

SUMMER 2018

HUDSON NEWS

**World-first
trial helping
premature
babies**



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Director's message

Professor Elizabeth Hartland



At Hudson Institute, one of our biggest priorities is nurturing future research leaders and encouraging our scientists to develop their research careers.

I'm delighted that a number of our emerging leaders have been recognised by the National Health and Medical Research Council (NHMRC), Australia's foremost medical research funding body, in the latest competitive grants and fellowships round.

Congratulations to Dr Rebecca Lim, Dr Jaclyn Pearson, Dr Samuel Forster and Associate Professor Flora Wong, who were awarded Career Development Fellowships, and Early Career Fellowship recipient Dr Vanesa Stojanovska.

This is recognition of their hard work, dedication and contribution to their field, as well as the calibre of their research. Crucially, these fellowships provide the support and momentum to develop their independent research careers.

Three of these 'scientists to watch' are featured in this edition of Hudson News.

You can read about Dr Lim's first-in-human clinical trial of a placental cell treatment for preterm lung disease (pages 3 and 7), Dr Forster's discovery of a 'bladder microbiome' (page 8) and Dr Jaclyn Pearson's path to success in science (page 6).

Fielding Foundation support

We need emerging scientists to foster new ideas and ensure the future of medical research, yet the path to success in medical research for young researchers is often uncertain.

Gaps in the career ladder can leave scientists establishing their careers vulnerable to leaving the profession

altogether. We know this is especially important for women in science.

We aim to provide strong pathways for our scientists to reach their full potential in science, and vital support from the Fielding Foundation has helped to cement these opportunities for six of our scientists over the past three years.

In 2015, the inaugural Fielding Foundation Fellowship was awarded to Dr Rebecca Lim to progress her research into clinical trials for preterm baby lung disease. This year, Dr Lim published these results, paving the way for a Phase II trial to prevent lung disease in at-risk premature babies. Without the support of the Fielding Foundation in those crucial early years, this life-saving work could not have progressed to reach patients.

We are extremely grateful to Fielding Foundation Chairman, Mr Peter Fielding, for his foresight and generosity in creating the Fellowship in 2015 to support early career researchers to establish their work and progress lifesaving medical research.

In 2018, the Fielding Foundation Fellowship was awarded to women's health researcher Dr Jemma Evans. You can read about Dr Evans' research in improving fertility outcomes for women, and how nutrition could play a role, on page 4.

Finally, thank you for your support over the past 12 months. I hope that you enjoy a safe and relaxing festive season with family and loved ones.

We look forward to sharing more life-changing research with you in 2019.

Best wishes

Professor Elizabeth Hartland
Director and CEO

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World-first trial helping premature babies



Flynn Minieri, now 19 months, who was part of the trial and Dr Rebecca Lim

A world-first therapy, using cells from the human placenta to repair the damaged lungs of premature babies, is giving hope to families of the most fragile infants like Flynn Minieri.

Flynn was born unexpectedly and extremely premature at just 25 weeks, weighing 990 grams. Like many babies born too early, he developed the chronic lung disease bronchopulmonary dysplasia (BPD) as a result of the lifesaving respiratory support he was on.

With parents John and Kirsty Minieri's consent, Flynn took part in a world-first safety trial, run by a team of scientists and clinicians at Hudson Institute, Monash University and the Monash Children's Hospital.

"There is no doubt that when Flynn was in hospital, he benefitted from treatments that were trialled on other babies, because of the brave decisions those parents made to take part in medical research," John and Kirsty said. "We wanted to pass that hope on to other families."

Now 19 months old, their 'little fighter' Flynn is a happy toddler, and he's slowly needing his home oxygen support less and less.

10 years of research

This first-in-human trial is the culmination of 10 years' research by a multidisciplinary team including Dr Rebecca Lim, Dr Atul Malhotra and Professor Euan Wallace. The results

were published in the journal *STEM CELLS Translational Medicine*.

"BPD is a devastating disease, and these babies often suffer severe and life-long conditions. When we tackle lung disease, the risk of developing many other life-long problems that go hand-in-hand with BPD, such as cerebral palsy, is also reduced," Dr Rebecca Lim, joint lead researcher, said.

"This is the first step towards a therapy for very vulnerable premature infants who currently have no other effective treatment."

Six premature babies with BPD were given a single low dose of amniotic

epithelial cells in the safety trial. These cells come from part of the placenta that surrounds the baby during pregnancy, and work by attaching themselves to damaged lungs and kick-starting the lung's own repair process.

The results were excellent, showing donor cells are well-tolerated and safe for use in babies, with some premature babies even showing a slight improvement.

The team is now starting a larger Phase II trial involving 24 extremely premature babies at risk of developing BPD to determine the optimum cell dosage and frequency.

Continued on page 7

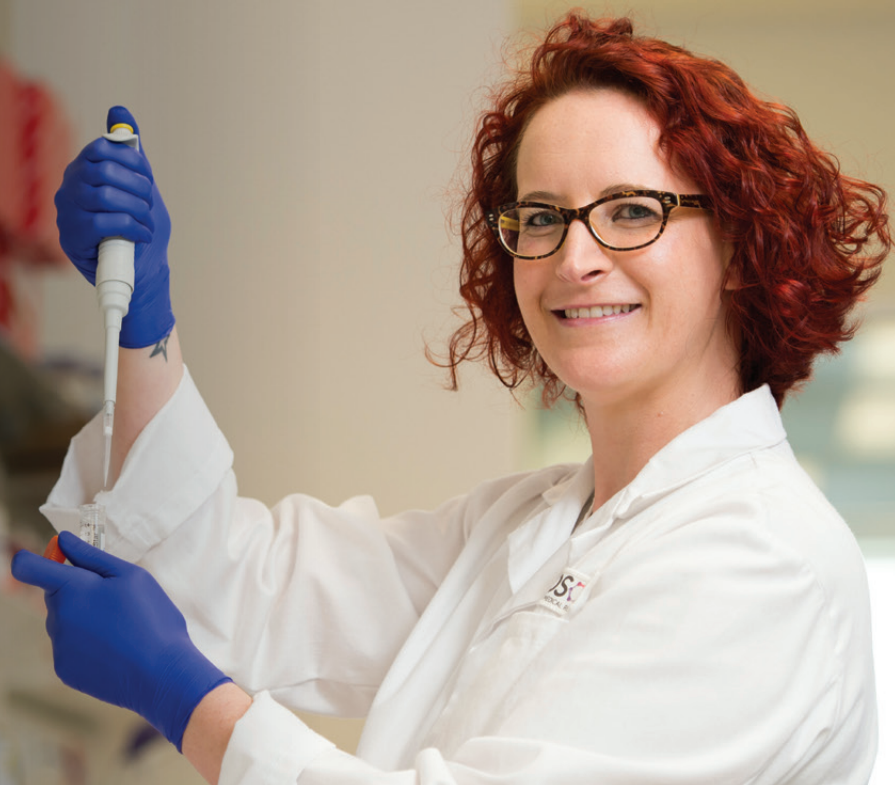
BPD FACTS

- Bronchopulmonary dysplasia (BPD) is the most common disease affecting premature babies. Up to 60 per cent of extremely premature babies will develop BPD.
- The smaller the baby, the greater the risk and the greater the severity of the disease.
- Babies with BPD may suffer severe lifelong complications, including impaired neurodevelopment, and are highly susceptible to airway infections that may lead to death.
- BPD affects the alveoli, the tiny sacs in the lungs that enable the entry of oxygen into the bloodstream and the clearance of carbon dioxide from the body.
- BPD occurs when immature newborn or premature lungs are exposed to mechanical ventilation and long-term use of oxygen. While life-saving, this breathing support can also cause damage to tiny developing lungs.
- There is currently no cure or safe and effective treatment for BPD.

What are amnion epithelial cells?

An amniotic epithelial cell is a stem-like cell extracted from the lining of the inner membrane of the placenta. They have ability to grow into any cell in the body, in a similar way to stem cells. Each placenta produces about 150-200 million amnion cells.

How sugary, fried and processed foods could affect female fertility



Dr Jemma Evans

We all know about the importance of maintaining a healthy maternal diet to ensure the health and development of the baby during pregnancy.

What is now becoming increasingly clear is that a woman's nutrition and diet prior to conception can also play an important role in fertility and pregnancy health.

A study led by Dr Jemma Evans has demonstrated how toxic proteins – produced in the body after consumption of sugary foods and found in browned and highly processed foods – may alter the environment in the womb and directly impact fertility.

The study, published in the journal *Human Reproduction*, looked at the effects of advanced glycation end products (AGEs) on the womb.

AGEs are formed when proteins in the body are exposed to high sugar levels. They can also be consumed by eating foods that are highly processed or cooked at high heat – for example, frying, grilling, caramelising or roasting – which changes certain proteins, causing them to become highly toxic.

"We analysed samples from the wombs of women with obesity, who generally have elevated levels of AGEs in the body as a whole and are more prone to infertility and pregnancy complications," Dr Evans said.

For the first time, the team demonstrated that levels of AGEs in these women were

elevated specifically within the womb where they triggered inflammation, making it more difficult for an embryo to implant and therefore reducing the likelihood of a pregnancy.

"We discovered that these toxic 'by-products' alter the cells in the lining of the womb," Dr Evans said. "They also interfere with placental development, which may contribute to pregnancy complications."

A simple change to boost fertility

AGE levels can be reduced using a drug or a highly controlled diet. A low-AGE diet has been shown to improve health outcomes in other diseases, such as insulin resistance in diabetes, in as little as four weeks, but it has never before been tested in infertility.

Dr Evans is planning a clinical trial of a simple eight-week dietary intervention aimed at reducing levels of toxic factors in the womb, to help more women fall pregnant and have healthier pregnancies.

Dr Evans said the womb is more likely to respond to a short-term intervention because, unlike the heart, kidneys or liver, the endometrium completely regenerates itself every 28 days.

"If successful, this simple dietary intervention may become a more holistic way to improve fertility and potentially avoid the need for costly measures such as IVF," Dr Evans said.

FACTS

Advanced glycation end products (AGEs) are compounds which are formed when proteins, lipids or nucleic acids change during exposure to sugar.

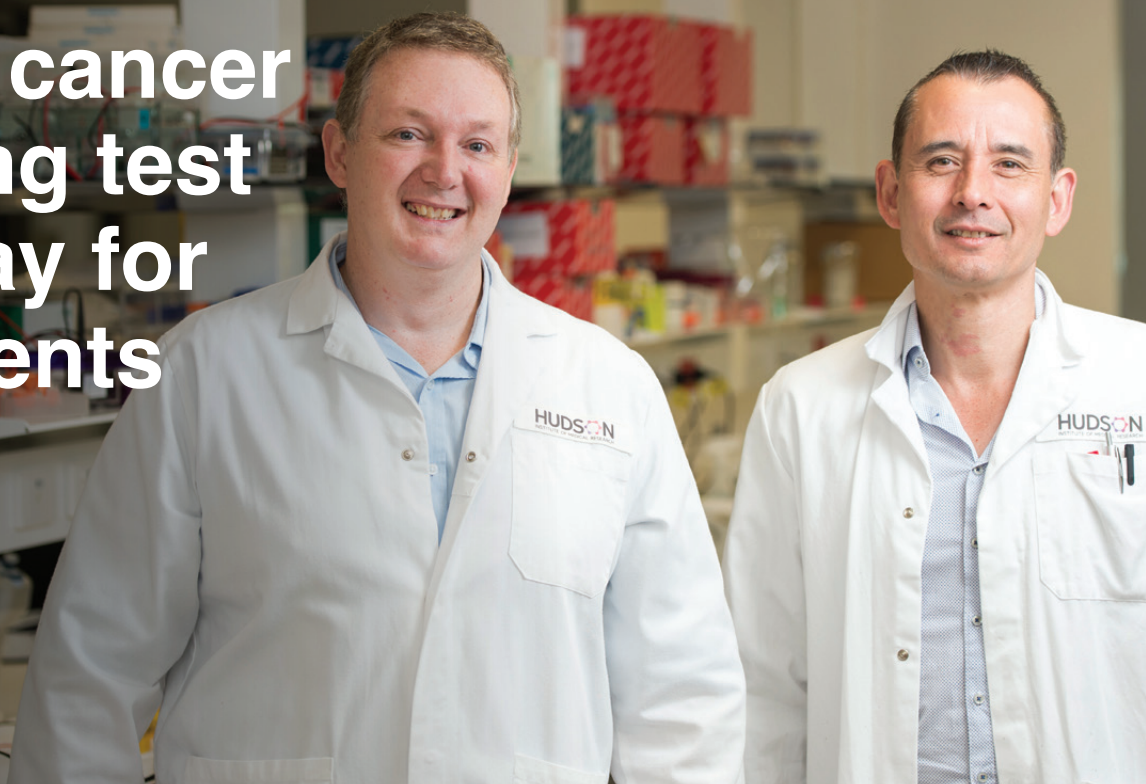
The pool of AGEs found in the human body can either be formed naturally within the body, or accumulate through dietary exposure to certain foods or beverages.

AGEs are formed in foods by heat-processing such as frying, grilling, caramelising or roasting (examples include browned meat or toast). Highly processed foods have a high content of AGEs.

Preclinical studies suggest that otherwise healthy proteins in the body can react with sugars (such as those consumed in foods or beverages) to form AGEs within the body.

AGEs are known contributors to oxidative stress and inflammation and have been linked to the recent epidemics of diabetes and cardiovascular disease.

Ovarian cancer screening test underway for 300 patients



L-R: Dr Andrew Stephens and Dr Simon Chu

Ovarian cancer is responsible for more deaths than any other gynaecological disease, yet it's known as the 'silent killer', due to an absence of symptoms and a devastatingly low survival rate of less than 50 per cent.

Unlike a mammogram for breast cancer, or a cervical screening test for cervical cancer, there is no early detection test for all types of ovarian cancer.

Ovarian cancer often comes without symptoms, while some women experience bloating, abdominal pain, fatigue or loss of appetite – all of which may be attributed to other conditions. Sadly, this means that ovarian cancer is often not detected until the advanced stages.

But there is hope on the horizon. Dr Andrew Stephens and his team are starting a trial of an early screening test, thanks to generous funding from the Ovarian Cancer Research Foundation (OCRF).

The three-year trial will involve around 300 at-risk women who have BRCA1 or BRCA2 gene mutations, to test whether a method developed by Dr Stephens' team in the laboratory to detect the most common type of ovarian cancer is also able to detect small or pre-cancerous lesions in women.

"Our 'Active Ratio Test' measures changes in a key immune process, to give an indication of the presence of a growing tumour," Dr Stephens said.

"We are excited about the potential for the test to detect the cancer when it is still confined to the ovary and at its most treatable. Ultimately we want to get the test into a routine screening program as a regular health check for women."

Combating chemotherapy resistance

For women whose ovarian cancer is detected at a later stage, or those women who experience recurrent disease, new treatments are needed to ensure that they survive for longer and have the best possible quality of life.

Dr Simon Chu and his team are working to improve treatment for a rare hormone-driven type of ovarian cancer, known as granulosa cell tumours (GCT).

Chemotherapy is initially effective at treating ovarian cancer in many women, but there is a high recurrence rate and often these aggressive tumours resurface up to 20 years later.

Dr Chu's team is working on a 'double hit' by combining an anti-diabetic drug with an anti-cancer drug targeting a protein known as XIAP, which drives GCT growth.

"This study could fundamentally change the way we treat GCT through a targeted approach," Dr Chu said.

"As these two drugs are already in clinical or pre-clinical use for other diseases, we are optimistic we could more quickly move these drugs from a testing phase into the treatment of ovarian cancer."

OVARIAN CANCER FACTS

- Ovarian cancer is the deadliest gynaecological disease.
- Every year, more than 1600 Australian women are diagnosed with the disease and it claims the lives of more than 1000.
- It is known as 'silent killer' because early stage ovarian cancer can have few symptoms.
- The disease is often not detected until the advanced stages when it has spread beyond the ovaries.
- The five-year survival rate is a devastatingly low 45 per cent.





Researcher spotlight Dr Jaclyn Pearson

What is your field of medical research?

I am a microbiologist by training and have an interest in understanding how gut bacteria such as *E. coli* and *Salmonella* cause disease.

Infections with these bacteria cause hundreds of millions of cases of severe gastrointestinal disease worldwide each year, resulting in at least 200,000 deaths, particularly in malnourished children.

An important part of my research is to understand the specific immune responses the body mounts to fight infections with these bacteria. By understanding these immune responses, we can aid the development of an effective vaccine and therapeutics.

In studying gastrointestinal infections, we also learn a lot about immune responses that contribute to inflammatory disorders of the bowel such as inflammatory bowel disease (IBD). I hope that my research will also impact treatment and prevention of IBD, a disease that is becoming alarmingly prevalent in our society today.

What drives and inspires you?

The excitement of discovery is the major driving factor in my everyday research. I love it, I feel so compelled by the idea that I might be seeing something for the first time, to be making a difference, even if in small steps. When you are committed to research long-term, these small steps often lead to large and important developments for human health. I also like the challenge of completing something difficult, solving a puzzle and ending up with new information that fits into a much larger scientific picture.

Can you tell us about a project you're working on at the moment?

Last year I was very fortunate to be one of six Australian female scientists to receive a L'Oréal-UNESCO for Women in Science Fellowship. The Fellowship provided \$25,000 towards starting my independent research career. I have used this money to help fund a project aimed at understanding how the gut microbiota contributes to disease outcomes during serious bacterial gut infection.

Recent funding from the National Health and Medical Research Council will also allow me to study a 'master regulator' of our immune system. This regulator is critical in maintaining balanced immune system function, especially in our gut. I am investigating the role of this regulator in protecting against serious bacterial gut infections and also its role in protecting against IBD.

What do you hope to have achieved by the time you retire?

Firstly, I hope to have and share a happy life with those close to me. I also hope that I can inspire young researchers to find what their real passion is and pursue that, in science or otherwise. I'd like to see women feel more empowered and confident in the workplace, to see everyone place confidence in strong female leaders and promote their careers. I'd also like to have contributed in some way to improving the health and wellbeing of people, even if it is just incremental.



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When you have a couple of hours free, how do you pass the time?

I mostly like to spend time with my family, especially outdoors, kicking the footy or going for a walk. I also love cooking, any excuse to be in the kitchen – I'll take it! I find it very relaxing and satisfying. My favourite food to cook is pasta. Finally, music is my other passion in life – I was the drummer in an all-girl rock band called Lash in the early 2000's and in a band called The Preytells from 2004-2009. Although I don't get as much time to do this anymore, I am hoping to break out the instruments again and introduce a Hudson Institute Variety Performance for staff and students at the end of each year!

Why is funding important in science?

All of the research that I have been able to do in the past 10 years, all of my major achievements and contributions to science, are due to the generous funding I have received via philanthropy and government support. Organisations such as L'Oréal, the CASS Foundation and The Centenary Institute have provided generous support in form of travel awards, research funds and support funds to enable consistency and longevity in my research endeavours. I cannot speak highly enough of these organisations – they not only bridge the gaps that we all inevitably face in achieving government funding but they provide flexible funds that can be used for childcare or travel to conferences. This kind of support allows early career researchers to engage in and foster exciting international collaborations and present their research on an international stage. The quality of medical research in Australia is exceptional and I feel very privileged to have the support to continue my work here and help inspire the next generation of early career researchers to do the same.



Flynn, who was born at just 25 weeks, with his mother, Kirsty

Continued from page 3

"Our long-term aim is to develop a treatment that could be rolled out in hospitals around the world," Dr Malhotra said.

An inspired investment in science

Dr Lim progressed the research as the inaugural Fielding Foundation Fellow in 2015-16. This Fellowship was established thanks to the generosity and foresight of Melbourne businessman and philanthropist, Mr Peter Fielding to support the careers of the Institute's emerging science leaders, and ensure their life-saving work reaches our community.



Dr Rebecca Lim and Mr Peter Fielding

"I remember well, back in 2015, when Dr Lim outlined to me the situation with one particular baby's premature birth, and all of the major complications this caused."

"When Dr Lim told me that this research could one day result in saving a life like this small baby's, all of our financial support was totally justified and seemed so insignificant. One small baby's life is priceless."

"We are delighted that Dr Lim's work in this area of medical research is progressing positively and if the results from these first trials continue to be replicated, the benefits for premature babies around the world will be breathtaking," he said.

"Of all the projects we have been honoured to be involved with, Dr Rebecca Lim's work on BPD has been the most emotionally gratifying," Mr Fielding said.

"I remember well, back in 2015, when Dr Lim

Help us protect premature babies from this devastating disease



"There is no doubt that when Flynn was in hospital, he benefited from treatments that were trialled on other babies. This treatment has the potential to help prevent extremely premature babies from developing chronic lung disease. Please make a donation to help pass this hope on to other families."

JOHN AND KIRSTY MINIERI (FLYNN'S PARENTS)

Discovery of bladder ‘mini-microbiome’ signals UTI treatment change

Dr Sam Forster examining a cultured bacterial sample

When the team examined the genetic profiles of these bladder bacteria, they found that startlingly, up to two thirds of the species found in the bladder were also common to the reproductive tract.

“This ‘crossover’ suggests the female bladder is not sterile, and forms part of an interconnected bacterial community with the female reproductive tract,” Dr Forster said, adding that this research has the potential to completely reshape treatment approaches for UTIs.

“More research is needed to find out whether bacteria associated with health or disease in the female reproductive tract can have the same positive or negative effect in the bladder, and vice versa.”

bacteria in patients with UTIs, could this also upset the balance of healthy bacteria that have a protective effect – much like in the gut?” he said.

The findings of a new study by Dr Forster with collaborators at the Wellcome Sanger Institute (Cambridge, UK) and Loyola University Chicago (USA) have been published in the journal, *Nature Communications*.

The team isolated and genome-sequenced 149 strains of bacteria found in urine samples from 77 healthy and symptomatic pre-menopausal women, then grew them in the laboratory to create a ‘living library’ of bacteria.



*Researchers from the Microbiota and Systems Biology Lab:
L-R: Gemma D'Adamo, Dr Sam Forster, Tambllyn Thomason*

It’s a slightly uncomfortable topic, yet a very common health condition that affects one in two women during their lifetime, and around one in 20 men.

Urinary tract infections, or UTIs, are painful infections that occur when bacteria enter the bladder, urethra or kidneys and multiply to cause infection.

A simple treatment of prescribed antibiotics usually kills the bacteria, yet each year, around 70,000 people are hospitalised with more severe kidney and urinary tract infections; which can even lead to death, particularly in older people.

With the rise of antibiotic resistance in the bacteria that cause many UTIs, such as *E. coli*, finding new and more effective ways of treating and managing UTIs is crucial.

Cutting edge genomics is now showing that, curiously, the female bladder is home to a community of bacteria – similar to the gut microbiome – even in the absence of infection.

“The female bladder has long been considered sterile except in women with UTIs caused by bacteria,” Dr Samuel Forster, research group head at Hudson Institute, explained.

“Now, using medical genomics, we are able to show that bacteria associated with health in the female reproductive tract are also able to colonise the bladder without causing clinical infection – superseding more than 100 years of medical dogma.”

“This also raises the question – if antibiotics are used to kill the ‘bad’

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