuals.

By focusing our collective research efforts, the Robinson Research Institute strives to understand how we can best protect current and future generations from disease, and to develop early interventions to ensure all children have the best start to life.

Our findings will improve the health and wellbeing of families around the globe through preventative interventions, and will reduce health inequality and the economic burden of chronic disease and disability.

Our discoveries are making a difference, and we continue to search for answers to the most pressing reproductive, pregnancy and child health needs.

Professor Sarah Robertson **RRI** Director



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# WHO WE ARE

**OUR VISION IS LIFE-TIME HEALTH FOR ALL CHILDREN AND FAMILIES, THROUGH RESEARCH EXCELLENCE.** 

the world.

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**OUR MISSION IS TO DELIVER** WORLD-CLASS ADVANCES IN HUMAN REPRODUCTION, **PREGNANCY AND CHILD HEALTH, INFORMING CLINICAL CARE, POLICY** AND PRACTICE TO IMPROVE **HEALTH ACROSS GENERATIONS** AND GLOBAL COMMUNITIES.

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 life events and determinants that build health and resilience in children and families over the life course and across generations, in Australia and around

We seek to enable a healthy start through fertility choices and intentional 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 SNAPSHOT**









## REFLECTIONS **ON 2018**

The Robinson Research Institute celebrated its 10th anniversary in 2018, building on 60 years of The University of Adelaide's research leadership in fertility, pregnancy and child health.

This milestone anniversary caused us to reflect on our achievements over the last 10 years, and to assess our direction for the next 10 years and beyond.

Our resolve to advance the health and wellbeing This new priority sets the RRI apart from of children, families and future generations through research excellence remains paramount. We made new ground in 2018, with science of reproduction and development, notable achievements including:

- Members awarded \$9.7m in new NHMRC Project Grants and Fellowships
- Launch of the Sex and Reproduction MOOC (Massive Open Online Course) in collaboration with AdelaideX
- Development of new international guidelines for the diagnosis and treatment of polycystic ovary syndrome, resulting from an extensive collaboration including 3,500 consumers, health professionals from 71 countries and 37 societies.

To guide evolution of our future direction and strategy, the RRI held a collaborative series of forums and events to determine our key area of focus. The most significant was our first interactive and collaborative Research Symposium, inviting input from a wide representation of stakeholders, including industry partners from several sectors and engaged health consumer representatives.

The input from this group was invaluable, providing new and unique perspectives on gaps and opportunities in early life research. The views we heard are vital to ensuring our direction meets the needs of stakeholders, and that our research achievements are meaningful to the community.

As a result, we have developed one overarching intention which captures the key focus of the Institute's work: reproductive and early life origins of health and disease.

In November 2018, the \$3.6 billion Adelaide BioMed City was officially launched. Home to the majority of our members, Adelaide other research institutions around the world. BioMed City (ABMC) is one of the largest It capitalises on our long history in the health and life sciences precincts in the it supports our important focus on the Southern Hemisphere. Being co-located first 1,000 days of life, and emphasises the in this space affords new collaborations and a compelling value proposition for vital significance of events before birth for imparting susceptibility or resilience to later building first-rate equipment and facilities life chronic diseases. And, it goes further accessible to all partners in the precinct. The to articulate the emerging international precinct model is already bearing fruit, as exemplified by the successful bid led by Dr consensus that health of prospective parents, their choices and environmental exposures, Kathy Gatford for a Vevo 3100 Ultrasound are fundamental for setting the life course Biomicroscope. Funding from the Ian health trajectory of the next generation -Potter Foundation resulted, in part, because with the most critical phase being before researchers across the whole precinct will conception commences. use the new imaging capability.

Our priority focus will cast new light on pre-conception events and determinants of health and disease. It will identify modifiable factors and develop interventions for conception planning that will benefit pregnancy progression and infant health. Through established translation pathways we will apply new knowledge to impart the next generation with the best possible start to life. We look forward to progressing research in this space in 2019 and communicating benefits from our research to the wider community.

This refreshed research focus will unfold as part of The University of Adelaide's exciting new strategic plan - Future Making. We are motivated by the central role identified for the RRI alongside the University's suite of research institutes to drive research success that delivers impact and benefit to local,



national and international stakeholders and builds partnerships with industry and the community

In 2018, our members produced an outstanding 483 publications, with many noteworthy advances, including: the discovery that cells causing the debilitating genetic disorder cystic fibrosis could be successfully replaced with healthy ones; demonstrating that metabolic syndrome in pregnant women increases their risk for pregnancy complications including preeclampsia and gestational diabetes by 2-4 times; uncovering that disrupted neurological pathways in cerebral palsy overlap with disruptions seen in autism supporting a common underlying lesion; discovering that disadvantaged children are prescribed antipsychotic medication more often than others; and demonstrating that women who eat fast food take longer to become pregnant and are less likely to conceive within a year.

Over the last three years, the RRI has directed renewed focus on extensive collaboration, particularly with nontraditional partners. We strategically recruited new expertise in this space, developed new funding programs for our members, and ran training sessions and workshops to provide members with the elements they need to develop and build new collaborative partnerships.

We are seeing the results of these investments with innovative new projects up and running and successes in external competitive grants focusing on collaboration. We are particularly proud of our researchers who have engaged health consumers and the community in research, often from the conception and design phase. Consumers and end-users are providing advice, guidance and views that were not previously given sufficient consideration. These partnerships are resulting in more meaningful projects that will inevitably lead to greater improvements in the health and wellbeing of our communities.

We congratulate two members for their outstanding achievements in 2018; firstly, to the RRI Director's Award recipient Prof Jennifer Couper. Jenny was awarded \$3.9 million in collaborative research funding to further the ENDIA project, which is seeking to uncover the pre-birth and early life causes of type 1 diabetes. ENDIA is an Australianwide project, recruiting 1,400 participants from seven cities across Australia. Secondly, to Professor Rob Norman AO, the inaugural Director of the Robinson Research Institute. Rob received the ASPIRE Lifetime Achievement Award for his superior achievement and compelling commitment



We are continually thankful to our Advisory Board, Executive Committee, EMCR Council and our brilliant members for their hard work and perseverance. Together we are making a difference to improve the health and wellbeing of families around the world.

Professor Sarah Robertson (Director) Professor Jock Findlay AO

(Chair of the Advisory Board) Professor Mike Brooks

(Deputy Vice-Chancellor, Research)







### Research Themes

# **FERTILITY AND CONCEPTION**

Conception is the foundation event for each new life. Every child's development, growth trajectory and health throughout their life is set in motion from the moment the embryo is formed.

Biological and social factors influence the events that facilitate (or interfere with) healthy conception. These factors ultimately determine not only whether pregnancy can commence, but also the progression of pregnancy, the growth of the fetus in utero, and the health of the infant after birth.

Achieving a healthy natural conception is a 1 in 6 couples, and 1 in 25 children are conceived by IVF. The reasons for infertility are often not easily identifiable, but age, health conditions and lifestyle factors are

The Robinson Research Institute is:

- Expanding knowledge of the molecular and cellular biology of each phase of the reproductive cycle
- Understanding developmental programming in gametes and embryos
- Understanding the role of the immune system in establishing a healthy pregnancy
- Uncovering the causes of infertility, including health conditions, genetics, lifestyle choices, environmental exposures and experiences
- Understanding the long-term implications of assisted reproductive technologies

challenge for many people; infertility impacts major contributors in both men and women.

- Empowering individuals to make informed decisions about their fertility, including pre-conception health, positive behavourial changes and alternative options to IVF
- Understanding the mechanisms of diseases that affect reproductive capability, including endometriosis, polycystic ovary syndrome and reprodutive cancers
- Developing new non-hormonal contraceptives

#### **Research advances in 2018**

- We discovered an immune and fertility defect in a mouse lacking a regulatory region linked to immune tolerance. Professors Simon Barry, Sarah Robertson and teams believe this could lead to a better understanding of how the immune system determines whether a fertilised egg should be tolerated, and a new pathway for unexplained infertility.
- We looked at the differences in fresh embryo transfer and frozen embryo transfer in women undergoing IVF without polycystic ovaries. The results from Prof Rob Norman and collaborators confirmed the safety and efficacy of frozen embryo transfers, which resulted in about the same live birth rate as fresh embryo transfers.

- We established an interdisciplinary team of biologists and physicists within the ARC Centre of Excellence for Nanoscale BioPhotonics to develop non-invasive tools to assess oocyte and early embryo health. Dr Kylie Dunning and Tiffany Tan are utilising the light naturally emitted by cells as an indicator of cell metabolism. This light is captured in images using sophisticated forms of microscopy and is being used to discern between good and poor quality oocytes and embryos.
- We analysed the antioxidant defence systems in granulosa cells throughout folliculogenesis, which revealed that GPX1 is the most important antioxidant enzyme. Together with the LRP8 selenium uptake receptor, Prof Ray Rodgers and Dr Katja Hummitzsch found it is positively correlated to the expression of steroidogenic enzymes involved in estradiol synthesis and therefore has a pivotal role in reducing the damaging effect of ROS on granulosa cells and oocytes.
- Across rodent species, we discovered the occurrence of relatively small testes mass co-evolved with less streamlined spermatozoa which have larger acrosomes and shorter tails, suggesting divergent processes of sperm-egg interaction and egg coat penetration at the time of fertilisation. E/Prof Bill Breed's findings indicate that sexual selection drives not only relative testes mass, but also sperm form and the cellular processes of gamete interactions during fertilisation.
- We identified the unique mechanism of action of the hormone progesterone in ovarian cells. Prof Darryl Russell's research shows this mechanism is important for understanding anovulatory infertility, and also includes novel targets for the development of new specific contraceptives.
- We found that the majority of adolescents with polycystic ovary syndrome (PCOS) are satisfied with their diagnosis experience. Dr Alexia Pena's findings contrast adult women who are often dissatisfied, with close to 60% of adult women with PCOS taking more than 1 year to achieve diagnosis after their first GP appointment.
- The Centres for Disease Control assembled data on all IVF clinics in the USA. We then analysed the increasingly common practice of using donor oocytes on the risk of adverse perinatal outcomes. Prof Michael Davies examined 204,855 singleton births, which revealed that use of donor oocytes was associated with increased risk for preterm delivery; whereas donor thawed embryo transfers increased the risk for being born small for gestational age.
- From a large survey of patients with period pain, we found that on average, women suffered from eight pain-related symptoms out of a potential of 14 symptoms - with 2.4% of women experiencing all 14. Dr

Susan Evans and A/Prof Louise Hull found that endometriosis was unable to be distinguished on the basis of symptoms from women with chronic pain, without a laparoscopy diagnosis.

- We looked at the function of a particular cell type in breast tissue that is associated with high breast density, called fibroblasts. A/Prof Wendy Ingman and Maddison Archer compared the function of fibroblasts isolated from women with high breast density with fibroblasts from women with low breast density, to understand whether fibroblasts from dense tissue could be driving increased breast cancer risk. They found that fibroblasts from women with high and low breast density are not inherently different, pointing to the immune system as a key driver of breast density.
- We assembled evidence for an invited review article on sleep disturbances in women with polycystic ovary syndrome (PCOS). Led by Dr Renae Fernandez, Prof Vivienne Moore and collaborators, the review found bidirectional pathways at play (physiological and lifestyle), which means that sleep disturbances may make PCOS worse, and vice versa. Quality of life for women with PCOS is likely to benefit from diagnosis and management of sleep disorders.
- We developed a unique high-throughput screening method for identification of new non-hormonal contraceptives. Prof Darryl Russell's research led to the discovery of previously unknown molecular pathways essential for ovulation and unique candidate drugs with promise as new contraceptives.
- We undertook the largest acupuncture trial in IVF comparing acupuncture with a sham acupuncture control. The first treatment was administered between days 6 to 8 of follicle stimulation, and two treatments were administered prior to and following embryo transfer. Prof Rob Norman and collaborators found no significant difference in live birth rates. These findings do not support the use of acupuncture to improve the rate of live births among women undergoing IVF.
- We are developing a completely new embryo creation and development paradigm to automate the IVF process. Prof Jeremy Thompson and Suliman Yagoub argue that delivering a micro-perfusion culture system, where media components change without culture 'interference', will significantly lift results, enabling more couples to become pregnant faster and more cost-effectively.
- We have shown that the addition of GM-CSF to oocvte maturation media can improve preimplantation embryo development in mice, pigs and cattle. Based on these finding A/Prof Mark Nottle has filed a patent and plans to extend this work to humans to overcome the need for hormonal stimulation in IVF.

- We undertook data acquisition and the development of a deep learning algorithm for improved detection of breast cancer from mammographic screening. Prof Lyle Palmer and collaborators hope this will lead to earlier detection of breast cancers to enable quicker and more effective treatments.
- We were the first laboratory to discover haemoglobin mRNA and protein in the mouse cumulus-oocyte complex, embryo and human granulosa and cumulus cells. Prof Jeremy Thompson and Megan Lim are now exploring haemoglobin mRNA's role in oxygen regulation and sequestering reactive oxygen species to evaluate its importance in healthy oocyte maturation.
- We demonstrated that the extracellular matrix molecule, hyaluronan, is increased in patients that develop chemotherapy resistance. Dr Carmela Ricciardelli and team are investigating strategies to target hyaluronan to overcome chemotherapy resistance in serous ovarian cancer patients.
- We demonstrated that maternal diet before conception impacts time to pregnancy and fertility. Dr Jess Grieger and Prof Claire Robert's paper published in Human Reproduction had a very high Altmetric score and attracted enormous media attention around the world.
- We identified interferon-gamma (IFNG) in male seminal plasma, the first known inhibitor of immune tolerance for pregnancy. Our studies in mice in vivo and human ex vivo, demonstrate that even low levels of IFNG suppress TGFB signalling to prevent GM-CSF induction, with adverse consequences for fertility and fetal development. This is significant as Prof Sarah Robertson and Dr David Sharkey have previously shown that IFNG is present in the seminal plasma of some men, and seems to fluctuate in response to environmental factors such as microbial dysbiosis and smoking
- We discovered that an endometriosis associated microRNA is essential for endometriosis leison development in mice. Null mutation of this microRNA caused the complete absence of glandular development in endometriosis-like lesions. Kavita Panir, Dr John Schjenken and A/Prof Louise Hull believe this microRNA may be a new target for endometriosis therapy.
- We concluded a series of studies examining the role of inflammatory molecules in mediating physiological events within the ovary. Prof Rebecca Robker and Drs Lisa Akison and Macarena Gonzalez found that progesterone signalling is required to produce inflammatory mediators such as interleukins and to recruit immune cells into the ovary at the time of ovulation. By analysing data from samples of human ovarian fluid Dr Macarena Gonzalez and Prof Michelle Lane found that

inflammatory molecules (such as TNF and IL6), were not related to obesity as expected, but were rather associated with high amounts of triglyceride and free fatty acid lipids in these women.

- We investigated the effect of a protein called CCL2 on how the fibroblasts function. CCL2 is part of the immune system and has been associated with breast cancer risk and breast density in mice. A/ Prof Wendy Ingman and Maddison Archer found that CCL2 treated mammary fibroblasts exhibited an increase in production of insoluble collagen, which is also observed in breasts of high density.
- We investigated the regulation of polycystic ovary syndrome (PCOS) candidate genes in cultured fetal fibroblasts, and found that INSR, C8H9orf3 and RAD50, as well as AR and its coactivator TGFB1I1, are regulated by TGF $\beta$  in vitro. This finding by Prof Ray Rodgers and Monica Hartanti further supports the idea that altered  $TGF\beta$ signalling during fetal development could contribute to the aetiology of predisposition to PCOS later in life.
- We have furthered our understanding of the role of cumulus after sperm penetration. Using time-lapse confocal and a specific calcium ion-fluorophore in a bovine model, Hanna McLennan has systematically shown that the behaviour of cumulus around the time of oocyte activation is different in the presence of sperm and especially when subsequent development takes place.
- We showed that all-trans retinoid acid (ATRA), an inhibitor of the Annexin A2-S100A10 signaling pathway, acts to suppress proliferation of serous ovarian cancer cells. The results by Dr Carmela Ricciardelli and Prof Martin Oehler show that ATRA is a potential novel therapy that warrants further evaluation.
- We are developing flow cytometry-based tests for quantifying and phenotyping T cells in women experiencing unexplained infertility and recurrent miscarriage, to better identify the immune causes of these conditions, and to underpin clinical studies to boost reproductive immune function. In future studies, Prof Sarah Robertson, A/Prof Louise Hull and Dr Lachlan Moldenhauer will trial targeted therapies to boost Treg cells to improve immune tolerance for pregnancy success.
- We demonstrated that repair of CRISPRinduced DNA breaks often generate large deletions in mouse embryos and pluripotent cells. These findings by Dr Fatwa Adikusuma and Prof Paul Thomas have far-reaching consequences, particularly for the use of CRISPR technology to correct pathogenic mutation in human zygotes.

• We defined the impact of polycystic ovary syndrome (PCOS) in women aged outside the peak reproductive years. Utilising data from a large, community-based survey of South Australian women, this study by Dr Jodie Avery shed light on the extent of under-diagnosis of PCOS among young, as well as peri and post-menopausal women. In addition, the findings identified previously unrecognised co-morbid conditions, particularly in young women with PCOS, such as arthritis. This reinforces the need for multi-disciplinary management of this complex condition.

- stressors influence ovarian somatic cell function, and in turn, impact oocvte and embryo health. Prof Darryl Russell found that these stress response mechanisms are of cancers of reproductive organs.
- We are progressing a large human clinical cohort to evaluate seminal fluid composition in men, to understand how this relates to fertility status and clinical outcomes in IVF, clinical and lifestyle factors, and immune response in the female partner. Next steps for Professors Sarah Robertson, Michelle Lane, Kelton Tremellen and Dr David Sharkey are



5-methylcytosine on the maternal DNA (red) and 5-hydroxymethylcytosine on the paternal DNA (green) of a one cell embryo. Prof Rebecca Robker and Yasmyn Gordon.

We showed that environment and lifestyle important in the initiation and progression

to develop algorithms to define the best predictive indices of male fertility that will add value to existing tests for sperm quality.

- We developed a new website on polycystic ovary syndrome (PCOS) as part of the NHRMC Centre for Research Excellence into PCOS with Monash University, led by Professors Rob Norman and Helana Teede. This website provides evidencebased information for women with PCOS, and links to the new AskPCOS App and Monash University's PCOS Program, which includes the newly developed international guidelines for the management and treatment of women with PCOS.
- We are seeking to improve herd genetics of cattle utilising in vitro embryo production (IVP). However, improvements are constrained as many immature oocvtes collected for IVP lack competency due to a lack of synchrony between nuclear and cytoplasmic maturation. Madeline Batsiokis and Prof Jeremy Thompson are undertaking trials focused on preventing nuclear maturation while supporting cytoplasmic maturation.

### Research Themes

## PREGNANCY **AND BIRTH**

Most prospective parents anticipate healthy, problem-free pregnancies. In reality, complications are common, with a quarter of Australian pregnancies affected by one or more of the following conditions: preeclampsia, preterm birth, fetal growth restriction or gestational diabetes.



Pregnancy complications can have serious life-long health implications for both the mother and her baby; identifying at-risk individuals and administering effective interventions is vital for healthy communities.

The Robinson Research Institute is:

- Defining the biological pathways and processes that enable healthy pregnancy and fetal growth
- Understanding the factors and pathophysiological events that lead to pregnancy complications
- Addressing the additional challenges facing disadvantaged communities
- Understanding the maternal immune response to implantation and the immune adaptations allowing placental formation, including vascular supply and nutritient transportation
- Understanding the immune and inflammatory mechanisms controlling the timing of labour, including preterm labour

- · Identifying all modifiable risk factors that affect pregnancy health
- Developing interventions to prevent or limit pregnancy complications
- Maximising maternal and infant health and wellbeing after birth
- Educating pregnant women on how to achieve a healthy pregnancy, including diet and lifestyle behaviours and timing of appropriate maternal vaccinations

#### **Research advances in 2018**

- We developed a tool and computational method to analyse reduced-representation DNA methylation data. Dr Jimmy Breen is applying these methods to large cohorts of placenta samples from the SCOPE study, led by Prof Claire Roberts.
- We showed that rytvela, a peptide inhibitor of interleukin-1A signalling, protects the fetus from inflammatory injury when exposed to infection-associated

inflammation in utero. With colleagues from Edmonton and Montreal, Canada, Dr Loretta Chin and Prof Sarah Robertson also found that treatment in utero is consistent with normal neurological, gastrointestinal and lung development, and healthy outcomes for offspring after birth.

- We developed and characterised a new model of restricted growth before birth in mice, that removes many of the confounders seen with natural variation, and where constraint occurs from early pregnancy. In this new model, Dr Kathy Gatford and collaborators found that maternal constraint and placental restriction both contribute to restricted fetal growth, similar to the effects seen in human twin and triplet pregnancies. The next step will involve using this model to test interventions.
- We provided the first complete atlas of developmental and tissue-specific expression of insulin-like growth factor system components in a mammal. The resource

developed by Dr Mani Ghanipoor-Samami and other students under the supervision of Dr Karen Kind and Prof Stefan Hiendleder, enables studies of programming effects on a epigenetic system that is crucial for growth and development.

- Maternal immunisation is an effective strategy to protect pregnant women and their infants from vaccine-preventable diseases. We undertook a study to estimate maternal vaccine uptake pre and post introduction of a midwife-delivered maternal immunisation program. The program enables registered midwives to administer vaccination during pregnancy using a standing medication order, without seeking permission from a referring medical doctor. Prof Helen Marshall and Haseen Mohammed's results demonstrate that the provision of maternal vaccinations by midwives at the place of antenatal service was a strong predictor of vaccination uptake during pregnancy.
- We analysed the use of Omega-3 fatty acid supplements in a pregnancy Cochrane Review. A/Prof Philippa Middleton and Emily Shepherd's publication shows clear evidence of reduced preterm birth; with findings released on World Prematurity
- Working in a collaboration across Adelaide and the University of Alberta, Dr Alison Care demonstrated the critical role for immune cells in regulating adaptation of maternal uterine arteries to ensure adequate maternal blood supply to the developing placenta and fetus. Using a mouse model enabling acute depletion of these cells, she showed that fetal loss is preceded by elevated vascular resistance and inflammation, providing extra insight for the critical role of Treg cells in successful pregnancy.
- Using scanning electron microscopy, we identified changes in the morphology of the ovarian surface throughout fetal development showing that in early and

Day, gaining extensive publicity.

mid-gestation, the surface cells are cuboidal, whereas late in gestation flat cells appear. Crater-like structures are seen on the surface from mid-gestation onwards and mark ovigerous cords which are not covered by a proper surface epithelium yet. These findings by Prof Ray Rodgers and Monica Hartanti provide a new insight into the formation of the fetal ovary.

• We demonstrated a novel method for the accurate assembly of an individual's complete genome as part of an international research team. The newly developed method partitions the two chromosome sets of an individual, inherited from each parent. This new assembly by Professors Stefan Hiendleder and John Williams with international collaborators has widespread biomedical applications, including improved identification of genetic variants and correct calling of genotypes that are required for application of genomics in personalised medicine.

**Research Themes** 

# EARLY ORIGINS OF HEALTH

The health of every child is profoundly influenced by events in early life.

Early life environment determines the trajectory of chronic disease later in life including metabolic and cardiovascular health, immune and reproductive health, and neurological function. Parental health and well-being prior to conception, during pregnancy and in early postnatal life determines the quality of this crucial early environment – a concept known as developmental programming.

Understanding the mechanisms underlying early life is essential in developing effective interventions, in identifying early prognostic markers of risk, and defining optimal parental health and lifestyle.

The Robinson Research Institute is:

- Defining the role of factors that affect early development, including: poor nutrition, lack of exercise, obesity, diabetes, asthma, infection and inflammation, shift work and stress
- Developing interventions that can be administered during pregnancy to improve the life-long health of the infant
- Demonstrating that even late preterm babies are at increased risk of impaired neurological function in childhood, and developing effective interventions
- Uncovering the impact of disadvantage in developmental programming and life-long health
- Demonstrating that paternal obesity and poor diet programs obesity and impaired metabolic health in the next two generations of offspring
- Utilising our knowledge to inform pregnancy care guidelines and public health policy
- Understanding the early life environments that program asthma and allergy development



#### **Research advances in 2018**

- We conducted a comprehensive systematic review and meta-analysis of the relationship between fetal growth and allergic diseases. Drs Kathy Gatford, Amy Wooldridge and collaborators found that increasing birth weight is associated with increased risks of childhood food allergy and eczema, independent of gestational age.
- We demonstrated that a novel microbial compound called OM-85 could be used in mice to prevent preterm birth, and to protect offspring from pre-birth programming of allergy susceptibility. This compound is utilised widely in Europe as a treatment for allergy and asthma, so there is a strong rationale to translate this finding to protect women at high risk of preterm birth. The next step for Prof Sarah Robertson, working with Dr Deb Strickland, Prof Pat Holt and colleagues at The University of Western Australia, is to demonstrate safety in phase 1 clinical trials in women.
- AusHealth is partnering with Prof Frank Grutzner to progress his research using comparative genomics in Australia's iconic native egg-laying mammals to explore potential treatment options for metabolic diseases in humans.
- We used transcranial magnetic stimulation to assess cortical excitability and neuroplasticity in 45 gestational diabetes mellitus (GDM)-exposed children and 12 control children aged 11-13 years. GDM-exposed children had reduced cortical excitability, neuroplasticity, and salivary cortisol when compared with control children. Jago Van Dam McDonald's findings suggest that GDM can contribute to subtle differences in child neurophysiology and possibly cortisol secretion, persisting into early adolescence.
- We investigated the effects of four consecutive simulated night shifts on glucose homeostasis, mitochondrial function and central and peripheral rhythmicities. Prof David Kennaway found that as few as four days of simulated night shift work in healthy adults is sufficient to reduce insulin sensitivity. Prolonged shiftwork can be expected to increase the risk of type 2 diabetes.
- We reported on the follow up of 18-month old children of women who participated in the LIMIT Randomised Trial, a trial of diet and lifestyle advice during pregnancy. Whilst Prof Jodie Dodd and team found no differences in measures of adiposity between children whose mothers received dietary and lifestyle advice and children whose mothers did not, we did observe that 46% of this cohort of children at high risk of childhood obesity had a BMI z score above the 85th centile for their age and sex. In addition we observed

high prevalence of at-risk obesogenic behaviors including increased screen time above recommendations, children not meeting fruit and vegetable consumption recommendations and high consumption of non-core foods including sugar sweetened beverages and salty snacks.

- We progressed our research on mechanisms which predispose children to the development of allergic diseases by showing that immediately following birth there is a very short 'window of opportunity' when epigenetic (nutrient) influences can operate to alter signalling pathways. Prof Antonio Ferrante's findings could lead to the prevention of allergy development in infants.
- We demonstrated that poor maternal metabolic health increases risk for gestational diabetes and preeclampsia independent of maternal BMI. The findings by Drs Jessica Grieger and Luke Grzeskowiak highlight the need to screen for poor metabolic health and to develop new interventions.
- We showed in a mouse model of periconception diabetes, there is a change in the maternal immune response, notably a decline in Treg cells and elevated inflammatory cells. Dr Hannah Brown and Ella Green's findings partly explains why hyperglycaemia at conception has such a potent adverse effect on fertility and provides new hints for the mechanisms linking metabolic dysfunction and infertility in women.
- We identified the pathological mechanism for PCDH19-Epilepy using multiple CRISPR/Cas9-generated mouse models. We showed that PCDH isoforms interact to form a molecular code that regulates cell-cell-adhesion of neuroprogenitors. Perturbation of this code in PCDH19 heterozygous females alters neural circuitry increasing seizure susceptibility. Dr Daniel Pederick and Prof Paul Thomas also identified for the first time, congenital brain malformations in affected females.
- We are identifying that ART-conceived children and survivors of extreme preterm birth may be at increased risk of type 2 diabetes and cardiovascular disease earlier in life. A/Prof Michael Stark and Professors Michael Davies and Rebecca Robker are investigating telomere length on these groups, including the potential interaction between the two, as a contributing factor to chronic disease.
- We randomised 524 women who were overweight or obese in pregnancy to take metformin or a placebo, in addition to receiving healthy diet and lifestyle advice. Prof Jodie Dodd and collaborators found that metformin was not effective in reducing the risk of delivering a baby with a high birth weight above 4 kg. Whilst there was a slight reduction in weekly gestational weight gain, there were no benefits observed in reducing the risk of adverse



outcomes associated with overweight and obesity in pregnancy, including gestational diabetes and high blood pressure.

- We found that feeding methyl donor supplements, including folic acid, to mothers in the last 1/5 of pregnancy partially removed the protection against allergy seen in adolescent offspring who were growth restricted before birth. Drs Kathy Gatford and Amy Wooldridge's findings supports other studies suggesting that taking folic acid in late pregnancy may increase the risk of allergy for the offspring in childhood, and is the first time this effect has been demonstrated in intrauterine growth restriction.
- In the course of recruitment for the Treatment Of BOoking Gestational diabetes Mellitus (TOBOGM) study, we identified that pregnant women attending the Women's and Children's Hospital were at a much lower risk of abnormal gestational carbohydrate intolerance than women at the Lyell McEwin Hospital. Prof Bill Hague's findings have led to interventional research focused at the Lyell McEwin Hospital where the need is greatest.
- We evaluated the effects of a simulated shift work protocol for 1/3, 2/3 or all of pregnancy, on maternal and pregnancy outcomes in sheep. Drs Kathy Gatford,

Tamara Varcoe and team found simulated shift work disrupted hormonal and cellular rhythms, and impaired maternal glucose tolerance during early pregnancy. Additionally, gestation length increased in twin pregnancies, while singleton lambs were lighter if mothers were subjected to shift work conditions in the first 1/3 of pregnancy. Exposure to rotating night and day shifts, even if only in early pregnancy, may adversely affect maternal metabolic and pregnancy outcomes.

### **Research Themes**

## **CHILD AND ADOLESCENT** HEALTH

The future health of our society depends on the health of our children; as many chronic physical and mental disorders originate in childhood.

> There is a clear need to develop safe and effective interventions to be administered in early life to prevent life-long conditions.

Our members consist of world-leading clinicians and researchers who are working to detect, prevent and treat serious childhood diseases, to improve the health of children, adolescents and families around the world.

- The Robinson Research Institute is:
- Improving the effectiveness of immunisation programs to prevent serious infections in children
- Establishing improved treatments for many disorders including diabetes, sleep and neurological disorders, allergies, joint disease and cystic fibrosis

- Identifying biomarkers to ensure early diagnosis and treatment of autoimmune disease, allergies and asthma
- Defining the genetics of intellectual disability, cerebral palsy, and epilepsy to provide targets for new treatment
- Working to prevent childhood diabetes and obesity
- Strengthening the mental health of mothers, young children and adolescents through e-learning programs
- Understanding the serious implications of generational disadvantage and working with government to comprehensively address these issues
- Running large clinical trials and cohort studies in the areas of obesity, gestational diabetes and type 1 diabetes

#### **Research advances in 2018**

- We discovered a novel molecular pathway in human T reg cells that is linked to metabolic homeostasis in fat tissues. Prof Simon Barry and Dr Tim Sadlon believe this is the key to understanding how type 2 diabetes may progress as BMI increases, and modulating this process in Tregs may reduce the incidence of type 2 diabetes
- We achieved recruitment of 1,221 participants at the end of December to the national ENDIA study, looking to find the causes of type 1 diabetes. Led by Prof Jenny Couper, the team achieved 87% of their target of 1,400 participants, with recruitment completing in 2019.
- We took oropharyngeal swabs from 421 first year university students, and repeated with an additional swab after 3 months. We identified that attending bars and engaging in intimate kissing is associated

with oropharvngeal carriage of Meningococcal B in South Australian university students. Prof Helen Marshall and Mark McMillen's findings support the implementation of adolescent meningococcal vaccine programs at school.

A/Prof David Parsons adapted a tiny human endoscope to target specific deep lung airways in small lab animal models. no knowledge of the dose distribution. Together with Dr Chantelle McIntyre they established a new procedure that will and tissue sampling.



• To develop treatments for cystic fibrosis, Previously dosing selected airways or lobes of the lung has not been possible, as desired locations are not visible and there has been improve our understanding of lung dosing, reduce animal use, and provide options for multiple-site dosing and lung environment

- We engineered anti-TNF biologics which bind to TNF and alter the cellular responses induced by this cytokine. While blocking the inflammatory response in disease models, the biologics did not pose a risk of increased susceptibility to infection, so have advantages over present anti-TNF therapy. Prof Antonio Ferrante believes this may be particularly useful in treating inflammatory diseases in childhood.
- We conducted the largest prospective screening study of its kind, screening for primary immunodeficiency diseases and examining the efficacy of an assay identifying newborns with T and/or B cell lymphopaenia. Dr Jovanka King reported two novel screening approaches, a strategy harnessing transcriptomics to identify hypogammaglobulinaemia, and a genotyping assay to identify genetic polymorphisms conferring specific disease susceptibility.

- We completed a study in mice and humans showing that time-restricted eating, with and without a phase delay, improved glucose control. A/Prof Leonie Heilbronn's findings help to build the understanding for more effective preventative interventions and treatments for diabetes and obesity.
- We compared the oral microbiome in healthy children and children with sleepdisordered breathing. Children with sleep-disordered breathing have distinctly different oral microbiome abundance before and after they sleep, suggesting the disorder may disrupt normal microbial colony maintenance. Given the oral cavity is the gateway to the gut, Jessica Carlson-Jones' findings suggest these changes may have consequence for gut microbiome, which may affect digestion and other vital organ function.
- We identified and functionally evaluated a number of rare DNA variants in the core of the mRNA export pathway, the THOC2 gene, in primarily children, with various neurodevelopmental disabilities including intellectual disability, epilepsy or autism. Taken together, Prof Jozef Gecz's data demonstrates that even subtle alterations to the canonical molecular pathways such as mRNA export, can be compatible with life but lead to neurodevelopmental disabilities in humans.
- We ran a study looking at influenza vaccine uptake and associations in a cross-sectional study of children with special risk medical conditions. The study used data from over 400 parents of children with a special risk medical condition attending the Women's and Children's Hospital to highlight that uptake of the influenza vaccine in these children remains sub-optimal. The work also showed that receiving a recommendation from a specialist or GP and having a parent receive the influenza vaccine annually was strongly associated with uptake. This work by Prof Helen Marshall and Jane Tuckerman, reinforces that a healthcare provider recommendations remains crucial, and offers new ways that healthcare professionals and policy makers could tackle low uptake in vulnerable populations.
- We validated a new tumour antigen target for cancer immunotherapy, nfp2x7. Prof Simon Barry and Dr Veronika Bandara hope this will lead to a new personalised immunotherapy for cancer. The Chimeric Antigen Receptor we generated to target this tumour antigen has proven effective on 12 different human cancer cell lines representing 6 types of cancer in lab-based assays.
- We conducted a systematic review and meta-analysis of 271 cases of individuals with mutations in the PCDH19 epilepsy and intellectual disability gene, which showed that the age of onset before 12 months is a strong predictor of a more severe

neurodevelopmental outcome. Prof Jozef Gecz's research also shows that even identical genetic mutation in the PCDH19 gene may have variable onset; about 80% of mutation-carrying individuals are unaffected.

- In a collaborative study, melatonin treatment of patients with delayed sleep wake disorder and delayed circadian phase, improved objective and subjective measures of sleep and sleep-related impairment. Prof David Kennaway found that improvements were achieved largely through the sleeppromoting effects of melatonin, combined with behavioural sleep-wake scheduling.
- We continued our X-ray imaging studies at SPring-8 Synchrotron in Japan, the Imaging and Medical Beamline at the Australian Synchrotron, and the Munich Compact Light Source. These studies have examined airway surface health and lung function in CF rats, and quantified the effects of Dr Martin Donnelley's airway gene therapy.
- Using mice that model mutations causing intellectual disability and seizures, A/Prof Cheryl Shoubridge's team demonstrated that treatment with a steroid hormone early in life leads to significant reductions in the frequency and severity of seizures. The team is seeking to understand how these improvements occur, and to identify potential treatments to improve the behavioural and life expectancy aspects of these disorders.

Dual-expression of GFP (green) and luciferase (red) reporter genes in a rat cell culture, used to track the targets and the efficiency of our lentiviral gene transfer vector used in studies of CF gene therapy. Dr Juliette Delhove.



- We used arterial myography on a child's artery, removed from tonsillar tissue (dorsal lingual artery). This is important as it is the first time researchers have a peripheral functional measure from the child, an ex vivo measure of vascular function and vascular structure. Dr Anna Kontos' work seeks to better understand the early origins of cardiovascular disease in sleep disordered breathing.
- We identified a lineage restricted transcription factor in human T cells which may be disrupted in inflammatory bowel disease (IBD). This factor could lead Drs Cheryl Brown, Chris Hope and Soon Wei Wong to understanding which cells in the immune system have become dysfunctional in IBD, enabling a diagnostic test, and a new target for intervention.
- Using new RNA sequencing technology to measure MRNA in cells from children with cerebral palsy, we showed that the neurological or signalling pathways that are disrupted in children with cerebral palsy, overlap with disruptions seen in autism. This research of Dr Clare Van Eyk, E/Prof Alastair MacLennan and Prof Jozef Gecz points to a common biological change in both cerebral palsy and autism.
- We studied a cohort of 6,987 children assessed by clinical geneticists to have severe neurodevelopmental disorders such as global developmental delay and autism, often in combination with abnormalities of other organ systems. Although the genetic causes of these neurodevelopmental disorders is expected to be almost entirely monogenic, Prof Jozef Gecz and collaborators have shown that 7.7% of variance in risk is attributable to inherited common genetic variation.
- We detected copy number variants from exomes of 186 children with cerebral palsy, and validated these findings using single nucleotide variants arrays, and compared this with RNA-seq outlier gene expression analysis from lymphoblastoid cell lines. We had previously identified likely pathogenic de novo or inherited single nucleotide variants in 14% of trios by exome sequencing and a further 5% from evidence of outlier gene expression using RNA sequencing. Dr Mark Corbett's research brings this total to 22.7%, as here we resolved an additional 3.7% of this cohort with pathogenic or likely pathogenic copy number variants, while a further 7.7% had copy number variants of uncertain significance.
- We undertook a study asking: are children with special risk medical conditions receiving influenza vaccination? This was the first study to provide data on the reporting of influenza vaccination to the national Australian Immunisation Register; finding only a third of influenza vaccinations were reported, and parental reporting over estimates confirmed

- influenza vaccination status and is affected by time and relationship to the child. Prof Helen Marshall and Iane Tuckerman's work contributes to under-
- in children with sleep-disordered breathing is significantly different from non-snoring children. Dr Benlee Yap's findings may lead to a more comprehensive understanding of the origins of the disorder and to better treatment options for patients.
- We were part of a national collaborative study evaluating the cases of severe hospitalised chicken pox (varicella) and exploring factors associated with severity. The study assessed 327 children admitted to hospital with confirmed varicella and found that the majority (71%) were not vaccinated. Prof Helen Marshall and collaborators also identified that whilst vaccination provided protection against requiring hospitalisation did still occur in some children vaccinated with a one-dose schedule, providing some evidence to consider funding of a two-dose varicella vaccination schedule.
- We assessed a novel method to condition the airway epithelium and provide space for Dr Nigel Farrow's findings showed that without the conditioning step, stem cell conditioning step, approximately 50% of
- We found that some mental health apps symptoms, promote medicalisation of normal mental states and imply individual responsibility for mental wellbeing. Prof Jon Jureidini, Dr Melissa Raven and collaborators believe that within the health care clinician-patient relationship, such messages should be challenged, when appropriate, to prevent over-diagnosis and
- We systematically reviewed evidence of the costs and resource utilisation relevant to acute infection and long-term sequelae of shows that the public health burden of the disease is substantial with significant increases in healthcare costs and resource
- Prof Alastair MacLennan and team hope to identify cerebral palsy in early life, facilitating new and improved interventions.

standing how parental recall could influence uptake of the influenza vaccine for children.

• We have shown the dento-facial morphology

more severe disease, breakthrough varicella

donor stem cells transplants in cystic fibrosis. transplantation is not successful and with the animals showed successful transplantation.

which claim to improve wellbeing or relieve to ensure supportive health care when needed.

invasive meningococcal disease. The review by Dr Bing Wang and Prof Helen Marshall use for meningococcal patients with sequelae.

• We are progressing a new project to deliver earlier diagnoses for children with cerebral palsy. Currently, most children with cerebral palsy receive diagnosis at 12-24 months. E/ that an early diagnostic assay using pre and peri-natal biomarkers will enable clinicians

- We added new genes to the list of genes for mutation analysis for primary immunodeficiency diseases; including identifications of mutations in the ARPCIb gene, which is important for actin polymerisation. Prof Antonio Ferrante and Dr Alex Quach characterised the functional consequences of this mutation in particular to neutrophil chemotaxis. These findings will help to understand why children with this mutation have distinct clinical presentations.
- We constructed a clinically-relevant lentiviral vector containing the CFTR transgene, which has an improved safety profile. Dr Juliette Delhove also constructed a version that allows us to track where the vector goes, enabling us to determine whether we are targeting the right cells with our gene therapy methods and vector for treating cystic fibrosis.
- We published a novel systematic and metaanalysis of non-cognitive skills in childhood and later outcomes. A/Prof Lisa Smithers and Prof John Lynch found some evidence that non-cognitive skills (such as attention, selfregulation and perseverance) associate with improved outcomes later in life, but there is need for further inter-disciplinary research.
- We demonstrated that a novel mouse strain modelling an intellectual disability and seizure gene mirrors the clinical features in affected patients. A/Prof Cheryl Shoubridge and Dr Matilda Jackson are now using this model to understand how this genetic mutation leads to intellectual disability and seizures.
- We conducted a critical, qualitative case study of regulation of the Australian mental health app market. Dr Melissa Raven and colleagues found current regulation focuses on the potential loss of commercial reputations and profits, rather than consumer protection. They believe policy makers in different sectors should work together to develop an overarching regulatory framework for health apps, with a focus on consumer protection.

## TRANSLATING FINDINGS THROUGH COLLABORATION

OUR MEMBERS COLLABORATE EXTENSIVELY WITH RESEARCHERS AND STAKEHOLDERS, BOTH LOCALLY, AND INTERNATIONALLY, TO TRANSLATE RESEARCH FINDINGS INTO IMPROVED CARE.



HOSPITALS Members are embedded within the 5 SA public hospitals.



ACADEMIC Collaborating with researchers at hundreds of institutions across 20+ countries.



CLINICIANS Many clinicians are RRI members, and we collaborate with fertility clinics, hospitals and other primary health organisations.



INDUSTRY

Research translation is facilitated through industry and pharmaceutical collaborations and our MRCF membership.



#### **HEALTH CONSUMERS**

Collaborating with health consumers ensures our research is relevant and facilitates access to unique perspectives and solutions.



#### PEAK BODIES

We advocate for the significance of our research through memberships and partnerships with peak bodies including AAMRI and PSANZ.



NOT-FOR-PROFITS We partner with not-for-profit organisations to support evidence-based impact.



#### GOVERNMENT

Our members collaborate with local, state and federal Government on projects to improve the health of the community.



### **BOOSTING PRETERM INFANTS' BRAINS**

Megan Bater is collaborating with the Department of Education and Child Development, SA Health and parents of preterm babies, to deliver a new education program to guide parents in promoting positive cognitive development for their preterm infants.

Babies born preterm are at increased risk of motor, speech, behavioural and learning difficulties, which can persist over their lives.

The good news is that these setbacks can be mitigated by positive early life environments, which is what Megan is tapping into.

The education program includes online videos and resources and two one-on-one sessions with parents and their infants to help parents facilitate their baby's brain development by: reducing stress, protecting sleep, facilitating bonding, supporting motor development and responding appropriately to their baby's cues, tailored to age and developmental stage.

Megan surveyed over 700 parents around Australia who either previously had or currently have babies in the Intensive Care Unit. These parents helped to shape the content of the resources based on their current or perceived needs and concerns, facilitated through Miracle Babies.

This study was piloted in the Women's and Children's Hospital during 2018 and received very positive feedback; 92% of the participants would highly recommend this program to parents of preterm babies. Megan is now analysing the results and hopes that this program will be rolled out across Australia to improve the developmental trajectory of babies born preterm.

### **TRANSLATING FINDINGS THROUGH COLLABORATION**

#### **Global Nutrition Report**

The 2018 Global Nutrition Report (GNR) shares insights into the current state of global nutrition, highlighting the unacceptably high burden of malnutrition in the world. In particular, the report stresses the need to address micronutrient deficiency surveillance and targets; the effect of fragility, conflict and violence on food security and nutrition; and investing in adolescent nutrition, particularly for girls and young women.

Dr Zohra Lassi was part of the global collaboration that authored this report. She particularly contributed to the section on burden of malnutrition in adolescence. GNR acts as the world's leading publication on the status of malnutrition around the world and acts as a report card on the world's nutrition.

#### **New PCOS International Guidelines**

New global guidelines for the diagnosis and treatment of polycystic ovary syndrome (PCOS) were developed through a remarkable collaboration involving 3,500 consumers, health professionals from 71 countries and 37 societies.

The NHRMC Centre for Research Excellence in PCOS ran this process, led by Prof Helena Teede from Monash University, with Prof Rob Norman as Co-Director. RRI members Prof Ray Rodgers and Dr Alexia Pena are also members of the International PCOS Network and contributed to this important research which has been endorsed by the NHMRC.

#### **Stillbirth Senate Committee**

The Australian Senate established the Select Committee on Stillbirth Research and Education to inquire and report on stillbirth research and education in Australia. Professors Claire Roberts and Gus Dekker provided a submission and contributed to the Adelaide committee meeting.

Included in their submission was: the need to regard stillbirth as a continuum of pregnancy complications; to standardise perinatal data collection across Australia and rigorously collect termination data; and they highlighted that trends in singleton stillbirth have decreased in South Australia.

#### **Obesity Select Committee**

The Australian Senate established the Select Committee into the Obesity Epidemic in Australia Stillbirth Research and Education to inquire and report on obesity in Australia. Professors Megan Warin and Vivienne Moore and Dr Lucy Farrell presented a submission to the committee and presented evidence in person in Melbourne.

Included in their submission was: the need to include a strong equity and gender focus; a multi-sector systematic approach to implementation; local solutions to be implemented rather than a one-size-fits-all approach; regulation of online marketing should be a high priority; and high importance should be given to ensuring appropriate language is used.

#### **Pregnancy Care Guidelines**

A/Prof Philippa Middleton continued her ongoing update of the NHMRC and the Department of Health Pregnancy Guidelines. In 2018, she contributed to guideline refreshment on the topics of chlamydia, syphilis, cytomegalovirus, cervical length and prolonged pregnancy, as well as lifestyle factors including diet and exercise. These guidelines are used exclusively by maternity services.

#### WHO Commissioned Review: Community **Health Workers in Low-Income Settings**

Dr Zohra Lassi contributed to the World Health Organization guidelines on Health Policy and System Support to Optimize Community Health Workers Programmes. These guidelines seek to support countries in designing, implementing, evaluating and sustaining effective community health worker (CHW) programmes. Dr Lassi contributed to the evidence related to CHW's pre-service training and selection, training curriculum and delivery modalities and CHW competency based formal certification.

#### The Food Fix Report

The Food Fix report, The role of diet in type 2 diabetes prevention and management, seeks to improve the health of Western Australians, by moving away from the mindset of 'living with type 2 diabetes' to 'beating type 2 diabetes'. Produced by the Western Australian Legislative Assembly and the Education and Health Standing Committee, this

comprehensive report demonstrates that type 2 diabetes can be reversed through positive health behavioural changes.

Prof Rebecca Robker was one of the contributors for this report, informing the committee that the seeds of obesity and diabetes are planted in early life. She stressed the importance of prospective parents making positive health changes before pregnancy, and explained that the environment the fetus is exposed to, plays a key role in future health of the child.

#### **Updates in Infertility Treatment**

Prof Sarah Robertson was an invited speaker at the Updates in Infertility Treatment education meeting in January 2018. Convened by Ferring Pharmaceuticals, this event was attended by more than 2,000 IVF clinical practitioners world-wide. Prof Robertson presented on the topic: Reproductive Immunology - what does biology tell us? Prof Robertson has also received support from Ferring Pharmaceuticals to progress research on stimulating immune tolerance in pregnancy.

#### **Genetic Testing Delivering Diagnoses**

Prof Jozef Gecz has developed genetic tests to uncover undiagnosed conditions for families across Australia and internationally, as well as interpreting variants of uncertain significance. Prof Gecz's works with clinicians and families in the areas of intellectual disabilities, epilepsies and cerebral palsies to facilitate precise genetic diagnosis.

His translational research forms an integral part of the Australian Genomics, where he is the national lead of the Neurodevelopmental Diseases Flagship. His research led to an international Phase II Clinical Trial of ganaxolone in PCDH19 Girls Clustering Epilepsy, currently conducted by Marinus Pharmaceuticals.

#### **Omega-3 Fatty Acid Findings**

A/Prof Philippa Middleton and Emily Shepherd are part of a team that has translated the omega-3 fatty acid literature from the Cochrane Review findings into specific guidance for pregnant women and health professionals. There is clear evidence of reduced preterm birth, particularly for women with low omega-3 levels.



Prof Jeremy Thompson and Marie Ellul from ART Lab Solutions

#### **ART Lab Solutions**

Prof Jeremy Thompson, Australian Reproductive Technologies and collaborators recently launched ART Lab Solutions, building upon decades of research into assisted reproductive technologies.

The company seeks to improve livestock reproduction, moving away from artificial insemination and towards cattle IVF. Their technology will provide greater flexibility in rapid genetic improvement, with the addition of sex selection, which is expected to be of significant benefit to the beef and dairy industries.

#### **Keeping Children out of Hospital**

Prof John Lynch contributed to the Australian Institute of Health and Welfare's proposed specification A potentially preventable hospitalisation indicator for general *practice*. This sought to reduce hospital admissions by focusing on conditions that could either be prevented or managed by general practice.

Prof Lynch's submission was based on his team's analyses of data from the South Australian Early Childhood Data Project that examined potentially preventable hospitalisations (PPHs) experienced by children. His submission supported reporting of PPHs by age groups, and the inclusion of hospitalisations that are

relevant to children in the definition. Additionally, he highlighted the value of linked data in enabling examination of the proportion of individuals who experience a PPH, rather than only being able to count hospitalisations.

#### **South Australian Paediatric Chronic Pain Service**

Until 2018, South Australia was the only mainland state without a co-ordinated chronic pain service for children. Chronic pain in children causes significant suffering for the child and family and affects physical and psychological factors, and most importantly, quality of life. An integrated, multidisciplinary approach is the most effective for treating chronic pain and commencing



Nicolle Flint MP, Greg Hunt MP and Dr Susan Evans at the launch of the National Action Plan

#### National Action Plan for Endometriosis

The Hon Greg Hunt MP, Federal Minister of Health, invited A/Prof Louise Hull and Dr Susan Evans to join the working group for the National Action Plan for Endometriosis. This working group consisted of clinicians, researchers, health consumers and the community, to formulate an Australianwide plan for endometriosis community engagement, clinical practice and research.

Launched in mid-2018, this plan is already improving awareness of endometriosis in the community, and has led to a series of clinical trials and new research projects aimed at improving the health and wellbeing of adolescents and women living with endometriosis. Additionally, the plan has enabled us to build new collaborations with groups such as Jean Hailes for Women's Health, resulting in new projects in a number of areas outside endometriosis.

> with a program of 2.5 days per week, The SA Health Model of Care for paediatric chronic pain was endorsed by The Ministerial Clinical Advisory Group in Feb 2018.

Dr Carolyn Berryman joined members of the Paediatric Chronic Pain Service in mid-2018 to instantiate a collaborative research program involving A/Prof Rachael Coakley, from Boston Children's Hospital. Dr Berryman won a prestigious Australia-Harvard Fellowship to bring A/Prof Coakley to Adelaide, and in July 2019, she will run her evidence based, one-day workshop for adolescents with chronic pain and their parents.

## **COMMUNITY CONNECTION**

Over the last three years, the Institute has deliberately sought to collaborate with the community, advocacy groups and not-forprofits, to deliver research that is higher quality, meets the needs of the community and is translatable.

We developed a suite of funding programs, training sessions and community events, to provide the support and resources our members require to develop and advance collaborations; and our members are reaping the benefits.

#### **Collaborative Research Symposium**

In 2018 the Institute invited its external stakeholders to the annual RRI Symposium, to work together on identifying and setting the RRI's future research priorities. The event attracted 200 attendees including 60 external stakeholders and health consumers.

The event was positively received and is greatly assisting us in developing our new priority which will be released in 2019.

#### **Endometriosis Co-creation Workshop**

On the back of Australia's first *National Action Plan for Endometriosis* (launched in February 2018 by the Federal Government), A/Prof Louise Hull led a co-creation workshop involving advocacy groups, clinicians, researchers and health consumers. This meeting resulted in a new collaborative project to develop a digital intervention for earlier diagnosis and treatment of endometriosis, responding to the needs of women living with this condition.

#### Birthing Kit Foundation Australia collaboration

In 2017 the RRI formed a new collaboration with the Birthing Kit Foundation of Australia (BKFA) to identify low cost evidence-based interventions to improve fertility and health of women and children in low and middle income settings.

Led by Dr Zohra Lassi and Zeshi Fisher (BKFA), the group has completed a research synthesis, a Cochrane Systematic Review and a Campbell Review on clean birthing kits which appear to be a promising strategy to reduce maternal and neonatal morbidity and mortality in low resourced countries.

The group is now commencing a new project in Uganda to improve adolescent sexual and reproductive health. Uganda has the highest proportion of the population under the age of 30 years (78%) than any other country in the world and the highest total fertility rate (5.4), with half of all births occurring in girls under 20 years of age, which is associated with higher morbidity and mortality for both mother and child.

**Preeclampsia Consumer Group** 

RRI members formed the Preeclampsia Consumer

Group to share experiences, build networks

and work together to improve outcomes for

pregnant women. This group involves five RRI

researchers (Professors Gus Dekker and Claire

Roberts, and Drs Tanja Jankovic-Karasoulos, Luke Grzeskowiak and Jessica Grieger) and seven health consumers with experience

of preeclampsia, eclampsia or HELLP

Sex and Reproduction MOOC

syndrome. Meetings will continue in 2019.

Developed by The University of Adelaide's,

Course (MOOC) in Sex and Reproduction

was launched in May. This self-paced course

AdelaideX, the first Massive Open Online

teaches users about human reproduction;

pregnancy and menopause. Research

discoveries from the Institute feature in

the MOOC, with many RRI members

contributing to course content.

from puberty and contraception, to fertility,

"In my head I had a wish list of where I'd like to take our sleep disorders research but I was unsure how to progress some of my ideas. At our 2018 symposium I sat next to a representative from a women's health organisation, we got talking about my research, and an instant collaboration formed. I now have a clear vision for the direction of my research...including access to women I didn't have previously."

Dr Anna Kontos





Clockwise from top: Endometriosis Q&A Panel: Dr Ryan Rose, Dr Susan Evans, Libby Parker, Ms Nicolle Flint MP and A/Prof Louise Hull; Attendees at the Collaborative Research Symposium; Dr Megan Penno at the Pregnancy, Babies and Children's Expo'

#### **Pregnancy, Babies and Children's Expo**

The Institute engaged with families by hosting a stall at the Pregnancy, Babies and Children's Expo. This provided members with the opportunity to engage with a key target audience to discuss research trials, Institute findings and proposed future collaborative projects.

#### **Endometriosis Q&A**

RRI and Healthy Development Adelaide co-hosted *The Endometriosis Q&A*, a public awareness forum. The panel members at this event were: Ms Nicolle Flint MP, A/Prof Louise Hull, Dr Susan Evans, Dr Ryan Rose and Libby Parker. This event included 90 minutes of Q&A-style discussion of current and future endometriosis treatments and research with approximately 100 participants.

#### Science Week

During Science Week the RRI highlighted the work of our up and coming researchers from the RRI's Early and Mid-Career Researcher Council. Five members developed short videos discussing their research and explaining what science means to them Additionally, Professor Paul Thomas presented the Science Week Public Lecture at SAHMRI on the topic *Big Science Public Lecture: It's as simple as cut and paste.* 

"I have dedicated a lot of my research career striving to understand the origins of polycystic ovary syndrome (PCOS). I followed a research direction investigating what clinicians and I thought was one of the biggest issues for women living with this condition. After meeting with a woman with PCOS who is well connected in the PCOS community, I learned that there were more pressing issues. This has changed my research direction and I now expect to have a bigger impact for women with this condition."

**Professor Ray Rodgers** 



#### Lloyd Cox Memorial Lecture

Prof Rob Norman AO presented the 2018 Lloyd Cox Memorial Lecture on the topic: *The reproductive revolution and how it changed science, sex and society.* Prof Norman impressed with his engaging presentation and clearly laid out why investment in the early years is so important, and how reproduction is instrumental in shaping societies around the world.

#### **Science Meets Parliament**

Drs Pallave Dasari and John Schjenken were among 200 scientists who converged on Canberra to bring science to the nation's decision makers, at Science Meets Parliament. They were led by luminaries of Australian science including Professor Alan Finkel (Australia's Chief Scientist), Dr Larry Marshall (Chief Executive, CSIRO), chief scientists from several government departments, as well as Nobel Laureates and Australians of the Year, who stressed the importance of science to Australia's future.

#### **Heart Health Consumer Engagement Workshops**

Dr Prabha Andraweera, together with Professors Claire Roberts and Gus Dekker, A/Prof Margaret Arstall, Dr Zohra Lassi and PhD students Michelle Plummer and Maleesa Pathirana, have been uncovering the links between pregnancy health and heart health later in life, for both the mother and child. During 2018 the group conducted four consumer engagement workshops at the Lyell McEwin Hospital with 26 health consumers.

Before the workship, none of the women knew of the association between pregnancy complications and cardiovascular disease (CVD), and they requested that more advice on cardiovascular health be provided during pregnancy. During focus groups, it was identified that screening for CVD within 5 years after the first pregnancy would be beneficial, and that the majority of women would be receptive towards screening during this time.

#### **Aboriginal Communities in SA**

The Aboriginal Gender Study is a collaborative research project between the Aboriginal Health Council of South Australia, The University of Adelaide and the South Australian Health and Medical Research Institute. Funded by the Lowitja Institute, this project encourages Aboriginal people in South Australia to talk about their understandings of gender, gender roles and gender equity within their community.

"Together with SA Health, we led the biggest Meningococcal B Herd Immunity study in the world. This study required a huge level of engagement and participation from the community, including students, teachers, school principals, parents, youth advisors and immunisation nurses. At every step of the process we had community partners who helped us with recruitment, messaging, contact with students and providing feedback on the study which was instrumental in us recruiting 35,000 high school students."

**Professor Helen Marshall** 

Dr Alice Rumbold co-led the study with staff from the Aboriginal Health Council of SA, and supported the research team to implement the project in three communities. The study revealed some important insights into how gender influences the experiences of Aboriginal women, men and LGBTQ people in South Australia. In addition, participants in the study described gender equity as women and men standing together and sharing responsibilities for family and the community. This is different to the way gender equity is generally discussed in non-Aboriginal society, where the focus is often on individuals and unequal power between women and men.

#### Science Meets Business

The Centre of Excellence for Nanoscale BioPhotonics, led by Prof Mark Hutchinson showcased its science and translation into exciting new commercial ventures at Science meets Business. The event brought national and international corporate leaders and entrepreneurs, venture capitalists and

angel investors together with Australian research and commercialisation pioneers, to help advance activity in the science and translation space.

Prof Jeremy Thompson shared his startup story in establishing the business ART Lab Solutions. The venture uses advanced reproductive technologies to accelerate the improvement of livestock quality.

#### **ENDIA Feedback Group**

Led by Dr Kelly McGorm, the ENDIA Feedback Group is composed of more than 20 families with experience of type 1 diabetes. The group provides input on several aspects of the Australia-wide ENDIA type 1 diabetes trial, including reviewing documents and contributing consumer perspectives to funding applications.

#### **Breast Density Workshop**

A/Prof Wendy Ingman hosted the Ethical and Legal Considerations in Breast Density workshop, which posed the question: Given that screening mammography is recommended for early detection of breast cancer in Australia, what are the ethical and legal issues regarding provision of information about breast density to women?

This event featured presentations by breast cancer researchers, ethicists, a lawyer, health consumers and clinicians, and facilitated interaction with the community and patients and their families.

Engagement with academic peers and health service delivery is necessary to advance the highest quality research and deliver tangible outcomes for the community. Here are some of the events we hosted and supported in 2018.

#### **Fetal Medicine Update**

Led by Professor Jodie Dodd, 140 midwives, obstetricians, neonatologists, sonographers, general practitioners and colleagues from Bali attended the Fetal Medicine Update. The topics covered the best evidence currently available for non-invasive screening for fetal anomalies in the first trimester, diagnosis and management of complex brain, heart and gut abnormalities and technique and interpretation of fetal sonography.

#### **New Frontiers for a Healthy Start to Life**

The RRI hosted the fifth New Frontiers thinktank conference, bringing together researchers from around Australia under the banner Environment and epigenetic impact on plasticity in reproduction and early development. This conference seeks to assemble multidisciplinary groups with disparate but overlapping perspectives to plan effective research agendas.





#### 28 Robinson Research Institute Annual Report 2018

Attendees at the SA Vaccinology Update

**ACADEMIC AND HEALTH CARE** CONNECTION

#### **SA Vaccinology Update**

Together with SA Health, the Women's and Children's Hospital and SAHMRI, the RRI hosted the fourth SA Vaccinology Update. This full day event for immunisation providers, doctors and researchers educates attendees about the latest developments in immunisation research, policy and programs.

#### **AAMRI Research Strategy Network**

The inaugural Australian Association of Medical Research Institutes (AAMRI) Research Strategy Network meeting occurred in 2018. The RRI Business Manager (Marcus Goddard) is Co-Chair of the Steering Group for this Network and facilitated a session on Improving the quality of grants. These events are building RRI's connection into the network of Australian medical research institutes, and our ability to ultimately deliver effective research-based outcomes.

- With the members in different disciplines and Societies
- · Joint seminars, sharing activities & opportunities
- · Website and publicity material

human health, agricultural productivity, environmental sustainability





To raise awareness of the exceptional benefits that Australian reproductive research brings to society, Reproductive Health Australia (RHA) was established as an advocacy group. Prof Jock Findlay, the RRI's Advisory Board Chair, established RHA, with the RRI being a founding partner of this new alliance.

#### **ANZPRA Satellite Conference**

Led by Prof Claire Roberts, the RRI hosted an ANZPRA Satellite Conference for 50 delegates from around Australia and New Zealand, to share the latest advances in placenta research. Topics explored on the day included: viral infections of the placenta and fetus, preeclampsia, prevention of stillbirth, and the roles of micronutrients, circadian rhythms and maternal age on placental development and pregnancy success.

#### **DOHaD ANZ SA Symposium**

Led by Dr Prabha Andraweera, the RRI co-hosted the first DOHaD ANZ SA Symposium for 64 researchers from across South Australia. The Symposium enabled exploration of the following topics: intrauterine growth restriction, impact of inflammation in pregnancy, genetics of lifecourse health, SA early childhood data project, animal models in DOHaD research and epigenetics.

#### WCH Co-hosted Grand Rounds

Continuing our collaboration with the Women's and Children's Hospital, the RRI co-hosted three Grand Rounds seminars in 2018: Prof Randy Jirtle, North Carolina State University - *Epigenetics* – *How genes* and environment interact in disease risk; Prof Jeffrey Keelan, The University of Western Australia – A clinician trial employing a novel screening test to prevent infection-driven preterm birth; and Prof Michael Davies, RRI – The implication of fertility and related treatments for obstetric and neonatal outcomes.

These seminars facilitate engagement with researchers and clinicians at the Women's and Children's Hospital.

#### **Partnership with SRB**

For the 13<sup>th</sup> year in a row the RRI sponsored the Society for Reproductive Biology at its annual joint meeting (with the Endocrine Society of Australia and the Asia and Oceania Thyroid Association). The Institute sponsored the Robinson Research Institute Award for Excellence in Reproductive Biology, awarded to Dr Tu'uhevaha Kaitu'u-Lino from the University of Melbourne.

#### **Sponsorship of ASMR**

Sponsorship of the ASMR Annual Scientific Meeting provides the opportunity to support early career researchers and students in career development. The Institute sponsored the Robinson Research Institute prize for the best presentation in the field of reproduction, pregnancy or child health, awarded to Ellen Potoczky from the Centre for Cancer Biology.

#### North Carolina State **University Collaboration**

The Institute received funding from the Northern Communities Health Foundation and the University's Division of Research to host Prof Randy Jirtle, a Professor of Epigenetics at the Department of Biological Sciences, North Carolina State University. This trip cemented the new research collaboration between the two universities.

Prof Jirtle's pioneering work in epigenetics and genomic imprinting has uncovered a vast territory of new understanding about geneenvironment interactions. In Randy's words, "Epigenetics means that a gene represents less of an inexorable sentence and more of an access point for the environment to modify the genome."





#### **The International Cerebral Palsv Genetics Consortium**

E/Prof Alastair MacLennan, Prof Jozef Gecz and collaborators established the International Cerebral Palsy Genomics Consortium, which seeks to foster collaboration between key, active cerebral palsy genomics groups around the world. Additionally, the group is working towards establishing the world's first genomics database of cerebral palsy.

The first meeting of the group occurred in March 2018 with members traveling to Adelaide from China, Canada, USA, Sweden, Turkey and Spain.

#### **ENDIA Symposium**

The 2018 ENDIA Symposium was held in Adelaide with 72 attendees from across Australia, including clinicians, scientists, research nurses, allied health professionals, software engineers, students and administrators, as well as a consumer and delegate representative from ENDIA's funding partner, JDRF Australia. The group spent two days deciding the strategic direction of ENDIA, reflecting on progress and future developments as they strive for their recruitment target of 1,400 - due to be reached mid-2019.

## Below: AskPCOS App platform.

## DIGITAL DEVELOPMENTS

#### **South Australian Early Childhood Data Project**

The South Australian Early Childhood Data Project (SA ECDP) is one of the most comprehensive population-based administrative research databases in Australia. It spans more than 30 different government administrative data sources spanning health, education, welfare, child protection and housing. It includes every birth cohort of South Australian children born from 1991 onwards, with over 555,000 children and their families included.

Led by Professor John Lynch, this resource informs research, service provision and policy around child health, development and human capability formation from the perinatal period into young adulthood. The SA ECDP has been a platform for a number of research and academic partnerships, including the South Australian Department of the Premier and Cabinet, Child and Family Health Service, SA Health, Department for Education, Department for Child Protection, Women's and Children's Health Network, The Council for the Care of Children, Wardliparingga Aboriginal Research Unit, and the Aboriginal Health Council

Approved researchers from universities and government departments in South Australia have access to the SA ECD platform. Together we work to build and utilise a public-good data resource that supports the best start in life for all South Australian children and enhances health and development through the life course.

#### **Digital Platform for Endometriosis**

More than 700,000 Australian women and girls live with endometriosis, with a delay between onset and diagnosis of 7-12 years. There are major health, education, employment, social and economic consequences for the 1 in 10 women and teenage girls who live with regular, significant and undiagnosed pain.

Together with endometriosis advocacy groups, Jean Hailes for Women's Health, researchers and clinicians around Australia, the RRI is co-developing an online platform to facilitate early diagnosis and improved awareness and outcomes for those living with endometriosis. This resource will apply digital health informatics research techniques to learn from those using the online platform and continually improve understanding on how to increase endometriosis awareness

and reduce time to diagnosis. The online platform will also be a central point for communication and engagement on endometriosis research being implemented through the National Endometriosis Clinical and Scientific Trials Network.

#### AskPCOS App

AskPCOS is the first Polycystic Ovary Syndrome (PCOS) App based on the best available evidence, developed in collaboration with women with PCOS. Prof Rob Norman, Prof Helena Teede and collaborators in the NHMRC CRE for PCOS developed this App to assist women with managing their condition.

AskPCOS includes a range of innovative features: a self-diagnostic quiz, videos by experts and a question prompt-list to take to health care professional appointments.

#### **Your Fertility Web tool**

Together with the Victorian Assisted Reproductive Treatment Authority and Flinders University, the RRI built the Healthy Conception Web Tool. This online platform provides tailored guidance to users based on the input of personal factors including age,

BMI, smoking and alcohol consumption, with the intent of improving their ability to conceive and have a healthy baby

There have been more that 140,000 unique visitors to the web tool over 2.5 years, of whom about 20% actively engaged with the tool. During 2018 the team collated information on usage of the web tool, and how it directed users to relevant information on the Your Fertility site. A paper is scheduled for publication in 2019 to provide base line information on the characteristics of users engaging with the Healthy Conception Tool and their behaviours. It will identify improvements to drive behavioural change and further analyses that could be undertaken.

#### **Cerebral Palsy Bioinformatics Database**

In 2018, E/Prof Alastair MacLennan, Prof Jozef Gecz and collaborators in the Cerebral Palsy Alliance, received ethics approval for the creation of the CP Commons, an international data repository to manage and securely store molecular, experimental, clinical and imaging data for cerebral palsy patients.

Currently under development, the group have sent anonymised clinical and genomics data to its software developers to shape the build. The CP Commons will aggregate data in a computational environment that can support the storage, sharing, querying and analysis of anonymised FAIR data (findable, accessible, interoperable, and reusable). Researchers and clinicians will be able to query the database at a population-level to build new cohorts, or investigate whether other participants within the database share similar phenotypic or genetic features.

#### eMums Plus

eMums Plus is an online, group-based, nurse-led program for new mothers with mild to moderate levels of depression and parenting problems. Developed by Professors Michael Sawyer, John Lynch and Dr Alyssa Sawyer, the program is delivered via a mobile phone app.

Mothers participate in an online group containing 12-15 women with similar-aged infants. A Child and Family Health Service (CaFHS) nurse leads the group and provides assistance and information about maternal depression and parenting problems. Women

Left: Emeritus Professor Alastair MacLennan (team leader), Dr Jimmy Breen, Dr Nandini Sandran, Sayaka Kayumi (Phd student), Dr Nader Aryamanesh, Dr Mark Corbett, Dr Dani Fornarino Professor Jozef Gecz, Kelly Harper, Dr Jesia Berry, Dr Clare van Eyk. Missing from Photo - Dr Luis Alberto Perez Jurado (clinical geneticist) and Dr Suzanna MacLennan (Paediatric Neurologist).



are provided with information and activities designed to reduce symptoms of depression and improve parenting skills.

#### **Genomics Data Repository**

As one of Australia's most research-intensive institutions, we need to be innovative in the way we collect, analyse and collaborate with our research data. The processing of massive datasets through the Genomics Repository and the High Performance Computer is key to achieving this goal and will deliver dividends in research outputs and impact.

Led by Dr Jimmy Breen, and in development phase, the Genomics Repository will have extensive data storage capabilities to enable researchers to store and process data in a timely manner with the assurance of regular data backup. The ability to share datasets within the repository will enhance collaboration across research groups. Bioinformaticians and non-computational researchers will benefit from this critical platform capability that can be utilised without specialist data processing knowledge.

## COMPETITIVE **FUNDING HIGHLIGHTS**

#### NHMRC

**Centre for Research Excellence** commencing in 2018

Prof Maria Makrides, A/Prof Philippa Middleton and team awarded \$2.5 million

Prof Maria Makrides (SAHMRI) awarded a CRE for Targeted nutrition to improve maternal and child health outcomes

#### **Project Grants commencing in 2018**

\$1.46 million to Prof Sarah Robertson *The male partner contribution to pregnancy* immune tolerance deficit in women

\$1.1 million to Prof Ben Mol Prediction and prevention of spontaneous preterm birth: An individual participant data meta-analysis comprising of prognostic and therapeutic data

\$987,047 to A/Prof Leonie Heilbronn Intermittent fasting versus daily energy restriction for improved human health

\$714,792 to Prof Michael Davies Identifying strategies to improve perinatal outcomes after assisted reproduction

\$690,821 to Prof Sarah Robertson Preclinical development of TLR signaling inhibitors for prevention of preterm labour and fetal inflammatory injury

\$562,194 to Prof Michael Davies Why is there an increased risk of severe adverse perinatal outcomes after the use of clomiphene citrate for infertility treatment?

\$536,978 to Prof Ray Rodgers Antioxidant enzymes counter reactive oxygen species from steroidogenic cytochrome P450 enzymes in the ovary to limit aneuploidy of embryos

\$287,316 to Prof Jodie Dodd

The effects of dietary and lifestyle interventions among pregnant women who are overweight or obese on longer-term maternal and early childhood outcomes: an individual participant data meta-analysis

#### **Project Grants awarded in 2018**

\$2.43 million to Prof Jodie Dodd The first 1,000 Days: in-utero and early life exposures and their contribution to child obesity



\$1.1 million to Prof Rebecca Robker A therapy to restore health of gametes from older males and females seeking pregnancy

\$980,692 to Dr Luke Grzeskowiak OPTimising Mothers' Own Milk supply in the neonatal unit – enhancing breast milk supply with Domperidone in mothers of preterm infants (OPTIMOM-D)

\$967,481 to Prof Claire Roberts Targeting micronutrients to tackle pregnancy disorders: an integrated approach?

\$861,345 to A/Prof David Parsons Translating gene-addition treatment for CF lung disease to the clinic

\$870,024 to Prof Jozef Gecz TREX nuclear mRNA export and healthy development

\$600,772 to Prof Darryl Russell Functional non-coding RNAs: New players in oocyte maturation and female fertility

#### ARC

#### **Discovery Projects**

\$490,000 to Prof Sarah Robertson Seminal fluid interferon-gamma: a potential inhibitor of reproductive success;

\$415,000 to Prof Paul Thomas Development of efficient CRISPR gene drives in mice

\$387,884 to Prof Gustavo Carneiro Deep reinforcement learning for discovering and visualising biomarkers

#### AusHealth

Prof Frank Grutzner awarded \$200,000 for Analysis of novel monotreme GLP-1 based receptor agonists for use in the management of metabolic disorders

#### **Channel 7 Children's Research Foundation**

RRI members were awarded seven project grants in 2018, totaling more than \$465,786. This includes \$74,517 to to Prof Megan Warin for Family by Family: Addressing childhood obesity through local understandings and local solutions

#### **CMV Group Foundation**

E/Prof Alastair MacLennan awarded \$90,000 to Facilitate an international cerebral palsy genomic database.

#### **Carina Biotec**

Prof Martin Oehler and Dr Carmela Ricciardelli awarded \$78,134 for Evaluating CAR-T cells on ovarian cancer using ex vivo and in vivo models

#### **Diabetes SA**

Dr Rebecca Thomson awarded \$50,000 for The impact of modifiable exposures in the parent's and child's environment on the risk of type 1 diabetes

#### **Ferring Pharmaceuticals**

Prof Sarah Robertson awarded \$210,000 for Development of novel immune-regulatory agents for boosting Treg cells to improve pregnancy success

#### JDRF Australia, JDRF International and **Helmslev Charitable Trust**

Prof Jennifer Couper awarded \$3.96 million in collaborative research funding to further the ENDIA project – to understand what is causing Type 1 diabetes with the aim of preventing the disease

#### **Ovarian Research Cancer Foundation**

Prof Martin Oehler awarded \$351,354 for two projects: Autoantibody biomarkers for ovarian cancer detection and Study Nurse and Research Assistant for Biospecimen Collection and Maintenance of Databases

#### **Rebecca L Cooper Medical Research Foundation**

Dr Luke Grzeskowiak awarded \$100,000 for Exploring the role of inflammatory mediators in the development and therapeutic management of lactation insufficiency in mothers of preterm infants

#### RIAT Support Centre

**Tenix Foundation and Cerebral Palsy Alliance** 

E/Prof Alastair MacLennan awarded \$900,000 for The genetic origins of cerebral palsy



Prof Jon Jureidini awarded \$USD 150,000 for TADSRIAT: Reanalysis of the most influential study of antidepressants in adolescents

#### The University of Pennsylvania Orphan Disease Center

Dr Nigel Farrow awarded \$73,926 for Airway Cell Therapy for Cystic Fibrosis Nonsense Mutations

#### Women's and Children's Hospital Foundation

RRI members were awarded seven project grants in 2018 totaling \$460,000. This included \$75,000 to Dr Alexia Pena for Does meditation improve quality of life and coping in adolescents with PCOS? A pilot randomised controlled trial

## **FELLOWSHIPS AND AWARDS**

#### **ARC FELLOWSHIPS**

#### **Commencing in 2018**

Postdoctoral Fellowship Dr Gabriel Maicas

#### Awarded in 2018

**Future Fellowship** Prof Mark Hutchinson

#### NHMRC FELLOWSHIPS

#### **Commencing in 2018**

Early Career Fellowships Dr Zohra Lassi, Dr Kisha Sivanathan and Dr Clare Whitehead

#### Awarded in 2018

Senior Principal Research Fellowship Prof Jozef Gecz

**Practitioner Fellowship** Prof Helen Marshall

**Early Career Fellowships** Dr Amy Keir and Dr Merryn Netting

#### **Other Fellowships (awarded 2018)**

#### Australian-Harvard Foundation

Dr Carolyn Berryman was successful in her application for an Australia-Harvard Fellowship to fund the visit of A/Prof Rachael Coakley

#### **CSIRO**

SynBio Fellowship Dr Fatwa Adikusuma

#### Lloyd Cox Fund

**Professorial Research Fellowships** Professors Claire Roberts and Ray Rodgers

**Career Development Fellows** A/Prof Alice Rumbold and Dr Luke Grzeskowiak

#### The University of Adelaide **Beacon Fellowship**

Dr Tanya Zivkovic

#### Japan Society for the Promotion of Science

**Overseas Research Fellowship** Dr Takashi Umehara and Prof Rebecca Robker

#### Women's and Children's Hospital Foundation

**MS McLeod Fellowships** Drs Nigel Farrow and Anna Kontos

PhD Scholarship Katherine Brown

#### **Awards and Prizes**

#### ASPIRE

Prof Rob Norman AO received the ASPIRE Lifetime Achievement Award

#### **Australian Bioinformatics and Computational Biology Society**

Melanie Smith received a CSL Travel Award

#### Australian Federation of University Women SA

Dr Jodie Avery awarded a Postdoctoral Grant; Tahlia Perry received the Graduate Women SA Centenary Bursary

#### **Citizens United for Research in Epilepsy (CURE)**

Prof Jozef Gecz received the CURE Innovator Award

#### Clarivate

Professors John Lynch and Lyle Palmer acknowledged as 2018 Highly Cited Researchers by Clarivate

#### **Professor Jennifer Couper**

Prof Jennifer Couper received the American Diabetes Association Presidents' Select Abstract Award for her contribution to scientific discovery and clinical medicine. She also received the 2018 RRI Director's Award for her outstanding contribution to the Institute

SAHMRI

Oozoa Award Finalist

Superstars of STEM

Shanghai Meeting

**The Heart Foundation** 



#### CUDOS

Dr Megan Penno awarded a poster prize at the Conference on Understanding Molecular Mechanisms in Cardiovascular Biology

#### **DOHaD ANZ Society**

Dr Prabha Andraweera and Michelle Plummer received Nestle Nutrition Institute Travel Grants

#### **Epigenetics Consortium of South Australia**

Melanie Smith received the AGRF People's Choice Award; Dr Dexter Chan received the Best Oral Presentation Award

#### JDRF

Drs Alexia Peña and Megan Penno were accepted into the JDRF Future Research Leaders Program

#### Lorne Genome

Ruby Dawson received the Lorne Genome Conference Student Poster Award

#### PSANZ

Tara Crawford received the Best Abstract Award at the PSANZ Annual Congress in Auckland

#### **SA Science Excellence Awards**

Prof Jozef Gecz was a finalist for the SA Scientist of the Year

Prof Helen Marshall and collaborator's study Meningococcal B Herd Immunity was a finalist for the Excellence in Research Collaboration category

### published in Nature • Highest Altmetric Score Publication of the Year - Dr Jessica Grieger, Dr Luke

associated with time to pregnancy published in Human Reproduction



Prof Paul Thomas received the Publication of the Year Award; Dr Fatwa Adikusuma received the Early Career Researcher Award

#### Society for Reproductive Biology

Dr Alison Care received the Newcastle Reproduction Emerging Research Leader Award: Dr Macarana Gonzalez was an

Dr Sanam Mustafa become a SuperStars of Stem from Science Technology Australia

#### The American Society for **Reproductive Immunology**

Bihong Zhang received the ASRI Best Poster Presentation Award at the 2018

Dr Alison Care received the SA Cardiovascular Research Showcase Poster Prize

#### **The Robinson Research Institute**

• Director's Award - Prof Jenny Couper

• Publication of the Year – Dr Fatwa Adikusuma, Prof Paul Thomas and team for Large deletions induced by Cas9 cleavage

Grzeskowiak, Prof Claire Roberts and team for Pre-pregnancy fast food and fruit intake is

#### The University of Adelaide

- Adelaide Medical School Honours Scholarship – Sabrina Sghirripa
- Adelaide Medical School Senior Research Award - Prof Rebecca Robker
- ARC Centre of Excellence for Nanoscale BioPhotonics Conference Awards -Director's Award: Prof Jeremy Thompson; Best Pitch and Best Student Poster: Vicky Staikopolouis: Best Poster: Tiffany Tan; Best Student 3 Minute Thesis: Florence Lees and Hanna McLennan
- Emerging Leadership Program Dr Kylie Dunning and Dr Jessica Grieger
- FHMS Research Infrastructure Funding Award - Dr Carolyn Berryman
- FHMS Research Travel Awards Dr Prabha Andraweera, Dr Jodie Avery, Dr Angela Gialamas, Dr Zohra Lassi, Prof Helen Marshall, Prof Claire Roberts, Melanie Smith and Qianhui Wan
- Ken Hall Plumbing Prize Holly Groome
- Llewellin and Margaret Davey Bequest Award – Dr Zohra Lassi
- Florey Postgraduate Research Conference, RRI Award for the Best Poster in Reproduction and Pregnancy Research -Ella Green: RRI Award for Best Poster in Child and Adolescent Health Alexandra McCarron
- The Alice Davey Award Dr Alexia Pena
- Women's Research Excellence Awards Dr Tina Bianco-Miotto and Dr Jessica Grieger

## **FINANCIALS 2018**



| NHMRC              | \$7,171,881 | Public Sector<br>Research Income | \$2,545,752 |
|--------------------|-------------|----------------------------------|-------------|
| ARC                | \$1,110,345 | Industry and<br>Philanthrony     | \$6,420,67  |
| Other Australian   | \$2,238,008 | i mantin opy                     |             |
| Competitive Grants |             | CRC Income                       | \$6,91′     |

## **RESEARCH GROUPS**

Our Research Leaders lead a diverse range of groups across the Institute's four themes.

### FERTILITY AND CONCEPTION GROUP LEADERS

#### **Prof Bill Breed** Comparative Reproductive Biology of Mammals

Comparative morphology of gametes and their interaction at fertilisation in Australian mammals

Group Members:

Senior Lecturer: Eleanor Peirce

Lecturer: Natasha Speight Research Officer: Chris Leigh

RRI Collaborators: Michelle Lane, Karen Kind and Nicole McPherson

External Collaborators: Steven Cooper (South Australian Museum), Chris Dickman (University of Sydney), Lawrence Heaney (Field Museum of Natural History) and Kevin Rowe (Museum Victoria)

#### **Prof Frank Grutzner Comparative Genome Biology**

Comparing genetic and epigenetic mechanisms in mammalian species to improve our understanding of how human diseases originate

#### **Group Members:**

Visiting Research Fellow: Dan Kortschak Lecturer: Tasman Daish Postdoctoral Researcher: Linda Shearwin PhD Candidates: Eunice Lee, Filip Paijpach, Tahlia Perry and David Stevens Research Associate: Shee Chee Ong Affiliated Research Fellow: Peggy Rismiller Masters Student: Jifei Huong Honours Students: Natasha Bradley and Praveena Chandrasegaran Casual Student: Isabella Wilson RRI Collaborators: Stefan Hiendleder, Martin Oehler, Carmela Ricciardelli and Darryl Russell

External Collaborators: Peter Donnelly (Oxford University), Briony Forbes (Flinders University), Henrik Kaessman (University of Lausanne), James Turner (Medical Research Council), Wesley Warren (University of Washington) and Guojie Zhang (University of Copenhagen)



#### A/Prof Leonie Heilbronn

**Obesity and Metabolism** 

Does when we eat matter more than what we eat to prevent type 2 diabetes?

**Group Members:** 

Postdoctoral Fellow: Amy Hutchison PhD Candidates: Rajesh Chaudhary, Bo Liu, Prashant Regmi, Xiao Ting Teong and Lijun Zhao

RRI Collaborator: Rebecca Robker



External Collaborators: Luigi Fontana, David James and Mark Larrance (Charles Perkin Centre), John Hawley and Evelyn Parr (Australian Catholic University)

#### **A/Prof Louise Hull**

Endometriosis

Developing diagnostic and therapeutic tools to treat pelvic pain and infertility caused by endometriosis

Group Members:

Gynaecologist and Laparoscopic Surgeon: Susan Evans

PhD Candidate: Kavita Panir

RRI Collaborators: Robert Norman, Sarah Robertson, John Schjenken, David Sharkey and Hannah Brown

External Collaborators: Neil Johnson and Cindy Farquar (University of Auckland) and Guying Nie (Hudson Institute)

#### **Prof Mark Hutchinson**

#### Neuroimmunopharmacology Laboratory

Exploring the real time contributions of the brain immune-like cell signalling at the neuroimmune synapse that contribute to behaviour

**Group Members:** 

Senior ARC Research Fellow: Sanam Mustafa

ARC Research Fellow: Georgios Tsiminis ARC Research Associates: Kelsi Dodds,

Jiajun Liu and Jacob Thomas

NHMRC Fellow: Alexandra Whittaker

Lab Manager: Vicky Staikopoulos

RRI Collaborators: Kylie Dunning, Wendy Ingman, Sarah Robertson and Jeremy Thompson





#### A/Prof Wendy Ingman **Breast Biology and Cancer**

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

#### **Group Members:**

Postdoctoral Researcher: Pallave Dasari

Research Nurse: Michelle Warnes

Research Officer: Leigh Hodson

PhD Candidates: Maddison Archer,

Vahid Atashgaran, Sarah Bernhardt, Amita Ghadge and Joe Wrin

RRI Collaborators: Simon Barry, Luke Grzeskowiak, Louise Hull, Mark Hutchinson, Sarah Robertson and Rebecca Robker

External Collaborators: Kara Britt (Peter MacCallum Institute), John Hopper (The University of Melbourne), Honor Hugo and Erik Thompson (Queensland University of Technology), Tim Price and Amanda Townsend (Queen Elizabeth Hospital), Wendy Rogers (Macquarie University) and Jennifer Stone (The University of Western Australia)

#### **Prof Rob Norman AO Reproductive and Endocrine Medicine**

Optimising outcomes in fertility treatments and preconception care

#### **Group Members:**

Senior Research Associate: Jodie Avery RRI Collaborators: Louise Hull, Alexia Pena, Rebecca Robker and Ray Rodgers

External Collaborators: Adam Balen (Leeds Teaching Hospital), Michael Barry and Ryan Rose (Fertility SA),

Jacqueline Boyle, Ben Mol and Helena Teede (Monash University), Roger Hart (The University of Western Australia), Martha Hickey (Melbourne University), Manh Tuong Ho and Lan Vuong (University of Ho Chi Minh), Joop Lavern (Rotterdam University), Rick Legro (Penn State University), Rong Li and Jie Qiao (Beijing University) and Zephne van der Spuy (Cape Town University)

#### A/Prof Mark Nottle **Reproductive Biotechnology**

Innovative approaches to regenerative medicine and human IVF

#### **Group Members:**

Research Fellow: Ivan Vassilev PhD Candidates: Gabriele Heruc, Zoe Kopsaftis and Anmol Saini

Research Assistant: Stephen McIlfatrick RRI Collaborators: Toby Coates, Stefan

Hiendleder, Michelle Lane and Jeremy Thompson

External Collaborators: Peter Cowan (St Vincents Hospital), Wayne Hawthorne (Westmead Millennium Institute), Andrew Lew (WEHI) and Johan Smitz (Free University of Brussels)

#### Dr Carmela Ricciardelli and **Prof Martin Oehler Reproductive Cancers**

Identification of novel biomarkers and therapeutic targets for ovarian cancer

#### **Group Members:**

Senior Scientist: Anne MacPherson Postdoctoral Researcher: Noor Lokman

PhD Candidates: Tannith Marie Nove and Zoe Price Honours Students: Hayley Chapman,

Janelle Cheung and Wanqi Wang Research Assistant: Anita Oehler

Visiting PhD Candidate: Masato Yoshihara RRI Collaborators: Frank Grutzner, Ray Rodgers and Darryl Russell

External Collaborators: Taran Andrei (University of Tubingen), Peter Hoffman (University of Adelaide), Stuart Pitson and Wang Shudong (University of South Australia) and Andrew Ruszkiewicz (SA Pathology)

#### **Prof Sarah Robertson Reproductive Immunology**

Understanding how the immune system enables healthy conception and pregnancy and is key in infertility and inflammatory disorders of pregnancy, including preeclampsia, fetal growth restriction and preterm birth

#### **Group Members:**

Postdoctoral Research Fellows: Alison Care and Kerri Diener

Senior Postdoctoral Researchers: Lachlan Moldenhauer and David Sharkey

Postdoctoral Researchers: Peck Chin and John Schjenken

PhD Candidates: Hon Yeung Chan, Ella Green, Holly Groome, Kavita Panir and Bihong Zhang

Honours Students: Jacqueline Humphries, Ricky Matias, Sebastian Overduin and Kavita Shah

Research Officer : Camilla Dorian

Research Assistant: Bridget Arman

RRI Collaborators: Simon Barry, Gus Dekker, Louise Hull, Mark Hutchinson, Wendy Ingman, Michelle Lane, Claire Roberts, Rebecca Robker and Jeremy Thompson

External Collaborators: Sylvain Chemtob (University of Montreal), Pat Holt, Jeff Keelan and Deb Strickland (University of Western Australia), David Olson (University of Alberta), Jelmer Prins (University Medical Center, Groningen), Kenner Rice (NIH Washington) and Kelton Tremellen (Repromed)



#### **Prof Rebecca Robker**

Discovering the biological mechanisms that drive ovulation and early embryo development

#### **Group Members:**

Postdoctoral Researcher: Sonja Frolich PhD Candidates: Macarena Bermudez Gonzalez, Yasmyn Gordon and David Kennedy

Research Assistant: Haley Connaughton

RRI Collaborators: Leonie Heilbronn, Michelle Lane, Robert Norman, Darryl Russell, Cheryl Shoubridge and Michael Stark

External Collaborators: Michael Barry and Ryan Rose (Fertility SA), John Carroll and Damian Dowling (Monash University), Mark Febbraio (Garvan Institute), Jon Hennebold (Oregan National Primate Institute), Jie Qiao (Peking University) and Teresa Woodruff (Northwestern University)

#### **Prof Ray Rodgers Ovarian Developmental Biology**

Understanding how the ovary produces oocytes and hormones, what can go wrong and why

#### Group Members:

Postdoctoral Researcher: Katja Hummitzsch PhD Candidates: Nicole Bastian, Katrina Copping, Monica Hartanti and Menghe Liu

Research Assistant: Wendy Bonner

RRI Collaborators: Michael Davies, Michelle Lane, Sarah Robertson and Darryl Russell

External Collaborators: Richard Anderson (University of Edinburgh), Ross Bathgate and John Wade (Howard Florey Institute), Hugh Harris (University of Adelaide), Helen Irving-Rodgers (Griffith University), Phil Knight (University of Reading), Lisa Martin and Dagmar Wilhelm (Monash University), Elizabeth New (The University of Sydney), Viv Perry (University of Nottingham) and William Rainey (University of Michigan)

#### **Prof Darrvi Russell Ovarian and Reproductive Cancer Cell Biology**

Defining the molecular mechanisms of hormone control of ovarian folluculogenesis

#### Group Members:

Research Fellow: Alaknanda Alaknanda PhD Candidate: Doan Thao Dinh

Masters Student: Minnu Jayapal RRI Collaborators: Simon Barry, Frank Grutzner, Michelle Lane, Carmela Ricciardelli, Claire Roberts, Sarah Robertson, Rebecca Robker, Ray

Rodgers and Jeremy Thompson

External Collaborators: Juan Carlos Rodriguez-Maneque (Genyo), Robert Gilchrist (University of New South Wales) and John Sandy (Rush University)









**Ovarian Cell Biology** 

#### **Prof Paul Thomas**

#### Neural Development

Generation and analysis of mouse models for epilepsy and intellectual disability

#### Group Members:

Postdoctoral Research Fellow: Fatwa Adikusuma, Alvaro Nieto and Stefka Tasheva

PhD Candidates: Ruby Moffat, Chandran Pfitzner, Louise Robertson and Ella Thomson

Research Assistants: Sandie Piltz and Melissa White

RRI Collaborator: Jozef Gecz

External Collaborator: Robin Lovell-Badge (Francis Crick Institute)

#### **Prof Jeremy Thompson**

#### **Early Development**

Understanding the impact of metabolic disruption to gametes, embryos and the reproductive tract

#### **Group Members:**

Postdoctoral Researchers: Hannah Brown and Kylie Dunning

PhD Candidates: Madeline Batsiokis, Megan Lim, Hanna McLennan, Tiffany Cheow and Suliman Yagoub

Masters of Science Candidate: Avishkar Saini

Manager IVF Solutions: Marie Ellul

Honours Students: Carl Campugan and Darren Chow

Research Assistant: Annie Whitty

Technical Officer: Anwar Fatoi

Visiting Students: Sandra Soto Heras, Clara Smonteiro and Gabi Vetleal

RRI Collaborators: Michael Davies, Louise Hull, Michell Lane, Mark Nottle, Sarah Robertson, Rebecca Robker and Darryl Russell

External Collaborators: Andrew Abell, Hayley McGrice and Yvonne Stokes (University of Adelaide), Michael Barry, Rob Norman and Ryan Rose (Fertility SA), Jose Burantini (Universidade Estadual Paul), Pablo Certica (Uni Buenos Aires), Michel DeVos and Johan Smitz (Vrije Universiteit Brussell), David Gardner and Mark Green (University of Melbourne), Brant Gibson, Andrew Greentree and Antony Orth (RMIT), Rob Gilchrist (University of New South Wales), Ewa Goldys and Nicole Packer (Macquarie University), Jen Kelly and Alan Tilbrook (SARDI), David Mottershead (Mottasis Review), Simon Walton (Australian Reproductive Technologies) and Deidre Zander-Fox (Repromed)





### **PREGNANCY AND BIRTH GROUP LEADERS**

#### Dr Jimmy Breen

**Bioinformatics and Computational Biology** Identifying new analysis techniques for biological datasets

Group Members:

PhD Candidates: Ning Liu and Melanie Smith

Research Assistant: Jacqueline Rehn RRI Collaborators: Simon Barry and

Claire Roberts

External Collaborators: Alistair Forrest (Harry Perkins Institute for Medical Research) and Kate Sanders (University of Adelaide)

#### Prof Jodie Dodd

Lifelong Health Research

Start early, stay healthy, stop obesity
Group Members:
Clinical Researchers: Chad Andersen

and Andrew McPhee

Senior Statistician: Lisa Yelland Statistician: Jennie Louise

Clinical Trials Manager: Andrea Deussen

Data Manager: Sasha Zhang

Research Coordinator: Angela Newman

PhD Candidates: Cecelia O'Brien, Casey Nottage and Amanda Poprzecny

Research Assistants: Ashlee Jacobssen, Lavern Kannieappan and

Caroline Sheppard

RRI Collaborators: Jenny Couper, Lynne Giles, Vivienne Moore and Jeffrev Robinson

External Collaborators: Annick Bogaerts (Limberg Catholic University), Karen Campbell, Rachel Laws and Julie Owens (Deakin University), Emma Carlsen, Nina Geiker and Kristina Renault (University of Copenhagen), Roland Devlieger (University Hospital Keuven), Jan Dickinson (King Edward Memorial Hospital), Adrienne Gordon (University of Sydney), Rosalie Grivell (Flinders University), Catherine Hovo (North Carolina State University), Mark Kilby (Birmingham Women's Hospital), John Kingdom, Greg Ryan and Rory Windrim (Mt Sinai Hospital), Berthold Koletzko (Ludwig-Maximilans University), Debbie Lawlor (Bristol University), Ritta Luoto (UKK Institute), Fionnula McAuliffe (University College Dublin), Dorte Moller (Odense University Hospital), Lisa Moran (Monash University), Susan Phelan (California Polytechnic State University), Lucilla Poston (King's College London), Phil Robinson (Women's and Children's Hospital), Richard Saffery (Murdoch Research Institute), Wendy Scheil (SA Pregnancy Outcomes Unit), Danielle Schoenaker (University of Wollongong), Mette Tanvig and Christina Vinter (University of Southern Denmark), Shakila Thangaratinam (QMUL) and Liliana Voto (Juan A Fernandez Hospital)

#### Prof Bill Hague Obstetric Medicine

Improving outcomes for pregnant women with medical complications

#### **Group Members:**

Research Coordinator: Suzette Coat Postdoctoral Research Assistant: Mansi Singh

PhD Candidate: Jago McDonald Van Dam

Research Assistants: Jacqui Aikens,

Mansi Dass Singh, Joanne Koch, Ann Kren, Angela Llewellyn and Jessica Marathe

RRI Collaborators: Jenny Couper, Jodie Dodd, Ben Mol, Julie Owens and Julia Pitcher

External Collaborators: Hanneke de Vries (Free University Hospital), Michael Fenech (CSIRO), Anand Hardikar (University of Sydney), Laura Magee (University of British Columbia), Marc Rodger, Mark Walker and Shi-Wu Wen (University of Ottawa), Janet Rowan (Auckland Hospital), David Simmons (University of Western Sydney) and Catherine Williamson (King's College London)

#### **Prof Stefan Hiendleder** Epigenetics and Genetics

Understanding epigenetic and genetic mechanisms and programming in prenatal development

#### Group Members:

Postdoctoral Researcher: Dana Thomsen PhD Candidates: Hanh Nguyen and

Entesar Shuaib RRI Collaborators: Kathy Gatford, David Kennaway, Karen Kind, Mark Nottle and Claire Roberts

External Collaborators: Daniela Bebbere and Sergio Ledda (University of Sassari), Amanda Chamberlain and Vicki Clifton (Mater Research Institute), Mike Goddard and Ruidong Xiang (University of Melbourne), Axel Janke (Biodiversity and Climate Research Centre), Julie Owens (Deakin University) Tim Smith (USDA), Susanne Ulbrich (ETH Zurich), John Williams (University of Adelaide) and Eckhard Wolf (Gene Center)



#### E/Prof Alastair MacLennan AO and Prof Jozef Gecz Cerebral Palsy

Uncovering the genetic causes of cerebral palsy and understanding the epigenetic interaction with genetic susceptibility

#### Group Members:

Clinical Geneticist: Pérez-Jurado Postdoctoral Fellow: Mark Corbett Postdoctoral Researchers: Clare Van Eyk

and Chenglong Yu Bioinformatician: Jimmy Breen

Data Manager: Jesia Berry

PhD Candidate: Sayaka Kayumi

Research Officers: Kelly Harper and Dani Webber

Summer Student: Ryan Pham

RRI Collaborators: Lynne Giles, Lyle Palmer and Cheryl Shoubridge

External Collaborators: Nadia Badawi (The University of Sydney), Gareth Baynam (Genetic Services of Western Australia), Hilla Ben-Pazi (Shaare Zedek Medical Center), Michael Fahey (Monash Medical Centre), Darcy Fehlings (University of Toronto), Sheng Jin (Yale University), Michael Kruer (Barrow Neurological Institute), Manju Kurian (Institute of Child Health), Richard Leventer (Murdoch Children's Research Institute), Sarah McIntyre (Cerebral Palsy Alliance Research Institute), Andres Moreno-De-Luca (Autism and Developmental Medicine Institute), Carlos Santos Ocaña (CIBERER\_ ISCII and University Pablo de Olavide), Xiaoyang Wang (University of Gothenburg), Richard Wintle (The Hospital for Sick Children) and Changlian Zhu (Third Affiliated Hospital of Zhengzhou University)

#### A/Prof Philippa Middleton Health of Women and Babies

Improving the care of women and babies through evidence-based clinical practice and policy

**Group Members:** 

External Collaborators: Caroline Crowther









#### Prof Claire Roberts and Prof Gus Dekker Placental Development

Identifying risk factors and implementing screening tests to understand and alleviate major pregnancy complications

**Group Members:** 

Research Fellow: Luke Grzeskowiak Senior Lecturer: Tina Bianco-Miotto

Postdoctoral Researchers: Natalie Aboustate, Prabha Andraweera, Jessica Grieger, Tanja Jankovic-Karasoulos, Shalem Leemaqz and Dale McAnich

Research Midwife: Samantha Pahl PhD Candidates: Emily Aldridge, Konstantinos Bogias, Julia Dalton, Amy Garrett, Nahal Habibi, Catherine McCormack, Martha Menberu, Maleesa Pathirana, Michelle Plummer, Melanie Smith, Qianhui Wan and Rebecca Wilson Visiting Postdoctoral Researcher:

Visiting Postdoctoral Researcher: Callista Mulder

Visiting PhD Candidate: Petra Verburg Research Assistant: Dylan McCullough



Honours Student: Erica Langley

RRI Collaborators: Kathy Gatford, John Lynch, Helen Marshall, Ben Mol, Sarah Robertson, Michael Sawyer and Michael Stark

External Collaborators: Lisa Amir (La Trobe University), Vicki Clifton (Mater Research Institute), Rosalie Grivell (Flinders University), Louise Kenny (University College Cork), Lesley McCowan (University of Auckland) and Alicia Smith (Emory University)

### **EARLY ORIGINS OF HEALTH GROUP LEADERS**

#### **Prof Michael Davies** and Prof Vivienne Moore Life Course and Intergenerational Health

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

#### **Group Members:**

Senior Postdoctoral Researcher: Melissa Whitrow

Postdoctoral Researchers: Stephanie Champion and Renae Fernandez

Teaching and Research Academic: Lynne Giles

Project and Data Manager: Anthea Hutchison

PhD Candidates: Ash Borqkvist, Tassia Oswald, Anna Roesler and Rachelle Warner RRI Collaborators: Alice Rumbold, Darryl Russell and Megan Warin

External Collaborators: Sheree Boulet

(Emory University), Bianca deStavola (University College London), Dmitry Kissin (Centers for Disease Control), Jennifer Marino (University of Melbourne), Lisa Moran and Helena Teede (Monash University), Mark Walker and Shi-Wu Wen (University of Ottawa)

#### **Dr Kathy Gatford** Early Origins of Health and Disease

Understanding how early life exposures increase risk of adult disease and developing interventions to improve longterm health

#### **Group Members:**

PhD Candidates: Harleen Kaur and Hong Liu

Honours Student: Kate Highfield

RRI Collaborators: Alison Care, Lynne Giles, David Kennaway, Karen Kind, Helen Marshall, Julie Owens, Claire Roberts, Jeffrey Robinson and Tamara Varcoe

External Collaborators - Robert Bischof and Tim Moss (Hudson Institute of Medical Research), Vicki Clifton (Mater Medical Research Institute), David Kleemann (SARDI), Janna Morrison (University of South Australia), Beverley Muhlhausler (CSIRO), Amanda Page (SAHMRI), Rebecca Simmons (University of Pennsylvania), Will van Wettere (University of Adelaide) and Megan Wallace (Monash Institute)

#### **Prof David Kennaway Circadian Physiology**

Understanding how circadian rhythms regulate metabolism, reproduction and fetal programming of disease

#### **Group Members:**

Research Fellow: Tamara Varcoe

Research Officer: Mark Salkeld Honours Student: Kate Highfield

RRI Collaborator: Kathy Gatford

External Collaborators: David Kleemann and Tim Kuchel (SAHMRI), Leon Lack (Flinders University), Glenn McConnell (Victoria University) and Shantha Rajartnam (Monash University)

#### **Prof Lyle Palmer Machine Learning in Medicine**

Applying artificial intelligence to healthcare, combining: deep learning, medical image analysis, genomics, genetic epidemiology, statistics, clinical research and translation

#### **Group Members:**

Professor of Computer Science: Gustavo Carneiro

Statistical Analyst: Kelly Hall

Postdoctoral Fellow: Gabriel Maicas

PhD Candidates: James Condon, Renato Hermoza Aragones, Alice Krige, Hossein Lyarjdameh, Luke Oakden-Rainer and Khan Pham

Honours Students: Tristan Bampton and Denghao Wu

Technology), Enrico Coiera (Macquarie University), Jamie Craig and Sutapa Mukherjee (Flinders University), Chris Hahn and Hamish Scott (SA Pathology), David Hillman (University of Western Australia), Elina Hypponen (University of South Australia) and Johan Verjens (SAHMRI)



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

#### Group Members:

Research Fellows: Carolyn Berryman and Mitchell Goldsworthy

PhD Candidate: Jago McDonald Van Dam

Research Assistant: Lynton Graetz

Honours Student: Sabrina Sghirripa RRI Collaborators: Jodie Dodd, Bill Hague and Michael Stark

External Collaborators: Femke Buisman-Pijlman (University of Adelaide), Angela Clow (University of Westminster), Paul Fitzgerald (Monash University), Lorimer Moseley (University of South Australia)





#### **A/Prof Alice Rumbold Equity and Healthy Futures**

Improving the lifelong health of women and children by reducing inequality in disadvantaged families

#### Group Members:

Arusyak Sevoyan

NHMRC Early Career Research Fellow Zohra Lassi

Lloyd Cox Career Development Fellow: Jodie Avery Senior Research Associate:

PhD Candidate: Jessica Dawson, Sophie Kedzior and Tassia Oswald Administrative Assistant: Courtney Hammond

RRI Collaborators: Michael Davies, Luke Grzeskowiak, Philippa Middleton, Vivienne Moore, Lisa Moran, Robert Norman and Megan Warin

External Collaborators: Zulfigar Bhutta (Sick Kids Toronto), Jacqueline Boyle and Helana Teede (Monash University), Stephanie Brown (Murdoch Children's Research Institute), Dominic Guerrera and Gabbie Zizzo (Aboriginal Health Council of SA), John Kaldor (Kirby Institute) and Renae Kirkham (Menzies School of Health Research)







RRI Collaborator: Toby Coates, Jozef Gecz and John Lynch

External Collaborators: Andrew Bradley (Queensland University







#### **A/Prof Michael Stark** Neonatal Medicine

#### Ensuring life-long health for newborns

born preterm

#### **Group Members:**

Clinical Researchers: Chad Anderson and Andrew McPhee

Consultant Neonatologist: Amy Keir

PhD Candidates: Megan Bater, Tara Crawford and Kathryn Martinello

Honours Student: Vinay Athreya



RRI Collaborators: Michael Davies, Bill Hague, Anna Kontos and Rebecca Robker

External Collaborators: Carmel Collins and Maria Makrides (SAHMRI), Haresh Kirpalani (Children's Hospital of Philadelphia), Barbera Lingwood (University of Queensland) and Ben Mol (Monash University)

#### **Prof Megan Warin**

#### **Biosocial Approaches to Health**

Examining the biological and social processes that are entangled in the gendered reproduction of bodies, families and environments.

#### **Group Members:**

Senior Postdoctoral Researcher: Tanya Zivkovic

Researcher: Lucy Farrell

RRI Collaborators: Michael Davies and Vivienne Moore

External Collaborators: Paul Bissell (Sheffield Institute for International Development), Emma Kowall and Maurizio Meloni (Deakin University), Jane Maree Maher (Monash University), Ian Olver (The University of Adelaide), Paul Ward and Carlene Wilson (Flinders University)



### **CHILD AND ADOLESCENT HEALTH GROUP LEADERS**

oso

#### **Prof Simon Barry** Molecular Immunology

Understanding the molecular basis for immune tolerance

#### **Group Members:**

Postdoctoral Research Fellows: Cheryl Brown and Timothy Sadlon Postdoctoral Researchers: Veronika Bandara and Chris Hope Research Assistants: Nicole Craig,

Batjargal Gundsambuu and Silvana Napoli PhD Candidates: Ying Ying Wong and Soon Wei Wong

Honours Student: Katherine Brown

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

External Collaborators: Marc Beyer and Joachim Schultze (LIMES), Dan Campbell and Thomas Duhen (Benorya), Greg Goodall (Centre for Cancer Biology), Shane Grey, Chris Goodnow and John Sprent (Garvan Institute), Randall Grose (SAHMRI), Kazu Kikuchi (Victor Chang Institute), Giovanna Lombardi and Tim Tree (King's College London), Kelli MacDonald (QIMR), Raymond Steptoe (Diamantia Institute) and Kathryn Wood (Oxford University)

#### **Prof Jennifer Couper** Diabetes

Preventing type 1 diabetes and its complications

#### **Group Members:**

| *                                                                          | ALC / POINT   |
|----------------------------------------------------------------------------|---------------|
| Clinical Partner: Alexia Pena                                              | 6 6           |
| Clinical Researcher: Pyria Augustine                                       |               |
| Project Managers: Megan Penno and<br>Rebecca Thomson                       |               |
| Research Dietitian: Rachel Battersby                                       |               |
| Research Nurses: Sarah Beresford, Alison<br>Gwiazainski and Meredith Krieg |               |
| Engagement Officer: Kelly McGorm                                           |               |
| Research Officers: Roger Gent, Dao Huyn                                    | h and Ben Ram |
| Senior Administration Assistant: Leanne Ca                                 | avenett       |
| PhD Candidate: Jessica Harbison                                            |               |
| Masters Student: Myff Gever                                                |               |

RRI Collaborators: Simon Barry, Jodie Dodd, Lynne Giles and Claire Roberts

External Collaborators: Peter Colman and John Wentworth (Royal Hospital Melbourne), Maria Craig and William Rawlinson (University of New South Wales), Jayne Danska (University of Toronto), Elizabeth Davies and Aveni Haynes (Telethon Kid's Institute), Emma Hamilton-Williams (University of Queensland), Mark Harris (Mater Health Service), Len Harrison and Tony Papenfuss (Walter and Eliza Hall Institute), Grant Morahan (Harry Perkins Institute), Richard Sinnott (The University of Melbourne), Georgia Soldatos (Monash Health) and Peter Vuillermin (Deakin University)

#### **Prof Antonio Ferrante Developmental and Genetic Immu**

Cellular signalling pathways in childhood allergy and inflammatory disorders

#### **Group Members:**

Paediatric Immunologist: Jovanka King

Pathologist: Tatijana Banovic Principal Scientist: Charles Hii

Senior Scientists: Nick Gorgani and

Alex Quach

PhD Candidates: Marwah Basin Khalah, Nikki Lansdown, Khalida Perveen, David Shields and Annabelle Small

Masters in Laboratory Medicine: Yen-Wei Chang, Hans Huang, Jasbir Kaur, Raxhael Pei-Jui, Ling Chen Liu and Suthan Muraleethasan Placements: Nancy Azzolini and Ling Chen Liu

RRI Collaborators: Simon Barry, Jennifer Couper, Jozef Gecz, Michael Gold, Declan Kennedy, Anna Kontos, Andrew McPhee and Patrick Quinn External Collaborators: Catherine Abbott (Flinders University), Sharon Choo (Royal Children's Hospital), Lennart Hammarstrom (Karolinska Institute), Peter Hofmann (University of Adelaide), Suresh Mahaligam (Griffith University), Susan Prescott (University of Western Australia), Susanna Proudman (Royal Adelaide Hospital) and Harald Renz (Phillips University)

### **Prof Jozef Gecz**

Investigating the genetics and biology of

#### **Group Members:**

Clinical Geneticist: Luis Perez-Jurado

Research Fellow: Atma Ivancevic

Postdoctoral Fellows: Mark Corbett and Lachlan Jolly

Postdoctoral Researcher: Claire Van Eyk

Research Officers: Sarah Heron, Duyen Pham, Raman Sharma and Dani Webber

PhD Candidates: Rebekah De Nys, Deepti Domingo, Sayaka Kayumi, Kristy Kolc and Debrah Renders

Research Assistants: Renee Carroll, Alison Gardner, Bree Hodgson, Brett Johnson, Thessa Kroes, Urwah Nawaz, Renee Schulz and Marie Shaw

Cheryl Shoubridge

Gareth Baynam (Genetic Services of Western Australia), Hilla Ben-Pazi (Shaare Zedek Medical Center), Michael Fahey (Monash Medical Centre), Darcy Fehlings (University of Toronto), Sheng Jin (Yale University), Michael Kruer (Barrow Neurological Institute), Manju Kurian (Institute of Child Health), Richard Leventer (Murdoch Children's Research Institute), Sarah McIntyre (Cerebral Palsy Alliance Research Institute), Andres Moreno-De-Luca (Autism and Developmental Medicine Institute), Carlos Santos Ocaña (CIBERER ISCII and University Pablo de Olavide), Xiaoyang Wang (University of Gothenburg), Richard Wintle (The Hospital for Sick Children) and Changlian Zhu (Third Affiliated Hospital of Zhengzhou University)

#### **Group Members:**

Associate Professor: Lisa Smithers

Senior Lecturer: Catherine Chittleborough

Postdoctoral Researchers: Angela Gialamas, Dandara Haag, Catia Malvaso, Rhiannon Pilkington, Alyssa Sawyer and Helena Schuch

#### Statistician: Murthy Mittinty

Research Associates: Janet Grant, Alicia Montgomerie and Alexandra Procter RRI Collaborators: Gus Dekker, Ben Mol, Claire Roberts, Michael Sawyer and Josephine Telfer

External Collaborators: Aluisio Barros (University Pelotas), Tony Blakely (University Otago), Deborah Cobb-Clark and Stelfi Schurer (University of Sydney), George Davey Smith and Neil Davies (University of Bristol), Pernille Due (Danish National Public Health Institute), Kathleen Falster and Louisa Jorm (University of New South Wales), Belinda Gabbe (Monash University), Steve Guthridge and Sven Silburn (Menzies Institute), Rosemary Korda (Australian National University), Catherine Law (Institute of Child Health) and Anna Pearce (University of Glasgow)

#### **Prof Jon Jureidini Critical and Ethical Mental Health**

Promoting safe, effective and ethical research and practice in mental health

Group Members:

**Prof Declan Kennedy** 

disorders and their effect on child

Director, Pulmonary Medicine:

Medical Scientist: Anna Kontos

Sleep Disorders

development

Iames Martin

Group Members:

Policy: Kurt Lushington

Postdoctoral Fellow: Melissa Raven Affiliate Senior Lecturers: Catalin Tufunaru and John Walsh PhD Candidate: Julie Klau

External Collaborators: Lisa Bero, Quinn

Grundy, Barbara Mintzes and Lisa Parler

(University of Sydney), Lisa Cosgrove (University of Massachusetts),

Peter Doshi (University of Maryland), Sammi Timmi (Lincoln

University) and Martin Whitely (Curtin University)







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### **Neurogenetics**

human neurodevelopmental disabilities

RRI Collaborators: Lynne Giles, Alastair MacLennan, Lyle Palmer and

External Collaborators: Nadia Badawi (The University of Sydney),



Sleep Lab Manager: Yvonne Pamula External Collaborators: Mathias Baumert and Scott Willoughby (University of Adelaide), Roger Gent and Melissa La Forgia (Women's and Children's Hospital), Quenten Schwarz (University of South Australia)







#### **Prof Helen Marshall**

#### Vaccines and Infectious Diseases

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

#### **Group Members:**

Clinical Researchers: Sue Evans and Suja Mathew

Visiting Research Fellow: Jacqueline Stephens

Research Manager: Michelle Clarke



Research Nurses: Louise Goodchild, Christine Heath and Mary Walker Research Coordinators: Su-san Lee, Mark McMillan, Kathryn Riley and Philippa Rokkas

PhD Candidates: Jane Tuckerman and Bing Wang

Masters Student: Marianne Yanni

Honours Students: Hassen Mohammed and Brianna Morello

Administrative Assistant: Manasa Arani Krishna

RRI Collaborators: Simon Barry, Gus Dekker, Jodie Dodd, Lynn Giles, Michael Gold, John Lynch, Andy McPhee, Ben Mol and Claire Roberts

External Collaborators: Ross Andrews (Menzies Research), Ray Borrow and Shamez Lantanti (Public Health England), Margie Danchin (Murdoch Children's Research Centre), Adam Finn (University of Bristol), Ann Koehler (SA Health), Stephen Lambert (Queensland Children's Medical Research Institute), Andrew Lawrence (SA Pathology), David Lynn and Steve Wesselingh (SAHMRI), Kristine Macartney and Nicholas Wood (University of Sydney), Martin Maiden, Jenny McLennan, Andy Pollard and Matthew Snape (University of Oxford) and Peter Richmond (University of Western Australia)

#### **A/Prof David Parsons** and Dr Martin Donnellev **Cystic Fibrosis**

Development and testing of genetic therapies for treating and preventing cystic fibrosis lung disease

#### **Group Members:**

Postdoctoral Researchers: Patricia Cmielewski, Juliette Delhove, Nigel Farrow, Chantelle McIntyre, Nathan Rout-Pitt and Freda Werdiger

PhD Candidates: Mark Gardner, Ryan Green, Ali McCarron, Harsha Padmanabhan and Thomas Goddard

Honours Student: Chantelle Carpentieri

Research Officer: Nikki Reyne

Administrative Assistant: Bernadette Boog

RRI Collaborators: Jimmy Breen, Emma Knight and Paul Thomas

External Collaborators: Ivan Bertoncello (Melbourne University), Susan Birket



(University of Alabama), Ric Boucher (University of North Carolina), John Finnie (SA Pathology), Uta Griesenbach (Imperial College), Adam Jaffe (University of New South Wales), Albert Juhasz and Ivan Lee (University of South Australia), Marcus Kitchen and Kaye Morgan (Monash University), Tim Kuchel (SAHMRI), Guy Maddern and Robert McLaughlin (University of Adelaide), Ivanka Prichard (Flinders University) and Graeme Zosky (University of Tasmania)

#### **Prof Michael Sawyer Child and Adolescent Mental Health**

Developing and evaluating populationlevel interventions for the health and wellbeing of mothers and children

#### **Group Members:**

Postdoctoral Researcher: Alyssa Sawyer Senior Project Officer: Jennifer Clark

Research Officers: Amy Kaim and Christy Reece

RRI Collaborator: John Lynch

External Collaborators: Harriet Hiscock and Tony Jorm (University of Melbourne) and David Lawrence (University of Western Australia)

#### A/Prof Cheryl Shoubridge **Intellectual Disability Research**

Defining molecular and cellular pathways for intellectual disability and seizures, and developing effective interventions

#### **Group Members:**

Postdoctoral Researchers: Matilda Jackson and Tessa Mattiske

PhD Candidate: Karagh Loring Research Assistant: Monica Thai

RRI Collaborators: Jozef Gecz, Claire Roberts and Rebecca Robker

#### **A/Prof Lisa Smithers** Paediatric and Perinatal Epidemiology

Understanding how early life events can influence later health and development.

**Group Members:** 

Lecturer: Wendy Cheung

PhD Candidates: Mumtaz Begum, Engida Derbie, Cherise Fletcher, Addya Gupta, Davi Macedo, Pedro Ribeiro Santiago and Molla Wassie

Honours Students: Anna Kalamkarian, Luke Spaiic and Xinvue Wang

RRI Collaborators: Cathy Chittleborough, Gus Dekker, Jessica Grieger, Luke Grzeskowiak, Dandara Haag, John Lynch, Murthy Mittinty, Rhiannon Pilkington and Claire Roberts

External Collaborators: Sohinee Bhattacharya (University of Aberdeen), Annette Braunack-Mayer (University of Wollongong), Tess Gregory (Telethon Kids Institute), Elizabeth Hoon, Lisa Jamieson, Matthew Sorrell and Jo Zhou (The University of Adelaide) and Ben Mol (Monash University)





## **INVESTING IN OUR MEMBERS**

#### **Core Facilities**

#### Adelaide Research Assay Facility (ARAF)

Led by Professor David Kennaway

The Adelaide Research Assay Facility provides specialised, high-throughput and high-sensitivity assays of physiologically important analytes for academic researchers and commercial customers Australia-wide.

#### **Bioinformatics Facility**

Led by Dr Jimmy Breen

Bioinformatics enhances the Institute's capability in next-generation sequencing and 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 powerful tools to investigating systems and processes in biology and disease.

#### **Biostatistics Facility**

Led by Dr Emma Knight The Biostatistics Facility is a collaborative research service that provides expertise

#### **Cohort and Intergenerational Studies Facility (CIS)**

Led by Professor Claire Roberts

The Cohort and Intergenerational Studies Facility underpins the strategic utilisation of unique Adelaide generated 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 data sharing between studies.



Past and present Early and Mid-Career Researcher Council Members. Luke Grzeskowiak, Duyen Pham, Jimmy Breen, Nathan Rout-Pitt, Carolyn Berryman, Jodie Avery, Alison Care, Tara Crawford, Amy Garrett, Martin Donnelley and Megan Penno.

in research design and statistical analysis. Statisticians advise researchers on appropriate study design and conduct, undertake statistical analysis and report on research findings.

#### Gene Silencing and Expression Facility (GSEx)

Led by Jason Gummow

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, adenovirus and retroviral vectors, and stock viruses for purchase by the microlitre.

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

#### **Funding programs**

#### **Designed for Success**

After the success of the pilot year, *Designed for Success* ran again in 2018. This program improves the scientific quality and significance of grant applications through the facilitated development of research projects over an extended period, including structured project development in set stages and significant external review.

Six research teams benefited from this intensive program in 2018, with results to be announced in 2019.

#### **Engaging Opportunities**

Engaging Opportunities supports the development of new relationships with key stakeholders to jointly address research priorities; sharing identification and ownership of the problem being addressed, and the path to understanding and progressing a solution.

Collaboration with groups such as health consumers, clinicians, business, industry, government and not-for-profits leads to more robust and relevant research projects, quicker development of solutions, and more effective translation of discoveries. This program resulted in the development of four new collaborative projects, including Prof Helen Marshall's project: *Protection against* gonorrhea with a meningococcal B vaccine; is it achievable?

#### **Investment for Success**

This program increases competitiveness for NHMRC funding by developing highly competitive (but as yet unfunded) project grant applications, into more competitive applications for subsequent submission. Support serves to enable proof-of-concept studies, experiments or analysis, rapid publication of a pivotal paper, or to increase scientific quality, significance and innovation.

In 2018, four projects were funded, with two participants going on to achieve NHMRC project grant funding:

- Prof Claire Roberts: Interactions between micronutrients, obesity, metabolic health and pregnancy outcome
- Prof Darryl Russell: Functional non-coding RNAs: New players in oocyte maturation and female fertility

#### Innovation Seed Funding

This program supports early and mid-career researchers to collaborate across research groups and themes to explore novel research questions. This program harnesses and progresses new ideas towards competitive, fundable research that addresses significant knowledge gaps.

Six collaborative projects were supported in 2018, bringing together 26 members and external collaborators.

#### **Travel Grants**

Supporting researchers to 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 important networking with peers, and the opportunity to develop future collaborations.

In 2018 the Institute awarded 17 travel grants to research staff and students to attend conferences, training workshops, and meetings with research partners, funders and key collaborators.

#### Visiting Speakers

The Visiting Speakers program enables external research leaders to visit the Institute and encourages collaboration between institutions, providing insight and new perspectives on our research priorities. Visitors present a seminar to the RRI and meet with relevant researchers to discuss research ideas. In 2018, the RRI hosted 12 visiting speakers:

• Dr David Dorman, North Carolina State University

- A/Prof Deshayne Fell, University of Ottawa
- Dr Emanuele Pelosi, The University of Queensland
  Prof Jeffrey Keelan, The University of Western Australia
- Prof Jus St John, Hudson Institute of Medical Research
- Prof Karen Moritz, The University of Queensland
- Dr Lisa Nicholas, University of Cambridge
- Dr Quentin Pittman, University of Calgary
- Prof Randy Jirtle, North Carolina State University
- Dr Shamez Ladhani, Public Health England
- Susanne Bendz, Cooper Surgical Origio
- Will Siero, Murdoch Children's Research Institute

Nancy Jirtle, Randy Jirtle, Michael Davies, Sarah Robertson and Claire Roberts

#### **Exchange Program**

The Exchange Program builds collaborations with international researchers to increase research capacity and facilitate access to international funding, databases and expertise. It achieves this by funding RRI members to spend time with collaborators overseas, as well as funding international collaborators to spend time with the Institute in Adelaide.

#### **Mentoring Program**

This program seeks to strengthen networks, build relationships, develop career pathways and enhance resumes, providing mutual benefit for both the mentee and mentor. In 2018 the Early and Mid-Career Researcher Council ran the program for students and early and mid-career researchers seeking a mentor.

An introductory workshop was held to ensure mentees maximised the opportunity and were prepared when meeting their mentors. In 2018, nine mentees were matched with a senior researcher by the EMCR Council.

#### **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 into prestigious journals that attract an international, interdisciplinary audience. It provides heightened credibility and esteem to our research achievements.

In 2018 five members received funding for their high impact publications.

#### Workshops

#### **EMCR Masterclasses**

Prof Mary Wlodek (University of Melbourne) ran Early and Mid-Career Researcher masterclasses, tailored for the career stage of participants. These sessions focused on developing effective strategies for career development, including how to build your CV, networking, developing effective collaborations, time management, work-life balance, and general tips and tricks for becoming a well-rounded researcher.

#### **Health Consumer Drop-in Session**

The RRI held an informal 'drop-in session' where members spoke with health consumers about their grant proposals. This session was held in collaboration with the Women's and Children's Health Network and provided invaluable external perspectives, with many members re-shaping areas of their grant proposals in response to feedback received.

#### **Researcher Q&A**

Members of the RRI's Early and Mid-Career Researcher Council hosted a *Researcher Career Q&A* in August where an expert panel including Prof Mark Hutchinson, Prof Rachel Burton and Dr Zoe Doubleday spoke openly about their careers, and answered questions from EMCRs across the Institute.

### **2018 FELLOWSHIPS AND SCHOLARSHIPS**



#### **Career Development Fellowship**

This fellowship funds the salary of 'Emerging Star' early career researchers for one year, supporting their career development to enable competitiveness for an NHMRC Career Development Fellowship or similar. In 2018 the fellowship was awarded to: Dr Luke Grzeskowiak to

progress his research: Guiding safe and effective use of medications in pregnancy and lactation to improve maternal, newborn and child health outcomes.



#### **Jeffrey Robinson Honours Scholarship**

Each year the Institute awards the *Jeffrey Robinson Honours Scholarship* to a top performing student, who commences honours under the supervision of a RRI Member. This scholarship is named after Emeritus Professor Jeffrey Robinson CBE, for whom the Institute is named after.

In 2018, the Institute awarded the *Jeffrey Robinson Honours* Scholarship to Vinay Athreya, to undertake the honours project The Frank-Starling relationship in very preterm newborns.



#### **Repromed Reproductive Health Scholarship**

The Institute partnered with Repromed in 2016 to establish the *Repromed Reproductive Health Scholarship*. This scholarship is awarded to a top student completing their honours year under the supervision of a RRI Member. Repromed are a South Australian fertility treatment company

offering a complete range of fertility treatments and options. The 2018 recipient of this scholarship was Casidhe Goldsworthy who completed her project: *The Effect of Embryo Biopsy on Embryo Health*, under the supervision of Prof Michelle Lane, Dr Deirdre Zander-Fox, and Dr Leanne Pacella-Ince.

#### **Summer Research Scholarships**

During the 2018/2019 break, the Institute funded two Summer Scholarships. These positions provide an insight into a research career and seek to encourage undergraduate students to consider postgraduate study.

The 2018/19 recipients were:

- Evangeline Lovell *The effect of regulatory T cell deficiency on early placental development.* Supervised by Dr Alison Care
- Jacqueline Scaffidi *Identification and quantification* of *Treg subsets in pancreatic islet cell transplant patients*. Supervised by A/Prof Toby Coates

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#### **Professional Staff**

Box, Ruth Eley, Sarah Goddard, Marcus Kenny, Ashleigh

## **REPRESENTATIVE PUBLICATIONS**

## The following 50 publications (out of a total of 483 peer-reviewed primary papers, reviews and book chapters) illustrate the scope and impact of our research outputs in 2018.

The full list of publications can be found at adelaide.edu.au/robinson-researchinstitute/research/publications.

1. Adikusuma, F., Piltz, S., Corbett, M., Turvey, M., McColl, S., Helbig, K., Beard, M., Hughes, J., Pomerantz, R., & Thomas, P. (2018). Large deletions induced by Cas9 cleavage. *Nature*, 560(7717), E8-E9.

2. Anderson, J., Couper, J., Toome, S., Mpundu-Kaambwa, C., Giles, L., Gent, R., Coppin, B., & Peña, A. (2018). Dietary sodium intake relates to vascular health in children with type 1 diabetes. *Pediatric Diabetes*, 19(1), 138-142.

**3.** Boulet, S., Kawwass, J., Crawford, S., Davies, M., & Kissin, D. (2018). Preterm Birth and Small-for-Gestational Age in Singleton In Vitro Fertilization Births Using Donor Oocytes. *American Journal of Epidemiology*, 187(8), 1642-1650.

4. Brennan, L., Broekmans, F., Dabadghao, P., Devoto, L., Dewailly, D., Downes, L., Fauser, B., Franks, S., Garad, R., Gibson-Helm, M., Harrison, C., Hart, R., Hawkes, R., Hirschberg, A., Hoeger, K., Hohmann, F., Hutchison, S., Joham, A., Johnson, L., Jordan, C., Kulkarni, J., Legro, R., Li, R., Lujan, M., Malhotra, J., Mansfield, D., Marsh, K., McAllister, V., Mocanu, E., Mol, B., Ng, E., Oberfield, S., Ottey, S., Peña, A., Qiao, J., Redman, L., Rodgers, R., Rombauts, L., Romualdi, D., Shah, D., Speight, I., Spritzer, P., Stener-Victorin, E., Stepto, N., Tapanainen, J., Tassone, E., Thangaratinam, S., Thondan, M., Tzeng, C., Van Der Spuy, Z., Vanky, E., Vogiatzi, M., Wan, A., Wijeyaratne, C., Witchel, S., Woolcock, J., & Yildiz, B. (2018). Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. Human Reproduction, 33(9), 1602-1618.

5. Brown, C., Dayan, S., Wong, S., Kaczmarek, A., Hope, C., Pederson, S., Arnet, V., Goodall, G., Russell, D., Sadlon, T., & Barry, S. (2018). FOXP3 and miR-155 cooperate to control the invasive potential of human breast cancer cells by down regulating ZEB2 independently of ZEB1. *Oncotarget*, 9(45), 27708-27727.

6. Brown, H., Green, E., Tan, T., Gonzalez, M., Rumbold, A., Hull, M., Norman, R., Packer, N., Robertson, S., & Thompson, J. (2018). Periconception onset diabetes is associated with embryopathy and fetal growth retardation, reproductive tract hyperglycosylation and impaired immune adaptation to pregnancy. *Scientific Reports*, 8(1), 2113-2114.

7. Care, A. S., Bourque, S. L., Morton, J. S., Hjartarson, E. P., Robertson, S. A., & Davidge, S. T. (2018). Reduction in regulatory T cells in early pregnancy causes uterine artery dysfunction in mice. *Hypertension*, 72(1), 177-187.

8. Choi, J., Jeong, Y., Kim, S., Lee, B., Ariyasiri, K., Kim, H., Jung, S., Hwang, K., Choi, T., Park, C., Huh, W., Carl, M., Rosenfeld, J., Raskin, S., Ma, A., Gecz, J., Kim, H., Kim, J., Shin, H., Park, D., Gerlai, R., Jamieson, B., Kim, J., Iremonger, K., Lee, S., Shin, H., & Kim, C. (2018). Targeted knockout of a chemokine-like gene increases anxiety and fear responses. *Proceedings of the National Academy of Sciences of the United States of America*, 115(5), 1041-1050.

**9.** Chong, S.Y., Chittleborough, C. R., Gregory, T., Lynch, J., Mittinty, M., & Smithers, L. G. (2018). The controlled direct effect of temperament at 2-3 years on cognitive and academic outcomes at 6-7 years. *BioRxiv*, 410506.

10. Couper, J., Haller, M., Greenbaum, C., Ziegler, A., Wherrett, D., Knip, M., & Craig, M. (2018). ISPAD Clinical Practice Consensus Guidelines 2018: Stages of type 1 diabetes in children and adolescents. *Pediatric Diabetes*, 19, 20-27.

11. Cutland, C., Nolan, T., Halperin, S., Kurugol, Z., Ahmed, K., Perrett, K., Richmond, P., Marshall, H., Ceyhan, M., Kolhe, D., Hezareh, M., & Van Der Wielen, M. (2018). Immunogenicity and safety of one or two doses of the quadrivalent meningococcal vaccine MenACWY-TT given alone or with the 13-valent pneumococcal conjugate vaccine in toddlers: A phase III, open-label, randomised study. *Vaccine*, 36(14), 1908-1916.

**12.** Dalton, J., Rodger, D., Wilmore, M., Humphreys, A., Skuse, A., Roberts, C., & Clifton, V. (2018). The Health-e Babies App for antenatal education: feasibility for socially disadvantaged women. *PLOS ONE*, 13(5), 0194318-0194337.

**13.** Davies, M. J., & Rumbold, A. R. (2018). Measuring Trends in Infant Mortality Due to Unintentional Suffocation. *JAMA Pediatrics*, 172(9), 886-887.

14. Dodd, J., Grivell, R., Deussen, A., & Hague, W. (2018). Metformin for women who are overweight or obese during pregnancy for improving maternal and infant outcomes. *Cochrane Database of Systematic Reviews*, 2018(7).

**15.** Duby, J., Lassi, Z., & Bhutta, Z. (2018). Community-based antibiotic delivery for possible serious bacterial infections in neonates in low- and middle-income countries. *Cochrane Database of Systematic Reviews*, 2018(1). 16. Farrow, N., Donnelley, M., Cmielewski, P., Roscioli, E., Rout-Pitt, N., McIntyre, C., Bertoncello, I., & Parsons, D. (2018). Role of basal cells in producing persistent lentivirusmediated airway gene expression. *Human Gene Therapy*, 29(6), 653-662.

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20. Grieger, J., Grzeskowiak, L., Bianco-Miotto, T., Jankovic-Karasoulos, T., Moran, L., Wilson, R., Leemaqz, S., Poston, L., McCowan, L., Kenny, L., Myers, J., Walker, J., Norman, R., Dekker, G., & Roberts, C. (2018). Pre-pregnancy fast food and fruit intake is associated with time to pregnancy. *Human Reproduction*, 33(6), 1063-1070.

21. Grzeskowiak, L., Smithers, L., Amir, L., & Grivell, R. (2018). Domperidone for increasing breast milk volume in mothers expressing breast milk for their preterm infants: a systematic review and meta-analysis. *BJOG: An International Journal of Obstetrics and Gynaecology*, 125(11), 1371-1378.

22. Kakoly, N., Khomami, M., Joham, A., Cooray, S., Misso, M., Norman, R., Harrison, C., Ranasinha, S., Teede, H., & Moran, L. (2018). Ethnicity, obesity and the prevalence of impaired glucose tolerance and type 2 diabetes in PCOS: a systematic review and meta-regression. *Human Reproduction Update*, 24(4), 455-467.

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26. Lynch, J., Werder, R., Loh, Z., Sikder, M., Curren, B., Zhang, V., Rogers, M., Lane, K., Simpson, J., Mazzone, S., Spann, K., Hayball, J., Diener, K., Everard, M., Blyth, C., Forstner, C., Dennis, P., Murtaza, N., Morrison, M., Cuív, P., Zhang, P., Haque, A., Hill, G., Sly, P., Upham, J., & Phipps, S. (2018). Plasmacytoid dendritic cells protect from viral bronchiolitis and asthma through semaphorin 4a-mediated T reg expansion. *Journal of Experimental Medicine*, 215(2), 537-557.

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**28.** Marshall, H., & Plotkin, S. (2018). The changing epidemiology of mumps in a high vaccination era. *The Lancet Infectious Diseases*, 19(2), 118-119.

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**30.** Mattiske, T., Tan, M., Dearsley, O., Cloosterman, D., Hii, C., Gécz, J., & Shoubridge, C. (2018). Regulating transcriptional activity by phosphorylation: a new mechanism for the ARX homeodomain transcription factor. *PLOS ONE*, 13(11), 1-24.

**31.** Mincham, K. T., Scott, N. M., Lauzon-Joset, J. F., Leffler, J., Larcombe, A. N., Stumbles, P. A., Robertson, S. A., Pasquali, C., Holt, P. G., & Strickland, D. H. (2018). Transplacental immune modulation with a bacterial-derived agent protects against allergic airway inflammation. *The Journal of Clinical Investigation*, 128(11), 4856-4869.

**32.** Mukaro, V., Quach, A., Gahan, M., Boog, B., Gao, X., Huang, Z., Haddad, C., Mahalingam, S., Hii, C., & Ferrante, A. (2018). Small tumor necrosis factor receptor biologics inhibit the tumor necrosis factor-p38 signalling axis and inflammation. *Nature Communications*, 9(1), 1313-1365.

**33.** Murray, C., Callender, C., Kulikoff, X., Srinivasan, V., Abate, D., Abate, K., Abay, S., Abbasi, N., Abbastabar, H., Abdela, J., Abdelalim, A., Abdel-Rahman, O., Abdi, A., Abdoli, N., Abdollahpour, I., Abdulkader,

R., Abebe, H., Abebe, M., Abebe, Z., Abebo, T., Abejie, A., Aboyans, V., Abraha, H., Abreu, D., Abrham, A., Abu-Raddad, L., Abu-Rmeileh, N., Accrombessi, M., Acharya, P., Adamu, A., Adebayo, O., Adedeji, I., Adekanmbi, V., Adetokunboh, O., Adhena, B., Adhikari, T., Adib, M., Adou, A., Adsuar, J., Afarideh, M., Afshin, A., Agarwal, G., Agesa, K., Aghayan, S., Agrawal, S., Ahmadi, A., Ahmadi, M., Ahmed, M., Ahmed, S., Aichour, A., Aichour, I., Aichour, M., Akanda, A., Akbari, M., Akibu, M., Akinyemi, R., Akinyemiju, T., Akseer, N., Alahdab, F., Al-Aly, Z., Alam, K., Alebel, A., Aleman, A., Alene, K., Al-Evadhy, A., Ali, R., Alijanzadeh, M., Alizadeh-Navaei, R., Aljunid, S., Alkerwi, A., Alla, F., Allebeck, P., Almasi, A., Alonso, J., Al-Raddadi, R., Alsharif, U., Altirkawi, K., Alvis-Guzman, N., Amare, A., Ammar, W., Anber, N., Andrei, C., Androudi, S., Animut, M., Ansari, H., Ansha, M., Antonio, C., Appiah, S., Aremu, O., Areri, H., Arian, N., Ärnlöv, J., Artaman, A., Arval, K., Asavesh, H., Asfaw, E., Asgedom, S., Assadi, R., Atey, T., & Atique, S. et al. (2018). Population and fertility by age and sex for 195 countries and territories, 1950–2017: a systematic analysis for the Global Burden of Disease Study 2017. The Lancet, 392(10159), 1995-2051.

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**36.** Panir, K., Schjenken, J. E., Robertson, S. A., & Hull, M. L. (2018). Non-coding RNAs in endometriosis: a narrative review. *Human Reproduction Update*, 24(4), 497-515.

**37.** Peirce, E., McLennan, H., Tuke, J., Leigh, C., & Breed, W. (2018). Evolution of the testis and spermatozoon in mice and rats (Subfamily Murinae) in the absence of sperm competition. *Journal of Zoology*, 306(1), 58-68.

**38.** Pels, A., Mol, B., Singer, J., Lee, T., Von Dadelszen, P., Ganzevoort, W., Asztalos, E., Magee, L., Gafni, A., Gruslin, A., Helewa, M., Hutton, E., Lee, S., Logan, A., Menzies, J., Moutquin, J., Murphy, K., Rey, E., Ross, S., Sanchez, J., Thornton, J., Welch, R., Hoac, T., Kirton, J., Trigiani, K., Zahid, A., Bracken, M., Crowley, P., Duley, L., Ehrenkranz, R., Thorpe, K., Chan, S., Shi, M., Yu, S., Martin, R., Bassi, M., Clara Caruso, M., Lagunas, V., Vera, F., De Duhalde, M., Roque, A., Roldan, P., Duhalde, E., Dip, V., Aguirre, J., Alicia Morales, E., Abreo, G., De Sagastizabal, T., Gomez, C., Rizzi, N., Arias, C., Bruno, R., Mahomed, K., Drew, A., Green, A., Hoare, J., Hague, B., Coat, S., Crowther, C., Muller, P., Trenowden, S., Walters, B., Parker, C., Graham, D., Pennell, C., Sung, E., Makris, A., Lee, G., Thornton, C., Hennessy, A., Farrell, L., Sass, N., Korkes, H., Ferreira, D., Moreira De Sa, R., Marques Abreu, M., Bornia, R., Da Silva, N., Oliveira Cardoso, F., Marques, C., Hornos, J., Davdt, R., Paula, L., Zanella, P., Inglis, G., Dillon, R., Docherty, A., Hutfield, A., Still, K., Lalji, S., Van Tent, T., Hotz, C., Messmer, T., Ray, J., Berger, H., De Souza, L., Lausman, A., Freire-Lizama, T., & Besel, K. (2018). Influence of gestational age at initiation of antihypertensive therapy: Secondary analysis of CHIPS trial data (control of hypertension in pregnancy study). Hypertension, 71(6), 1170-1177.

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