HUDSON
INSTITUTE OF MEDICAL RESEARCH

SUMMER 2017

HUDSON NEWS

‘40 weeks’: New research is changing clinical practice to prevent stillbirth

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Director's message

[Professor Elizabeth Hartland]

Welcome to the summer edition of Hudson News. It is my great pleasure and honour to write to you in my new role as the Director and CEO of Hudson Institute of Medical Research.

Since arriving in August, I have been getting to know more than 300 Hudson Institute scientists and postgraduate students, and understanding how their research fits into our broader mission of improving human health across the entire lifespan.

I am genuinely excited about the groundbreaking work being undertaken here and the possibilities that lie ahead. I hope you will experience the same optimism when you read about our research discoveries in this edition.

For me, the opportunity to join Australia's leading scientists in innate immunity research at Hudson Institute was incredibly appealing. My own research focuses on how bacteria cause disease and in particular how these tiny organisms use biochemical tricks to shut down our immune response. This knowledge will help in the design of new vaccines and antimicrobial therapies.

Another key attraction for me in joining Hudson Institute was the application of fundamental laboratory science to clinical and translational outcomes. This crossover is possible through our partnerships with Monash Health (Victoria's largest health service) and Monash University (Australia's largest university), enabling our scientists to directly improve the lives of patients through medical research.

A fantastic example of this relationship is a new pancreatic cancer study and clinical trial involving Hudson Institute's Professor Brendan Jenkins and his PhD student, Mr William Berry, in collaboration with Dr Daniel Croagh, a Monash Health hepatobiliary surgeon and Monash University lecturer.

By optimising a technique to screen tumour samples, and identifying a new drug that could be used to treat up to 10 per cent of all pancreatic cancer patients, the team has now commenced a new trial that is aiming to lift survival rates. You can read all about the work on page 5.

Giving back to our community by sharing knowledge and scientific discoveries with the general public is also a key part of our role as a medical research institute. In early October, more than 100 women with endometriosis, their friends, partners and family members attended our free public forum titled 'Endometriosis – Moving towards a pain-free future' at the Melbourne Museum Theatre.

Our panel of scientists, clinicians and experts shed light on endometriosis, a condition affecting an estimated 1 in 10 women, by explaining how medical research can help.

Discoveries such as Professor Caroline Gargett's identification of stem cell markers is one such breakthrough for women's health that could lead to early diagnosis and non-invasive treatments for endometriosis. Read about this work on page 6.

Finally, I wish to thank Professor Bryan Williams for his stewardship of Hudson Institute over the past four years and also for eight years prior to the merger as Director of Monash Institute of Medical Research. Prof Williams has played a crucial role in expanding our influence on the world stage, and guiding the Institute through a merger and an uncertain funding environment.

Prof Williams will continue to lead his own research program in our Centre for Cancer Research, and leaves the Institute in a strong position primed for future growth.

I hope that you enjoy reading about the great science being performed at Hudson Institute. I wish you and your families a safe, relaxing and joyful holiday season.

Best wishes

Professor Elizabeth Hartland

IN THIS ISSUE

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‘40 weeks’: Rethinking pregnancy length could help prevent stillbirth

[Discovery impact: Stillbirth **]**

Dr Miranda Davies-Tuck with Neelima Kota and baby Arjun (centre)

Stillbirth is one of the most devastating outcomes to a pregnancy that a parent could imagine. Yet, in Australia, it remains common – one in 135 births will result in a stillbirth and this figure has not improved in two decades, but there is hope on the horizon.

New research by Dr Miranda Davies-Tuck is changing the way women are cared for in the final weeks of their pregnancy to better ensure the good health of their baby and reduce the rates of stillbirth.

Dr Davies-Tuck’s research redefines a ‘term’ birth by showing the average length of a pregnancy is not always the universal 40 weeks that has been widely applied. Her findings show pregnancy length may differ, based on a mother’s ethnic background or country of origin.

“These findings could completely change how we define what a ‘term’ and ‘post-term’ birth is in clinical care,” says Dr Davies-Tuck, a research fellow in The Ritchie Centre.

Ethnicity is ‘an independent risk factor for stillbirth’

The study of almost 700,000 births and stillbirths in Victoria between 2000 and 2011 found that pregnant women born in South Asian countries, such as India, Sri Lanka or Afghanistan, were at an increased risk of having a stillbirth in late-term pregnancy.

What is stillbirth?

Stillbirth is when a baby dies before or during birth. Stillbirth can occur at any time from 20 weeks until full term (40 weeks) or later.

The average natural onset of labour occurred earlier in women born in South Asia, at 39 weeks, compared to 40 weeks for women born in Australia or New Zealand, suggesting the time at which a placenta can no longer sustain a fetus may differ across ethnic groups.

“Currently, a mother’s country of birth is considered a risk factor for stillbirth, but only in the context of migration and socioeconomic factors. This study confirms a mother’s country of origin or ethnicity is an independent risk factor for stillbirth,” Dr Davies-Tuck says.

Setting the ‘placental alarm clock’ earlier

Current clinical guidelines advise that pregnant women undergo fetal surveillance or have the option of having their labours induced at 41 weeks of gestation to best prevent stillbirth.

“For women born in South Asia and Africa, 41 weeks may be too late, and we may need to set the placental ‘alarm clock’ earlier, for example at 39 weeks of gestation, to help prevent stillbirth in these women,” Dr Davies-Tuck says.

Based on the findings, Monash Women’s has started a trial of ethnic-specific guidelines to better monitor women during pregnancy and reduce the rates of stillbirth.

“It is vital that we identify which mothers are most at risk of stillbirth, and exactly when that is. Our study is leading to changes in clinical practice that may reduce the rates of late-term stillbirth,” Dr Davies-Tuck said.

The research, co-authored by Professor Euan Wallace of Monash Women’s, and Monash University Research Fellow, Dr Mary-Ann Davey, was published in the journal *PLOS One*.

Team

Dr Miranda Davies-Tuck, Professor Euan Wallace, Dr Mary-Ann Davey

STILL BIRTH FACTS

Findings from the study of births and stillbirths in Victorian hospitals between 2000 and 2011.

The overall stillbirth rate for mothers born in South Asia was 5.1 per 1000 births, compared to 3.3 stillbirths for mothers born in Australia and New Zealand.

The stillbirth rate was also higher in mothers born in Africa and the Middle East (4.4 per 1000 births), and lower in mothers born in South East Asia (2.4 in 1000 births).

Mothers born in South Asia were 27 per cent more likely to experience stillbirth than mothers born in Australia.

Women born in South Asia, the Middle East and Africa were more likely to have a late-term stillbirth (after 37 weeks of gestation) than women born in Australia, New Zealand, Europe or South East Asia.

Researcher spotlight Dr Simon Chu

What is your field of medical research?

Ovarian cancer, a disease affecting 4000 Australian women. Five-year survival rates for ovarian cancer are less than 50 per cent. I hope my work can go some way toward improving these outcomes.

My research examines the role of female reproductive hormones in ovarian granulosa cell tumours, a subtype of ovarian tumours affecting two to five per cent of patients. My work is aimed at finding new treatments to prevent the growth and spread of these tumours.

Why are you passionate about science – and women's health?

Studying ovarian cancer not only fascinates me – it is also challenging and exciting. There can be no better motivation for me to come to work when I know our discoveries have real potential to revolutionise treatment for women.

From a scientific point of view, my work is a 'best of both worlds' scenario, as I get to study endocrinology in the context of cancer. Endocrinology looks at the roles of hormones in the body and disorders created by their actions. The ovary is an organ that both makes and responds to hormones.

Endocrine therapy has probably been the most important systemic therapy for hormone-dependent cancers, including breast cancer, so there is real potential to make a difference for ovarian cancer through new hormone-based therapies.

What drives and inspires you?

I am very fortunate to have been supported in my research by the Ovarian Cancer Research Foundation (OCRF). Through the foundation, I have had the immense privilege and pleasure of meeting many ovarian cancer patients, both survivors and women who sadly have lost their battle. Every woman I have met through the OCRF has shown incredible bravery and grace. These women act as great ambassadors and trailblazers for the ovarian cancer cause, and support our work to find an early detection test and better therapeutic options. They inspire me and other ovarian cancer researchers at Hudson Institute to do our very best.

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

Part of my research is in developing an innovative new treatment for ovarian cancer. We are examining whether a combination of drugs could be used to target two key pathways in ovarian tumour development. One of these drugs is already used in the clinic, while the other is currently in phase III clinical trials for other types of cancer, so there is great potential for their use to treat ovarian cancer patients in the clinic quickly.

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

I hope the research we do here at Hudson Institute will make a difference, and even provide a cure for some women with this disease. As with any type of medical research, there are hurdles to overcome. However, I believe we are on the right path with our current research focus. To know that we could save one woman's life would make it all worthwhile.

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

There's nothing better than jumping on a bike and exploring Victoria's cycling routes. I can recommend 'The 1 in 20' plus 'The Wall' through the Dandenong Ranges, and the East Gippsland Rail Trail. One of the best things I've ever done is the 520 km Murray to Moyne Relay Ride for Research with Hudson Institute a couple of years ago. My favourite place to cycle is the Puglia Aqueduct in Cisternino, Italy – it has amazing views!

OVARIAN CANCER FACTS

- In 2017 it is estimated that 1580 new cases of ovarian cancer will be diagnosed in Australia.
- Ovarian cancer is estimated to be the eighth most commonly diagnosed cancer in females in Australia. On average, four Australian women are diagnosed with ovarian cancer every day.
- The five-year survival rate for ovarian cancer is around 45 per cent. In groups of women with high-grade tumours, the five-year survival rates can be as low as 10 per cent.
- Ovarian cancer is the sixth most common cause of cancer death in Australian women.
- There is no early detection test currently available for ovarian cancer.

A gift in your Will is a legacy that leaves the world a healthier place for this and future generations.

"Our research focus is on finding new cures for diseases to enhance the quality of life for this and future generations."

Professor Elizabeth Hartland

You can leave a legacy to support an area of medical research that is important to you. It's a simple process. For a confidential discussion or to receive a copy of our bequest brochure, please contact Hudson Institute's fundraising department.

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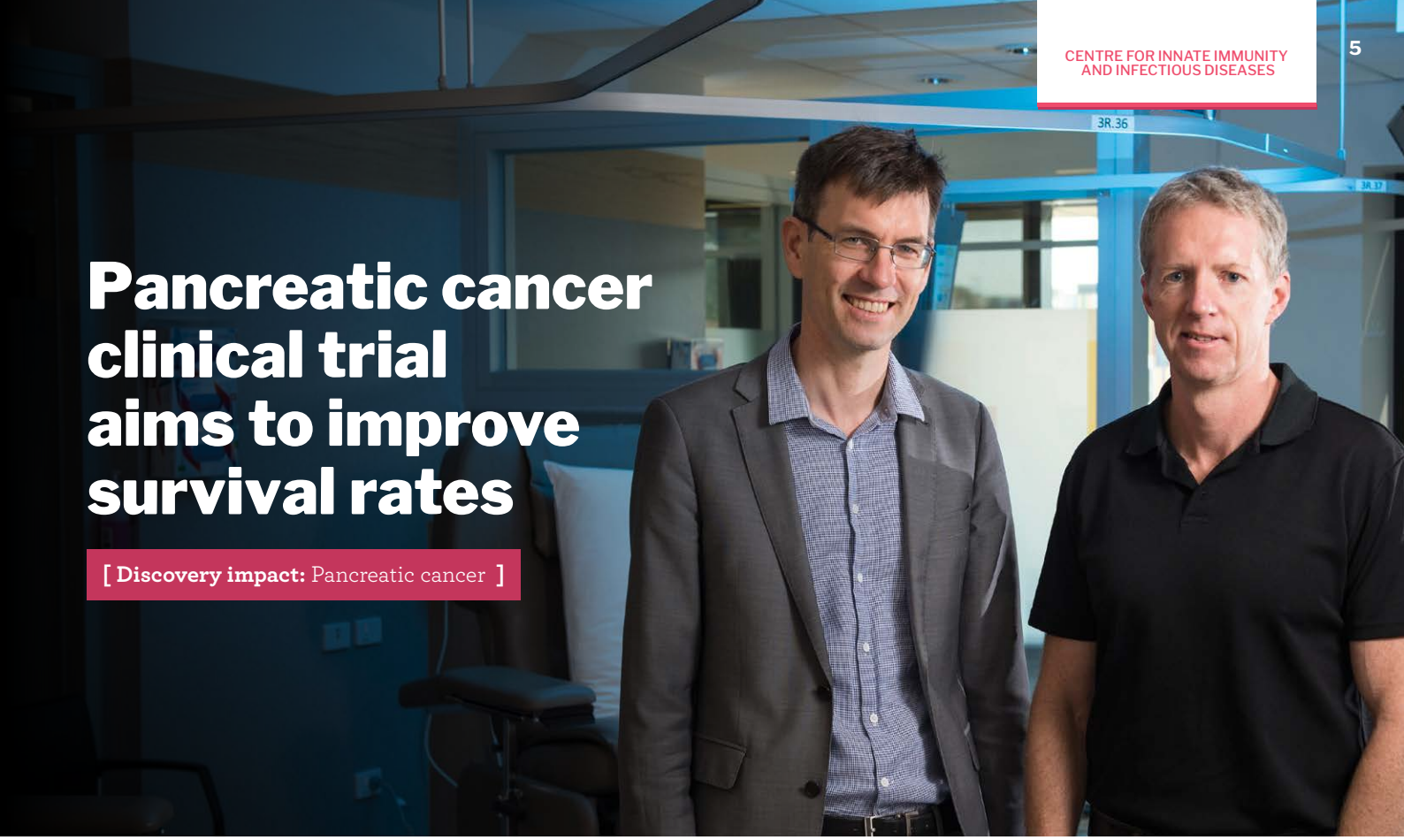
Pancreatic cancer clinical trial aims to improve survival rates

[**Discovery impact:** Pancreatic cancer]



Dr Daniel Croagh and Professor Brendan Jenkins

Pancreatic cancer has one of the lowest survival rates of any major cancer. Sadly, the statistics have not changed significantly over the last 40 years.

Patients have just a five to seven per cent chance of surviving five years after diagnosis and two-thirds of pancreatic cancer patients will die within the first 12 months of diagnosis, making every extra day spent with loved ones extremely valuable.

A new study by Professor Brendan Jenkins, PhD student Mr William Berry and Dr Daniel Croagh, a hepatobiliary surgeon from Monash Health, has led to a new clinical trial that is aiming to improve survival rates with a drug that is currently used to treat colon cancer.

"Treatment options must improve if patients are to be given the best chance at surviving for longer," says Prof Jenkins, from the Centre for Innate Immunity and Infectious Diseases.

Clinical trial underway

The study, published in the *International Journal of Cancer*, laid the groundwork for the trial by showing around 10 per cent of patients with a specific genetic tumour profile could benefit from the drug, called an epidermal growth factor receptor inhibitor.

The Victoria-wide trial, led by Dr Croagh and already underway at Monash Health, will see between 150 and 200 patients screened for suitability with the drug.

"We are taking the guesswork out of treatment for pancreatic cancer," Prof Jenkins says. "Instead of a 'one size fits all' approach of chemotherapy currently used, the drug is selected for the patient based on the genetic make-up of their tumour and how likely it is an individual will respond to the treatment – an approach known worldwide as precision medicine."

In the study, the team also refined an endoscopic technique used to extract biopsies of tumours, so tumour samples can be used to genetically screen patients for compatibility with new drug.

World-first application of precision medicine

"Currently, less than 50 per cent of patients are able to undergo genetic screening. This new, optimised technique overcomes the limitations of extracting samples from patients with inoperable, metastatic tumours – opening up genetic screening to virtually all patients, even those with advanced cancer."

Prof Jenkins and Dr Croagh are hopeful the clinical trial will lead to more targeted treatment approaches to improve responsiveness to drugs and give patients a better chance at surviving for longer.

"While there is no silver bullet, we hope this is the beginning of a shift towards better patient outcomes," they said.

"If successful, this clinical trial will be one of the first applications of precision medicine – targeting cancer treatment to the genetic profile of the tumour – in pancreatic cancer anywhere in the world."

Team

Professor Brendan Jenkins, Mr William Berry, Dr Daniel Croagh

PANCREATIC CANCER FACTS

- In 2017, an estimated 3271 new cases of pancreatic cancer will be diagnosed in Australia (1722 men and 1548 women).
- Pancreatic cancer is the fifth-leading cause of cancer death in Australia.
- Pancreatic cancer has the highest mortality of all major cancers. Two-thirds of pancreatic cancer patients die within the first year of diagnosis.
- Pancreatic cancer makes up 2.4 per cent of all new cancer cases diagnosed in 2017.
- Survival rates for pancreatic cancer have not changed significantly in nearly 40 years.

Miracle regenerative tissue provides hope

[Discovery impact: Women's reproductive health, endometrial cancer, endometriosis, adenomyosis, Asherman's syndrome **]**

Professor Caroline Gargett, Ms Dorien O and Dr James Deane

Solutions for women's reproductive health conditions including endometriosis and endometrial cancer, the most commonly diagnosed gynaecological cancer in Australia, will be accelerated thanks to a discovery by Professor Caroline Gargett's team in The Ritchie Centre.

The team has found an identifying marker, or unique signature, that could play a significant role in developing new treatments for female reproductive health disorders like endometriosis and endometrial cancer.

The marker, N-cadherin, is a protein expressed by adult stem cells called endometrial epithelial progenitor cells (eEPs) and can be used to identify and isolate these rare cells in the uterus.

Miracle tissue

"The endometrium is an incredibly regenerative tissue. It regrows each month when an embryo does not implant, for approximately 400 times in a woman's reproductive life. We believe these adult stem cells could play an important role in this process and in menstrual disorders," Prof Gargett says.

"This discovery means we can investigate the role of these adult stem cells in conditions such as endometrial cancer, endometriosis, adenomyosis and Asherman's syndrome, which are not well understood," Prof Gargett said.

Adult stem cells have the remarkable ability to differentiate or grow into functional cells of the tissue. In the uterus, endometrial stem cells are like germinated seeds that can rapidly grow into the new tissue that lines the uterus every month.

Significantly, Prof Gargett's team believes endometrial epithelial progenitor cells may be responsible for regenerating glands that prepare the womb for the next menstrual cycle, and help in sustaining an embryo until the placenta is fully formed.

"This discovery means we can examine when these cells are behaving normally, such as in menstruation, and when they exhibit uncontrolled growth, such as in endometrial cancer or endometriosis, to find new treatment solutions for women."

The research, a culmination of eight years of work for the team, was published in the prestigious reproductive biology, obstetrics and gynaecology journal, *Human Reproduction*.

Cancer Council Victoria CEO Todd Harper says, "I would like to congratulate Prof Caroline Gargett and her team at Hudson Institute on this exciting development in further enhancing our knowledge about endometrial cancer."

"Last year, 747 women were diagnosed with uterine cancer in Victoria alone. Research findings, like those of Prof Gargett, provide hope to cancer patients, as well providing more targeted treatment with fewer side effects."

Team

Professor Caroline Gargett, Dr Hong Nguyen, Dr Li Xiao, Dr James Deane, Dr Fiona Cousins, Ms Ker Sin Tan, Dr Hirotaka Masuda, Dr Carl Sprung, Associate Professor Anna Rosamilia

WOMEN'S REPRODUCTIVE HEALTH FACTS

ENDOMETRIOSIS: A condition affecting an estimated 1 in 10 women of reproductive age. Endometriosis occurs when tissue that normally lines the uterus is found outside of it, usually in the pelvic cavity. Symptoms can include severe pelvic pain, infertility, heavy periods and nausea.

ADENOMYOSIS: A condition affecting an estimated two per cent of women, where cells that normally line the uterus also grow in the muscle wall of the uterus. Symptoms include abnormal or heavy menstrual bleeding and painful periods.

ENDOMETRIAL CANCER: The most commonly diagnosed gynaecological cancer in Australia, it affects an estimated 1.7 per cent of women. Endometrial cancer arises from the lining of the uterus (endometrium). Endometrial hyperplasia is a condition that can be a precursor of this type of cancer.

ASHERMAN'S SYNDROME: A rare condition where scar tissue is present in the uterus or cervix. This often occurs after a number of surgeries on the uterus, or after a miscarriage. Symptoms can include absent periods, repeated miscarriages and infertility.

Run Melbourne success

In July, more than 50 of our scientists, staff and students ran or walked in the Run Melbourne event to raise funds for new equipment. Thanks to the generosity of 280 supporters, we raised $30,000 towards a virtual scanner microscope to assist our researchers in carrying out their life-saving work.

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L-R: Ms Steph Forman, Professor Bryan Williams, Ms Hui Kheng Chua, Dr Daniel Gough, Mrs Naama Neeman, Ms Caroline Drinkwater, Associate Professor Ron Firestein, Dr Dhanya Sooraj, Dr Jason Cain, Dr Peter Downie

Hudson Institute joins international paediatric cancer consortium

Hudson Institute scientists will share expertise with leading international research institutions to progress research and improve treatments for children and adolescents with brain cancer.

Hudson Institute has been announced as the first Australian member of the US-based Children's Brain Tumor Tissue Consortium (CBTTC) and joins a collaborative, multi-institutional research program dedicated to the study and treatment of childhood brain tumours.

Our scientists will work alongside 15 institutions from the US, Europe and China, including Weill Cornell Medicine, Stanford University and the Children's Hospital of Pittsburgh of UPMC, combining knowledge to discover cures.

Associate Professor Ron Firestein, Head of Hudson Institute's Centre for Cancer Research, says the consortium enables scientists from across the world to pool data from the collection and analysis of high-quality brain tumour biopsy specimens.

"While geographically we may work on opposite sides of the world, as researchers, our ultimate aim is the same – to improve treatment outcomes for paediatric brain cancer patients and their families," A/Prof Firestein says.

"Our scientists will share local expertise in developing patient-derived tumour models and drug/genomic screens with leading institutions, to identify ways to better treat young patients and save lives."

Hudson Institute expertise

A/Prof Firestein says Hudson Institute's strengths in paediatric cancer include its expertise in developing clinically relevant 'avatar' models of patients' tumours and its clinical collaborations with Monash Children's Hospital.

"Our tumour cell lines can be used to test hundreds of new or existing drugs on a model of an individual patient's tumour in the laboratory, to determine how effective a treatment is before it reaches the patient. As researchers, we are also working directly with oncologists to respond to clinical need," he explained.

Childhood Cancer Research Symposium

Members of the consortium will be keynote speakers at a Childhood Cancer Research Symposium that will be hosted by Hudson Institute in February 2018.