

WINTER 2021

HUDSON NEWS

A photograph of a woman with dark hair tied back, smiling warmly. She is hugging two young girls. The girl on the left is wearing a white shirt and has her eyes closed, smiling. The girl on the right is wearing a grey shirt and is laughing joyfully. They are standing in front of a rustic wooden wall.

**Spotlight on
women's health**

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Director's message

Professor Elizabeth Hartland



Welcome to *Hudson News* Winter 2021

I'm sure, like us, you are all breathing a collective sigh of relief that vaccines against COVID-19 are being rolled out and are already having an impact on reducing daily infection and death rates around the world. It's thanks to science and medical research that these rapid advances in vaccine development have been possible.

While our research into COVID-19 treatments and the development of a National Centre for Inflammation Research at Hudson Institute (see back page) continues, so do our other crucial research programs.

This year, the first edition of *Hudson News* is coinciding with Mother's Day and we are highlighting our world-leading research into women's health. **I'm proud that our researchers are making important discoveries into these neglected conditions that have a big impact on women's lives.** This includes our research into ovarian cancer. Our teams are making significant progress towards developing early detection tests and promising new

treatments for the most prevalent forms of ovarian cancer, as well as a rare form which can even affect babies.

You may know someone affected by endometriosis, a painful debilitating condition where endometrial tissue grows outside the uterus, or you may know someone who has suffered pelvic organ prolapse (POP), often as a result of birth trauma. **Historically, conditions like these have been considered something 'women just put up with' but we believe these patients deserve better.**

Lastly, I want to acknowledge that Mother's Day can be a difficult time for some, for a variety of reasons. The stories you will read about in this newsletter illustrate the importance of the work we're doing in women's health to improve the quality of life for women here and around the world.

We would welcome your generous support to help us solve some of the biggest health issues facing women today.

Professor Elizabeth Hartland
Director and CEO

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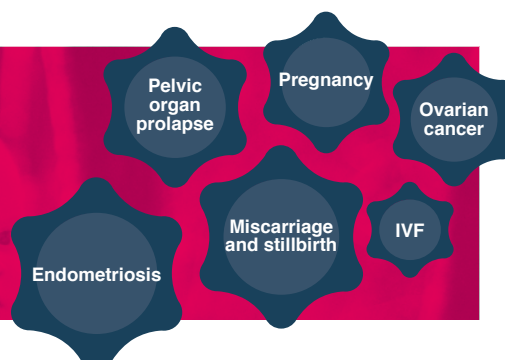
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WOMEN'S HEALTH AT HUDSON INSTITUTE

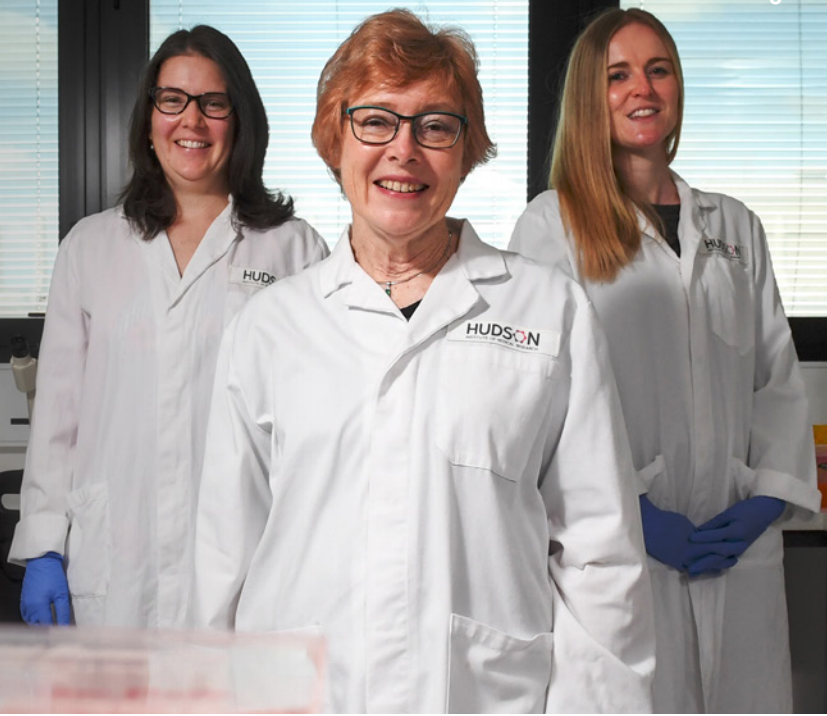


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Your endometriosis questions answered



Hudson Institute researchers Professor Caroline Gargett, Dr Caitlin Filby and Dr Fiona Cousins are investigating the potential causes of endometriosis. If we can understand more about how endometriosis emerges and develops, this could lead to the development of less invasive diagnostic tests and more effective treatments.

What is endometriosis?

Endometriosis or 'endo' is a debilitating, chronic inflammatory condition where tissue fragments with similar properties to the womb lining attach to other organs and grow into lesions outside the uterus. Initially, these lesions are still responsive to female reproductive hormones that trigger menstruation and may bleed during a woman's period, causing inflammation.

The conditions can cause chronic pelvic pain, bowel and bladder dysfunction, back pain, heavy menstrual bleeding, nausea, pain during sex, and infertility. There is no cure. Treatments include hormonal based therapies and surgery to remove lesions to reduce pain and improve fertility. But much better treatments are needed.

What causes endometriosis?

This is the key question facing endometriosis researchers today. We are working on the hypothesis that

endometriosis is caused by retrograde menstruation – where menstrual fluid containing cells that initiate endometriosis flows backward through the uterus, out of the fallopian tubes and into the pelvic cavity. These cells somehow evade the immune system, attach to organs, and form lesions.

What does your research involve?

We believe there are two types of endometrial stem cells shed during menstruation that could be forming lesions following retrograde menstruation into the pelvic cavity. The ability for stem cells to grow and proliferate are qualities that enable the endometrium – the lining of the uterus – to renew each month after shedding during the menstrual cycle.

“

This is a disease affecting young women in the prime of their lives. It prevents them from reaching their full potential – personally, professionally, financially. We desperately need new ways to diagnose and treat endo. We want to give the millions of women with endometriosis their quality of life back.”

Prof Caroline Gargett


You may wonder then why all women don't have endometriosis? We believe the answers might be in the DNA of

ENDOMETRIOSIS FACTS

- Affects **1 in 10** women – **176 million** women worldwide
- Up to **10 years'** wait for diagnosis
- Annual costs: Australia **\$9.7 billion** | UK **GBP 8.5 billion** | US **\$53.8 billion**

women's endometrial cells. We are working in collaboration with Professor Grant Montgomery from the University of Queensland to investigate how variations in the DNA sequence (genomics) that give rise to endometriosis risk genes could be giving these stem cells an advantage to grow into lesions. The role of inflammation and the immune system is also important in allowing lesions to survive.

There is an urgent need to improve the lives of women with endometriosis. To achieve this, we need to understand which cells form the lesions, how they spread to other organs, and what factors govern their ability to survive and invade other tissues. This will enable us to develop new therapies that will hopefully prevent endometriosis, saving women from the debilitating pain and discomfort caused by this condition.

 **Collaborators** Professor Grant Montgomery, University of Queensland; Professor Luk Rombauts, Monash IVF

 **Funders** US Department of Defense, NHMRC

Meet the scientists at the forefront of ovarian cancer research

Ovarian cancer is a silent killer. It is often asymptomatic and goes undetected until the advanced stages, when the cancer is widespread. Only a handful of new treatment options have emerged in the past 30 years and these typically become ineffective as the cancer develops resistance to chemotherapy. Our research teams tackle ovarian cancer from different angles to make a difference to women's lives.

New treatment options

In 2004, Professor Paul Hertzog's laboratory discovered interferon epsilon in the female reproductive tract. An interferon is a type of protein called a cytokine, which regulates the immune system. The team showed that interferon epsilon can activate immune cells to provide a protective inflammatory response to ovarian cancer in preclinical models.

“This new treatment could be groundbreaking for women in the late stages of ovarian cancer who have developed chemotherapy resistance.”



Prof Paul Hertzog
Associate Director
Hudson Institute

These promising findings have led to a multi-million-dollar investment by international venture capital fund Morningside Ventures, resulting in the spin-out company, Epsila Bio, Inc.

What we are working on

- Developing a new treatment for metastatic ovarian cancer
- Progressing treatment to clinical trials
- Understanding the role of interferon epsilon in other conditions like endometriosis

Early detection

Around 4000 women live with ovarian cancer in Australia, with less than half surviving longer than five years after diagnosis. The disease has few early symptoms, and even with treatment, most patients will relapse within a short space of time.

Headed by Dr Andrew Stephens, the Ovarian Cancer Biomarkers group is actively developing and trialling new cancer therapies and detection tests with the support of the Ovarian Cancer Research Foundation (OCRF), to help create a future free from the spectre of this disease.

What we are working on

- Development and preclinical testing of a new cancer drug
- Creation of early detection tests
- Precision medicine approaches to rapidly personalise therapy

“The fact is that no early detection test for ovarian cancer exists – it's a simple necessity we owe women.”



Dr Maree Bilandzic
Senior Postdoctoral Researcher

Rare ovarian cancer

Approximately five per cent of ovarian cancer sufferers have a subset of the disease known as granulosa cell tumours (GCTs), which can develop at any age, even in children. The condition has a high rate of late recurrence, meaning even if surgery is effective, women live for years in constant fear that their cancer might return.

“To know that we can contribute to bringing hope to these women makes my line of work very rewarding.”



Dr Simon Chu
Research Group Head

Dr Simon Chu's Hormone Cancer Therapeutics group is striving to bring hope for this somewhat neglected disease – through better diagnosis, early detection and more targeted treatment. A \$10,000 donation from Rare Ovarian Cancer Incorporated enabled the group to kickstart a world-first study into juvenile GCTs.

What we are working on

- Establishing a cost-effective, highly specific diagnostic test
- Personalised treatments based on GCT molecular processes
- Identifying the genetic mutations causing the disease

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VALI'S STORY

A devastating diagnosis

Diagnosed with ovarian cancer at age 19, Vali Creus feared she would never have children.

Vali Creus wanted to have kids for as long as she could remember. So when she was diagnosed with ovarian cancer at 19, one of her first thoughts was: "What does this mean for my fertility?"

Known for its deadly stealth, ovarian cancer is a 'silent killer' because it is often asymptomatic. But as an elite athlete Vali knew there was something wrong. She was playing basketball at state level, while also studying anatomy and biology. She was a fit young woman who understood physiology and knew that she should be in peak physical condition. Instead, she was exhausted. All the time.

Vali had reported vague symptoms to doctors since she was about 16 but had only been prescribed paracetamol. If Vali has one

regret, it's that she wasn't more assertive. She wonders whether her low-key style helped or hindered on the long road to an accurate diagnosis.

At 18, Vali found herself in front of yet another new doctor. By now she was nearing her wit's end, ticking off her symptoms in a long list – intense and escalating pain, particularly in her lower back, erratic periods followed by bleeding for weeks, strange food allergies and aching, bone-crushing fatigue.

Fortunately, her new doctor ordered a barrage of tests, correctly diagnosing Vali with endometriosis. Ovarian cancer was found during surgery for this condition and effectively treated, achieving Vali's first remission. The cancer recurred when Vali was 24, but constant monitoring meant this recurrence was detected early and, again, it was treated successfully. However, this time the treatment cost Vali her fertility. Both her ovaries were removed but one was frozen. Her doctors in 2003 anticipated that science would one day catch up and Vali would be able to achieve her dream of children.

At 27 Vali met the love of her life. They married four years later and the question of fertility again became front of mind. In 2013 Vali had the world's first successful pregnancy using the pioneering tissue graft methodology developed by Melbourne scientists. She gave birth to her twin girls, Alexis and Kaia, in November that year.

Unfortunately, when Vali's girls were born via caesarean doctors discovered the cancer had returned. It was removed in the same surgery and Vali, now 41, remains cancer free. But huge doses of chemotherapy have left her lungs permanently damaged. With the emergency of COVID-19, Vali is in a high-risk category.

"I've had a hard time, but I consider myself one of the lucky ones," Vali says. "I've got a good prognosis. I've got my girls – these amazing little people. They're too young to understand why they're extraordinary – I'll explain when they're older. For now, they just know that they are special and Mummy was very lucky to have them."



Stem cell therapy for pelvic organ prolapse

Pelvic organ prolapse (POP) is a hidden disease – while the injury happens during childbirth, the patient will not know about the damage until many years later, often during late menopause.

The potential new stem cell treatment, which is being developed in the laboratory but is not yet ready for human clinical trials, could potentially be given to women immediately after a traumatic childbirth. It means that invasive surgery could be avoided later in life.

This treatment is based on new research led by Dr Shayanti Mukherjee and PhD student Kallyanashis Paul. It follows on from earlier research by Hudson Institute researchers led by Professor Caroline Gargett that showed endometrial stem cells had tissue healing properties.

“What is really fascinating about this work is that we can potentially use a woman’s own stem cells from her endometrium, delivered in a natural plant-based product – an aloe vera-based hydrogel – to heal the woman’s own tissue injury,” Dr Mukherjee said.

What does the latest pelvic organ prolapse research show?

The study, published in *Applied Materials Today*, suggests that local delivery of endometrial stem cells in an aloe vera hydrogel could reduce or eventually replace the need for pelvic floor

Key points

- Pelvic organ prolapse develops when tissues, pelvic floor muscles and ligaments that support the pelvic organs (bladder, uterus and bowel), become damaged, usually in vaginal childbirth, causing organs to shift or ‘drop’ into or outside the vagina.
- The new treatment would reverse the decline of pelvic floor function by delivering therapeutic endometrial stem cells (eMSCs) via an aloe vera hydrogel soon after childbirth to repair an injury.
- One in four women experience pelvic floor disorders, of which one is POP.
- Hudson Institute researchers are developing a world-first new treatment using stem cells from the endometrium to heal childbirth injury.

reconstructive surgeries through early tissue repair and regeneration.

The research found that vaginal childbirth can damage tissue biomechanics, detectable at the nanoscopic level, and that this can be restored following the treatment. The study explored the hidden nature of this birth injury in preclinical models, and also validated the protective treatment delivering cells vaginally in the aloe vera-based hydrogel.

“Although birth trauma injuries occur during childbirth, its impact is often seen much

later in life when women start developing symptoms such as vaginal bulge or a dragging sensation, and bladder, bowel, and sexual dysfunction,” Dr Mukherjee said.

The study’s first author Kallyanashis Paul added: “POP is a hidden pandemic for women. It significantly disrupts their quality of life. This study, which contributes to a body of research aiming to create a tissue engineering treatment for childbirth injury to avoid women developing POP, could really make a big difference to the lives of women with the condition.”

What is the significance of the research?

There is no reliable cure for POP. Transvaginal mesh implants have been used to treat it. However, complications and side effects have resulted in an Australian Senate inquiry into its use, resulting in a recommendation that these only be used as a last resort for POP. A number of class actions have been brought against manufacturers of the mesh implants by women who suffered debilitating complications from their use.



Collaborators Monash University, Melbourne Centre for Nanofabrication (MCN)



Funders International Postgraduate Research Training and Monash Graduate Scholarships, CASS Foundation Science and Industry Endowment Fund, CSIRO, NHMRC, Victorian Government Operational Infrastructure Support Program

JESS'S STORY

Hidden pain of POP

Six months after the birth of her third child, Jess*, 35, felt something wasn't right. As she was walking 200 metres to the beach one day with her baby in a carrier, she felt an uncomfortable dragging sensation in her pelvis and had to sit down.

Jess visited her obstetrician and a pelvic floor physiotherapist and, after a 4D ultrasound, was diagnosed with severe pelvic organ prolapse.

"I could not believe this was happening to me," Jess says. "I went from feeling so happy and content in life to so scared about my future health and depressed."

Jess wears a cube pessary to support her uterus which needs to be put in place

and removed every day. While it helps with the dragging feeling, she finds it embarrassing, humiliating, and by the end of the day she is in pain. The pessary also limits many of her usual physical activities. "I still feel like I can't run or jump and do high intensity exercises," she says.

Her medical advice is to wear the pessary for as long as possible, because without it, surgery is the only other option and despite this, the prolapse can recur/reoccur.

"With the current surgical options available, things are looking bleak. I am tired of constantly thinking about it and worrying about it. I just want it fixed so I can move on and enjoy life with my beautiful babies and husband," says Jess.

Jess says it was only after confiding in friends that she discovered two others in their mid-thirties had also suffered pelvic organ prolapse and had surgery. "It's a very embarrassing thing to have happen, especially in your thirties. That's why people don't talk about it.

"The only thing that is keeping me going is reading about Professor Caroline Gargett's team's research into a potential stem cell treatment for POP," Jess says. "I am desperate for a better treatment option. The thought of having to live with a pessary for the rest of my life or having surgery now only for it to more than likely come back and need more surgery, is just not good enough. It makes me sad that this is my life now.

"I hope the stem cell team have all the funding they need to continue their very important work to find a treatment for this condition and make it available sooner rather than later."

Jess says the research investigating solutions soon after birth trauma occurs is especially important. "If there was a way to repair the damaged muscles after birth trauma, that would be absolutely ideal. It would prevent future prolapse and a life-long battle with a chronic condition."

*Jess has chosen to remain anonymous

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State-of-the-art National Centre for Inflammation Research proposed



The COVID-19 pandemic gripping the world since 2020 is a lesson in the dangerous and often fatal effects of inflammation following infection. But did you know more than half of all deaths worldwide are also caused by conditions linked to inflammation?

That's why we're proposing to establish a world-leading National Centre for Inflammation Research (NCIR) at Hudson Institute.

The centre was kickstarted with \$1 million in funding from the Victorian Government, announced in October 2020 by the Hon Jaala Pulford, Minister for Innovation, Medical Research and the Digital Economy. This funding is being used to assist with detailed planning to establish the NCIR at Hudson Institute, co-located with Monash Medical Centre in Clayton, as

well as critical seed funding to accelerate inflammation research.

Hudson Institute is home to the largest group of inflammation researchers in Australia. Scientists at the new NCIR will investigate cell and gene therapies, immunotherapies and the microbiome to treat chronic and dangerous inflammation during infection, cancer or chronic diseases.

The state-of-the-art centre will cement Victoria as a global leader in medical research and enhance the state's capability and capacity to respond rapidly to current and future health challenges, including pandemics.

The building will include facilities to manufacture therapeutics, increased capacity for clinical trials and much-needed PC3 containment laboratories to study infectious disease outbreaks and multi-drug resistant bacteria. More than 950 jobs will be created throughout the project.

Further State and Federal government and philanthropic funding will be sought to complete the project, which is expected to attract significant international commercial investment.

“If we can short circuit the pathways that lead to severe and chronic inflammation, we can have a real impact on major human diseases like sepsis, cancer, endometriosis and other inflammation-related conditions. We're calling for a national focus on this area to accelerate much needed progress.”

Prof Elizabeth Hartland
Director and CEO



“Your contribution will make a real difference to people's lives.”

Professor Elizabeth Hartland
Director and CEO

You can help improve the lives of women everywhere by supporting our women's health research today.

“I hope researchers have all the funding they need to continue their very important work to find a treatment for this condition.”

Jess
pelvic organ prolapse sufferer

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