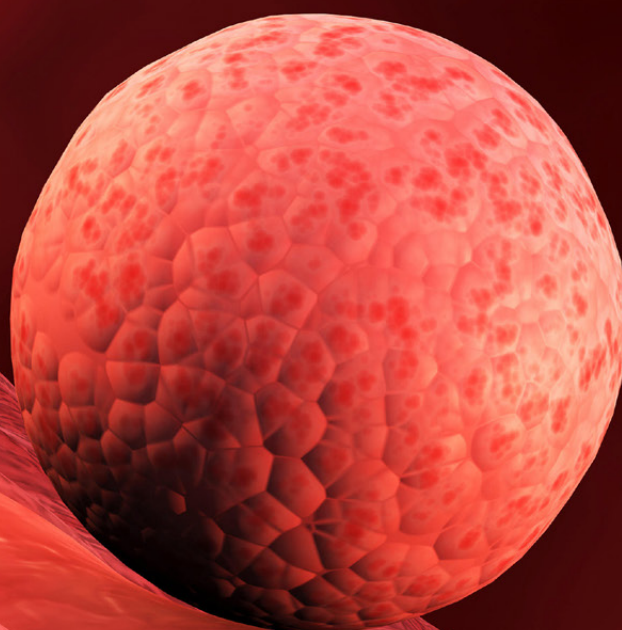


WINTER 2018

HUDSON NEWS

**Mystery
signal key
to life**



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Director's message

[Professor Elizabeth Hartland]



Every scientist wants their work to have lasting impact.

The most transformational scientific discoveries often start with bold out-of-the-box thinking and behind each of these discoveries is a person or organisation with the foresight and vision to back a promising, but high-risk, idea.

Philanthropic support plays a vital role in enabling our scientists to make medical research discoveries that change and save lives. It allows scientists to follow blue sky ideas with less predictable outcomes than traditional funding streams would allow.

We are very grateful to our many supporters and who play a crucial role in progressing life-saving medical research. Without this support, many scientific discoveries would remain unrealised ideas.

How life-saving ovarian cancer research can progress rapidly with philanthropic support is exemplified on page 5 by Dr Maree Bilandzic's journey in science.

Dr Bilandzic says, "I owe my career and the fact that I am able to continue my research to our supporters. It was philanthropic support that gave me the chance to establish my own independent stream of research and the means to tackle an 'old' problem – treating ovarian cancer – with a fresh approach."

In February, thanks to generous funding support from the Children's Cancer Foundation, we launched the truly innovative two-year \$1.3 million Hudson Monash Paediatric Precision Medicine Program. The program, a collaboration with our clinical partners at Monash Children's Hospital, is helping the 950 Australian children diagnosed with cancer each year.

We want to ensure that all Australian children diagnosed with brain cancer and solid tumours benefit from advances in precision medicine treatment.

Importantly, the Children's Cancer Foundation is supporting five new research staff with expertise in specialist areas including biobanking (creating a 'living library' of tumour samples) and organoids (lab-grown mini-tumours), to train and grow our valuable workforce.

On page 6, you can read about the lasting contribution made by the family of medical practitioner, Dr Sue Fowler in establishing the Dr Sue Fowler Scholarship in Ovarian Cancer research in her memory, to support the work of PhD student, Mrs Nazanin Karimnia.

Thank you once again to our supporters and community – without you, our transformative research wouldn't be possible. I hope that reading about our progress leaves you feeling inspired. Because of you, our work is helping children and families right now.

There is always more work to be done. Our world-leading scientists have so many more promising discoveries to progress, but they need your support to make them happen.

We've already accomplished so much with your support in 2018 and I look forward to sharing more of our highlights (and some challenges along the way) with you later in the year.

Professor Elizabeth Hartland
Director and CEO

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Mystery signal key to life

[Discovery impact: Fertility]



Professor Eva Dimitriadis

Women and couples in Australia and New Zealand now undergo more than 70 000 IVF treatment cycles each year in the hope of starting a family or having more children.

Around a third of couples who undergo IVF will have a baby as a result of their first cycle. This rate increases to 54 to 77 per cent by the eighth cycle.

Yet, for many of the couples affected by infertility, the embryo fails to attach to the lining of the uterus – like a seed in soil – or the woman miscarries at 6 to 12 weeks, causing significant heartache, as well as financial strain.

Despite advances in IVF technology, the reasons why some embryos fail to latch onto the cells in the womb remain unknown.

“Repeated implantation failure or recurrent miscarriage can be devastating,” Professor Eva Dimitriadis, Head of Hudson Institute’s Embryo Implantation laboratory, explains.

“It’s thought that around half of all embryos that fail to implant are chromosomally abnormal. The other 50 per cent – we don’t know why they fail. It’s a mystery.”

Now, Prof Dimitriadis’ research is offering hope by intercepting an embryo’s subtle cues to the body.

The team has identified a small molecule, released by a human embryo in the womb, which could be the key to understanding why some embryos fail to implant.

In a study published in the *Reproduction, Fertility and Development* journal, Prof Dimitriadis found that the pattern in which this message, or small molecule called microRNA-661, is released to a woman’s body reflects whether or not the embryo will implant during IVF.

Her team also showed that this small molecule regulates the way an embryo attaches to the cells that line the uterus.

Next steps

Prof Dimitriadis says the finding could help IVF clinicians to select embryos that are most likely to result in a healthy pregnancy, or to create the ideal environment for a pregnancy when an embryo is transferred to the womb.

“Often embryos look normal, yet they don’t implant,” Prof Dimitriadis explains.

“Now that we are beginning to understand how fertilised eggs ‘talk’ to the womb, we could help IVF clinicians to choose the embryos with the best potential to implant, and help more women to achieve a successful pregnancy.”

Clinical collaborator, Professor Luk Rombauts, Group Medical Director of Monash IVF, says, “We are learning more and more about how to select the best embryo for implantation but it has remained hard to determine when the womb is ideally prepared for its arrival.

“Our research collaboration with Prof Dimitriadis is starting to unravel the dialogue that happens between the embryo and the womb. That is important because it can help us find more successful strategies to help IVF patients fall pregnant.”

FERTILITY / IVF FACTS

- Infertility affects about one in six couples in Australia.
- 77 721 IVF cycles were performed in Australia and New Zealand in 2015.
- 14 791 babies were born from assisted reproductive technologies including IVF in 2015.

Did you know?

During the 1980s, Hudson Institute Distinguished Scientist, Professor Alan Trounson and his colleagues developed groundbreaking IVF technologies including the use of fertility drugs to time ovulation, systems for egg collection and embryo donation and techniques for egg and embryo freezing. More than seven million babies around the world have been born as a result of these technologies.

From discovery to saving lives

How a simple blood test could decrease risk of stroke and heart attack

[Discovery impact: Hypertension]



Dr Jun Yang and patient, David Dent

Australia's largest study of a common yet underdiagnosed cause of high blood pressure is now underway at Hudson Institute to help prevent heart attack and stroke.

Almost six million Australian adults have high blood pressure, or hypertension, which remains the leading risk factor for heart disease and can lead to a heart attack, stroke or kidney disease.

For between 5 and 15 per cent of patients, the underlying cause is primary aldosteronism (PA) – a potentially curable form of high blood pressure resulting from overproduction of the hormone aldosterone from the adrenal glands. Crucially, many patients aren't even aware they have this little known condition.

"Primary aldosteronism often doesn't have specific symptoms other than high blood pressure, so it's easy to miss," Dr Jun Yang, an endocrinology clinician-researcher and lead investigator says.

"An estimated 1 in 10 people with high blood pressure have PA, but only 1 in 200 are diagnosed because many doctors do not screen for it. As a result, many patients with undiagnosed PA are taking blood pressure medications that won't help."

The lack of awareness around PA can be life-threatening. Hudson Institute group head, Dr Morag Young showed that

aldosterone is more harmful to the heart and blood vessels than just high blood pressure alone. If left undiagnosed, the condition can get worse over time, leaving sufferers more prone to stroke and heart attack at a younger age.

GP referral clinic

In 2016, Dr Yang and Professor Peter Fuller, Hudson Institute Centre Head, established the Endocrine Hypertension Service at Monash Health, where GPs and specialists can refer patients with suspected PA for early diagnosis and targeted treatment to prevent permanent damage.

The clinic was established after Dr Yang streamlined the complex diagnostic tests for PA, leading to a dramatic rise in detection at Monash Health, from three patients per year in 2011 to more than 60 in 2017.

Next steps

The next phase is a research study asking GPs to screen hypertensive patients using a simple blood test to find out exactly how common PA is in the community.

"If this simple screening process is found to be cost-effective, it will inform new management guidelines so that more patients with hypertension can benefit from the early detection, treatment and cure of PA," Dr Yang says.

David's story

For nearly eight years, David Dent experienced routine dizzy spells, but he dismissed them as being nothing out of the ordinary.

A friend suggested that David get his blood pressure checked. The advice was timely and ultimately life-saving because David's blood pressure was dangerously high.

Referred to Dr Yang and the Monash Health service by his GP, David underwent adrenal vein sampling, showing he had PA caused by a tumour in his left adrenal gland. The tumour produced high levels of aldosterone, leading to very high blood pressure.

Within four weeks of diagnosis, David underwent surgery to have the benign tumour removed. Now, eight months on, his life – and his blood pressure – are returning to normal. He now takes just one instead of eight blood pressure tablets per day.

"I don't take nearly as much medication as I used to. I'll be glad to be off it."

"Dr Yang has just been amazing. I'm coming good and my blood pressure's coming back down to normal," David says.



Researcher spotlight Dr Maree Bilandzic

What is your field of medical research?

I am an ovarian cancer researcher with a strong interest in metastatic disease (where cancer spreads to other parts of the body). While there are many stories of survival and resilience around cancer, this is not the case for many women with ovarian cancer. Through my work, I hope to change the outlook for ovarian cancer patients to a more positive one.

What drives and inspires you?

I'm so honoured and privileged to do what I do. I come to a workplace that I love and make a positive impact on women's health. Ovarian cancer survival rates have remained dramatically low for decades at around 30 per cent, especially compared with diseases such as breast cancer, which has an 88 per cent survival rate. I want to give women hope for a disease-free future. This hope inspires me.

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

Firstly, thanks to long-term support from the Ovarian Cancer Research Foundation (OCRF), we are getting closer to a world-

first early detection test for ovarian cancer. If the cancer is detected early, the chances of surviving after five years increase dramatically from 30 per cent to over 90 per cent.

Secondly, thanks to discovery research funding from the CASS Foundation, we identified a protein that 'leads' invasion in a small population of ovarian cancer cells. We believe this population is crucial to relapse and resistance to chemotherapy. In essence, our discovery means we have found a way to stop these cancer cells.

Now, thanks to funding support from the Fielding Innovation Award, I'm really excited that this discovery will get the chance to be developed into a treatment. So many life-changing discoveries never make it because they aren't funded. I'm incredibly grateful to be able to realise the full potential of this research.

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

Do scientists ever retire? I can't see myself retiring because I love it so much. I am looking forward to improving survival statistics for ovarian cancer patients through an early detection test and a new treatment.

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

I have two young boys (aged one and five). Both my sons are like scientists embarking on a journey of learning and discovery. More than anything I love observing and nurturing their curiosity about the world around them and seeing their determination to learn.

Why is funding important in science?

I owe my career and the fact that I am able to continue my research to philanthropy. It is so important, as it often steps in where traditional funding isn't available for innovative research with a high risk but potentially high reward. Support from the OCRF, Fielding Foundation and CASS Foundation has enabled me to establish my own independent stream of research and tackle an 'old' problem of improving ovarian cancer survival rates with a fresh approach. It's great that philanthropy recognises we need new ways of looking at old problems and is prepared to back young, keen minds to do it!



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

You can leave a legacy to support an area of medical research that is important to you. For a confidential discussion or to receive a copy of our bequest brochure, please contact us.

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Dr Sue Fowler Scholarship in Ovarian Cancer

[**Discovery impact:** Ovarian cancer]



Nazanin Karimnia

The inaugural Dr Sue Fowler Scholarship in Ovarian Cancer has been awarded to PhD student, Nazanin Karimnia to support her research into new ovarian cancer therapies.

There is an urgent need for new therapies to improve the long-term survival of ovarian cancer patients. Ovarian cancer is a disease with a five-year mortality rate of around 70 per cent.

While most patients are initially responsive to chemotherapy, 90 per cent of patients relapse and develop drug-resistant disease.

Nazanin, a PhD candidate with the Ovarian Cancer Biomarkers laboratory, is investigating how targeting a unique signature, or marker, could help to disrupt the cells that lead tumour invasion.

The marker, called Keratin14, is expressed by cancer cells that control how ovarian tumours invade and implant into healthy tissues. By disrupting this process,

Nazanin hopes to develop a new therapy to treat ovarian cancers, at all stages of progression.

"These cells are like the tip of the invading arm in the 'army' of cancer cells," Nazanin explains.

"By targeting these 'leaders' through the Keratin14 marker, we could potentially disrupt the initial invasion of the cancer cells and prevent further tumour dissemination.

"Our aim is to develop a novel, effective and non-toxic anti-cancer strategy that can stabilise or regress disease and enhance the effectiveness of existing ovarian cancer treatments.

"Women diagnosed at any stage of ovarian cancer will benefit from the outcomes of this research."

The goal of the scholarship is to assist outstanding students to start a career in ovarian cancer research and to improve treatment and diagnostic approaches for women with ovarian cancer.



Mr John Fowler and inaugural recipient of the Dr Sue Fowler Scholarship in Ovarian Cancer, Nazanin Karimnia

OVARIAN CANCER FACTS

- Every year, approximately 1500 Australian women are diagnosed with ovarian cancer, most of them with an advanced stage of the disease.
- Ovarian cancer is the sixth most common cause of cancer death in Australian women.
- On average, four Australian women are diagnosed with ovarian cancer every day.
- Six out of ten ovarian cancer cases occur in women over the age of 60. The risk of ovarian cancer increases with age.

The scholarship was established in honour of the late Dr Sue Fowler, to support a Hudson Institute PhD student undertaking research into ovarian cancer.

Dr Sue Fowler was a dedicated and caring medical practitioner and Hudson Institute is grateful for the generous and foresighted support of her family in creating this important scholarship in her memory.



L-R: Mr Jeremy Smith, Chairman, Children's Cancer Foundation; Professor Elizabeth Hartland, Director and CEO, Hudson Institute; Associate Professor Ron Firestein, Centre Head, Centre for Cancer Research, Hudson Institute; Ms Aileen Boyd-Squires, CEO, Children's Cancer Foundation; Dr Peter Downie, Head of the Children's Cancer Centre at Monash Children's Hospital; Mr Nigel Garrard, Board Member, Hudson Institute

Childhood cancer program set to improve treatment

A truly innovative program launched in February to improve treatment outcomes for children diagnosed with brain and solid tumours is already achieving results, helping clinicians, children and their families.

The Hudson Monash Paediatric Precision Medicine Program is a collaboration with the Monash Children's Hospital Cancer Centre and is funded with a generous \$1.3 million investment from the Children's Cancer Foundation. This funding has enabled 12 researchers, oncologists and pathologists to work together towards a cure.

Each year, 950 Australian children are diagnosed with cancer, almost half of them under the age of four. The program aims to improve these statistics and reduce the long-term health impacts of chemotherapy and radiation on children.

"Every child's tumour is genetically unique and responds to cancer treatment in a different way. This program is aimed at ensuring children with cancer benefit from major advances already being made in adult solid tumours," Lead researcher, Associate Professor Ron Firestein says.

"We know the difference this program can make for children, so we hit the ground running. We have already generated several 2D and 3D organoid models of childhood tumours. Importantly, our work is starting to identify appropriate drugs to treat specific tumour subtypes. In the future, we hope that these findings provide new treatments for children with cancer," A/Prof Firestein says.

Our scientists are establishing a living biobank of childhood brain tumours and solid cancers – including organoids, three-dimensional lab-grown 'mini-tumours' that mimic the genetic profile of the child's tumour – to identify the most effective treatment for each child.

The living biobank is established using tumour biopsies taken when children are surgically diagnosed at Monash Children's Hospital and The Royal Children's Hospital.

The tumours' sensitivity to thousands of drugs will be tested by using specialised genetic and drug screens to identify potentially novel and more effective therapies. While currently in a preclinical phase, it is hoped that in future this vital information will be fed back to oncologists to help inform the management of individual patient's tumours.

"Current treatment options can have devastating long-term health effects for childhood cancer survivors. Our aim is to identify the most effective, targeted treatments with the least side effects for these young patients," he says.

"The potential to improve the quality of life, and improve survival rates for paediatric cancer is enormous," program researcher, Dr Jason Cain says.

Hudson Institute is grateful to the Children's Cancer Foundation for its foresight in supporting this program and its commitment to advancing research into paediatric cancer.

Ms Aileen Boyd-Squires, Chief Executive of the Children's Cancer Foundation, says, "The Children's Cancer Foundation is proud to fund this innovative program, which draws on Australian and international expertise and collaboration across hospitals and research institutes. We hope that one day, all Australian children and adolescents with cancer will benefit from this research program."

Help us help children with brain cancer



"Research is the key to finding a cure for children with brain cancer, so it's important that scientists are funded to find new treatments. In your darkest hour, having hope for a brighter future helps you face each day. Please help by making a tax deductible donation."

PAUL GIANNONE (LUCIA'S DAD)



From fear to hope for children with brain cancer

Children with brain cancer now have a better chance at a healthier future, thanks to a groundbreaking new program at Hudson Institute.

Dancing around to music and feeding chickens at her grandparents' home, Lucia Giannone is now the picture of a happy, loving three-and-a-half year old girl.

Yet, just over a year ago, Lucia's parents, Maree and Paul, received devastating news. Lucia was diagnosed with a brain tumour.

"Receiving a diagnosis like that for your child stops your world – it rocks you to the core," Paul says.

Treatment options for Lucia were limited. Her tumour was too large and intertwined in the delicate brainstem to undergo surgery.

After consultation with Dr Peter Downie, Lucia's oncologist at Monash Children's Hospital, a tiny portion of Lucia's tumour was sent for genetic testing on our site. A specific mutation in the gene, BRAF V600, was identified which meant that Lucia could immediately be started on a drug called dabrafenib, a personalised 'match' for the mutation.

Incredibly, in the 12 months since starting treatment, Lucia's tumour hasn't grown and it has even reduced slightly in size. "She has progressed beyond expectation," her father Paul says gratefully.

With your help we can do more

In the past, Lucia's treatment would have been limited to one-size-fits-all chemotherapy and radiation treatment with devastating side effects, to which the tumour may not have responded.

"Every child's tumour is genetically unique and responds to cancer treatment in a different way," Head of Hudson Institute's Centre for Cancer Research, Associate Professor Ron Firestein, says.

A/Prof Firestein is leading a new research collaboration between Hudson Institute and Monash Children's Hospital, which aims to develop more targeted therapies for children with brain tumours, like Lucia.

"Our new on-site tumour testing platform means we will soon be able to help clinicians identify treatments to match the tumour type, with fewer side effects and hopefully better results," A/Prof Firestein says.

The future is promising

Lucia takes the treatment as a tablet at home twice a day and there are no hospital visits for invasive chemotherapy or radiation.

"Using this drug to treat paediatric brain tumours is a new approach that is only being done in a few places in the world," says Dr Downie.

While there is still a long road ahead for Lucia, her treatment is allowing Paul and Maree to look to the future.

"The fear of what comes next is always there, but we've now got hope for a normal childhood for Lucia," Paul says.

"It's all because of research partnerships like this, where targeted therapies provide hope to parents and their children with cancer. It really gives you the drive when you need it."

We urgently need your support to expand this program to help more children like Lucia. Please make your tax deductible donation today.



'Thank you for your kind support'

Professor Elizabeth Hartland
Director and CEO, Hudson Institute

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