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INVESTIGATING THE POTENTIAL OF A HUNGER STIMULATING HORMONE TO SLOW BREAST CANCER TUMOUR GROWTH

DR KRISTY BROWN EXPLAINS

"Taking discoveries out of the lab and transforming laboratory research into new treatments, diagnostic tools, and preventions for disease, 'translational research', is at the forefront of what we do here at Hudson Institute of Medical Research."

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DIRECTOR'S MESSAGE

I often talk about the importance of translating medical research into tangible outcomes for patients. Taking discoveries out of the lab and transforming laboratory research into new treatments, diagnostic tools, and preventions for disease, 'translational research', is at the forefront of what we do here at Hudson Institute of Medical Research.

It is by working together with our clinical partners, scientific collaborators and colleagues that our discoveries are transformed into medically relevant information, with the potential to change the lives of many.

Hudson Institute and its predecessors have a proud history of research discovery, innovation and translation. A number of life-changing medical advances that are now taken for granted were born in our labs.

Our scientists have shaped current IVF technology, changed practices for the prevention of SIDS and discovered Inhibin, which led to important diagnostic tests for Down syndrome and for certain types of ovarian cancer.

The next step of this journey has now begun, with the official opening on March 10 of the new Translational Research Facility (TRF), at the Monash Health Translation Precinct, by the Australian Minister for Health, the Honourable Sussan Ley.

New era in medical research

The opening of the TRF places Hudson Institute at the forefront of translational research and medicine in Australia.

Our Centre for Cancer Research and The Ritchie Centre (women's and baby health) researchers have moved into the new facility, where they are co-located with clinical and academic colleagues from our partners, Monash University and Monash Health.

The facility was born out of a long-term vision for an end-to-end story of health innovation, and significantly transforms our research capability and impact on health. It is a unique facility and enables Hudson Institute researchers to translate ground-breaking discovery research into patient care faster than ever before.

The benefits of hosting researchers, clinicians, technology platforms and a dedicated clinical trials floor within one facility are immeasurable.

As well as being unique, the environment within the TRF is collegiate. Our scientists work alongside clinicians, academics and commercial entities, creating an environment rich with opportunities to spark collaboration, innovative research and commercialisation.

The facility ensures the most efficient use of funding for optimum outcomes, ensuring we remain competitive and innovative in a difficult funding environment.

You can read more about the TRF opening on the next page.

World-first cancer trial

We are already seeing the positive impact of patient-centred collaboration in our research through the TRF.

A team, co-led by the Head of our Centre for Cancer Research, Associate Professor Ron Firestein, will soon commence a world-first clinical trial to test the effectiveness of a new class of drugs in treating two of the most commonly diagnosed cancers in Australia, prostate and colorectal cancer.

The team, including collaborators from Monash Health and Cabrini, will look to develop a test for cancer patients to assess their genetic compatibility with BET inhibitor therapy. This discovery could positively impact up to 50% of patients who may have the genetic marker.

The team is optimistic about the potential to improve survival rates and the move towards personalised cancer therapies. I hope you enjoy reading about this and other ground-breaking research in this issue of Hudson News.

Hope Funds for Cancer Research

In April, I returned from the Hope Funds Cancer Research Meeting in New York which I co-organised and spoke about research to accelerate new treatments for people with difficult-to-treat cancers.

The event brought together world experts to focus on different areas of cancer research including the cutting-edge field known as 'big data'. It was an inspirational event which included two Nobel Laureates, two Lasker Awardees and two Breakthrough Prize winners. Also present were the major contributors to the drugs Neupogen, Rituxan, and the 7-plus-3 therapy for acute myeloid leukemia.

Along with the growth and availability of new technologies, the way cancer researchers collect and store genomic biological and statistical data is changing rapidly. How we interpret and use this powerful data has real potential to accelerate new targeted treatments for cancer patients. Collaboration is a critical component in enabling the most beneficial outcomes from data interpretation for cancer patients. Participants at the meeting explored novel ways of increasing scientific collaboration particularly around 'big data'.

Professor Bryan Williams
Director, Hudson Institute of Medical Research

ADVANCING HEALTH DISCOVERY

The Translational Research Facility is set to transform the Hudson Institute's research capability

Hudson Institute researchers are better placed than ever before to translate their basic research discoveries into clinical treatments, with the opening of the new $87.5 million Monash Health Translation Precinct (MHTP) Translational Research Facility (TRF) in October 2015.

Set across five levels, the TRF co-locates Hudson Institute researchers with both Monash University researchers and Monash Health clinicians to enhance collaboration and links that expedite the translation of vital research discoveries to patients.

Driving this research translation is an entire floor dedicated to clinical trials and clinical research, including a 30-bed clinical trials centre, and medical imaging facilities. Other key features of the new facility include:

- Integrated translational research laboratories.
- An entire floor of specialised research platforms to support MHTP research: medical genomics, micro imaging, proteomics and cell based therapies.
- Integrated capacity for molecular pathology, tissue banking, bioinformatics, bio statistics and PC2/PC3 facilities.
- A vibrant learning and engagement hub, comprising a 250-seat lecture theatre and associated conference rooms with state-of-the-art audio-visual technology.

This state-of-the-art facility creates a unique environment where researchers and clinicians work side-by-side, positioning the MHTP and Hudson Institute as an innovator in translational research.

"There is no other facility in Australia so ideally positioned to translate basic research into life-changing and life-saving discoveries that will drive solutions to our most pressing diseases," Hudson Institute Director, Professor Bryan Williams, said.

The Ritchie Centre and Centre for Cancer Research researchers from Hudson Institute have moved into two dedicated floors within the TRF, alongside the clinical research floor and an another entire floor housing sophisticated cutting-edge technologies.

The total investment in the TRF is $87.5 million, of which $71 million has been provided by the Commonwealth Government.

The Translational Research Facility will transform the Hudson Institute's research capability, accelerating our research to make a far greater impact on health.

Inset photo: Australian Minister for Health, the Hon Sussan Ley MP with translational research patient Mark Wilken.

Investigating the potential of a **hunger stimulating hormone** to slow breast cancer tumour growth

One in eight women - mothers, daughters, sisters, friends - will be diagnosed with breast cancer during their lifetime, and eight women die of the disease in Australia every day.

Dr Kristy Brown

Centre for Cancer Research scientist, Dr Kristy Brown will investigate the potential of a hunger-stimulating hormone to slow breast cancer tumour growth, thanks to a National Breast Cancer Foundation (NBCF) Career Development Fellowship.

Dr Brown and her team discovered a mechanism to explain why being overweight or obese increases a woman's risk of developing oestrogen-dependent breast cancer after menopause. These women are also less responsive to treatment and more likely to die from the disease. The team is now investigating an appetite-stimulating hormone produced by the gut, called ghrelin, and its role in preventing and treating breast cancer in these women.

Dr Brown discovered that this 'hunger hormone' can stop the body producing oestrogen, effectively starving the tumour and halting its growth.
Dr Brown explains, "Oestrogen, in addition to being produced by the ovaries, is also produced by fat cells, and the majority of obesity-related breast cancers are oestrogen-dependent.

"We have found that ghrelin not only stops the production of oestrogen from the breast fat and the growth of oestrogen-dependent breast cancers, it also acts on tumours that are not dependent on oestrogen and for which there are limited treatments available"

"Ghrelin is a naturally occurring hormone, with limited toxicity, meaning most women would be able to tolerate it," Dr Brown said.

While the research is currently at the preclinical phase, Dr Brown is hopeful of moving this research into a pilot study and clinical trial within the next two years.

"Our lab is also investigating the possible interaction between breast inflammation, the metabolism of cells within the breast, and the production of oestrogen that drives tumour growth.

"This will help us identify new therapy options for the effective treatment and prevention of breast cancer," she said.

Through her work at Hudson Institute, Dr Brown hopes to contribute to the NCBF's goal of "zero deaths from breast cancer by 2030."

CLINICAL TRIAL BRINGS PERSONALISED TREATMENT FOR PROSTATE AND BOWEL CANCER A STEP CLOSER

Dr Arun Azad (left) with Associate Professor Ron Firestein

Prostate and colorectal cancers are two of the most commonly diagnosed cancers in Australia. More than 3000 men die of prostate cancer and over 4100 lives are claimed by colorectal cancer every year in Australia.

Targeted genetic treatment for these diseases is now a step closer, with a world-first clinical trial at Hudson Institute and Monash University set to test the effectiveness of a new class of drugs called BET inhibitors in treating prostate and colorectal cancer.

A team of clinicians and researchers will lead the innovative three-year trial, involving 24 patients with stage four prostate and colorectal cancer, for whom all other forms of treatment have failed.

The project builds upon work done by co-lead of the project and head of Hudson's Centre for Cancer Research, Associate Professor Ron Firestein, at Genentech in the US, where he identified a genetic marker that may explain why only some patients respond to BET inhibitors.

"BET inhibitors are a relatively new class of cancer drugs that target tumour cells at a genetic level by essentially 'switching off' the expression of certain cancer genes," Associate Professor Firestein said.

"Clinical trials of BET inhibitors around the world are showing results that are promising, but ours is the first to target the treatment to patients with a specific genetic marker."
Associate Professor Firestein says the aim is to develop a test for use in cancer patients to assess their genetic compatibility with BET inhibitor therapy.

Co-lead, consultant medical oncologist at Monash Health and Monash University Senior Research Fellow, Dr Arun Azad, believes around 50% of prostate and colorectal cancer patients have the RNA biomarker and predicts these patients will respond well to the new class of drug.

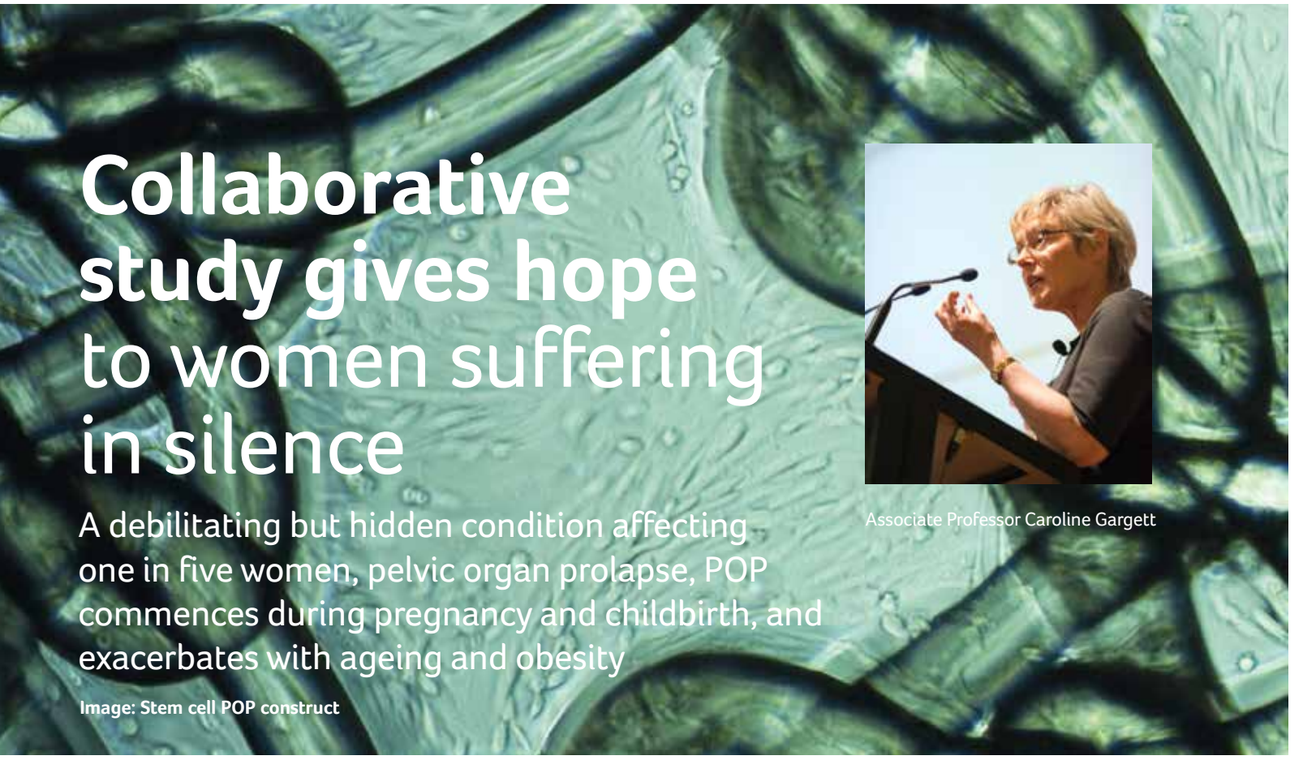
"We're ultimately hoping to increase the range of therapeutic options available to prostate and colorectal cancer patients," added Dr Azad.

"We need to use these treatment options the smartest way we can and not use the scattergun chemotherapy approach where we give all patients the same treatment, and if 20% respond, that's great. What about the other 80% of patients for whom chemo was never going to work, who suffered unnecessary toxicity, and wasted time, effort and a lot of money?" Dr Azad said.

Dr Azad and Associate Professor Firestein are very optimistic about the potential for epigenetic therapies like BET inhibitors.

"Improving the effectiveness of targeted cancer therapies not only improves survival rates, it also provides more options to patients who invariably develop chemotherapy resistance," Associate Professor Firestein said.

This project is being funded by a $2 million grant from the Victorian Cancer Agency.



Collaborative study gives hope to women suffering in silence

A debilitating but hidden condition affecting one in five women, pelvic organ prolapse, POP commences during pregnancy and childbirth, and exacerbates with ageing and obesity

Image: Stem cell POP construct

Associate Professor Caroline Gargett

New treatment for millions of women affected by a hidden condition, pelvic organ prolapse (POP), will be the focus of Dr Shayanti Mukherjee's novel bioengineering project.

Dr Shayanti Mukherjee

A debilitating but hidden condition affecting one in five women, POP commences during pregnancy and childbirth, and exacerbates with ageing and obesity.

Dr Mukherjee is investigating new stem cell therapies for this condition using surgical meshes. She is being trained for the project by A/Prof Caroline Gargett from The Ritchie Centre and Dr Jerome Werkmeister from CSIRO, thanks to a highly competitive Science and Industry Endowment Fund (SIEF) John Stocker Postdoctoral Fellowship.

"At present, millions of women worldwide suffer from POP with very limited treatment options," said Dr Mukherjee, from The Ritchie Centre - Hudson Institute and Monash University.

"POP is associated with sexual, bladder, and bowel dysfunction, including incontinence that profoundly affect the quality of life and daily functioning of sufferers; in Australia, more than $200 million was spent on urinary incontinence in 2009."

In the last decade, pelvic support using surgical meshes (primarily synthetic) has been heavily employed with reports of successful outcomes. However, the US Food and Drug Administration (FDA) issued Public Health Notifications in 2008 and 2011 due to significant and unacceptable mesh-related complications, leading to the withdrawal of several brands of vaginal surgical meshes from the market.

Dr Mukherjee said there are currently no clinical trials on cell-based therapies for POP incorporating surgical implants in or outside Australia.

"With the elderly population expected to double by 2030, POP is expected to become more prevalent without any reliable treatment options, representing a significant health and economic challenge for Australia and world-wide," added Dr Mukherjee.

To address this major health challenge, Dr Mukherjee's project will develop new surgical constructs for the prevention and treatment of POP, using hydrogels to deliver stem cells to the vaginal walls or pelvic floor muscles to prevent women developing pelvic organ prolapse.

"POP is a hidden burden — women don't talk about it, they suffer in silence," said Dr Mukherjee.

"My project will also develop new options and long term surgical treatment options for women with POP."

This important project significantly adds to a large collaborative study currently funded by NHMRC, involving researchers and clinicians from The Ritchie Centre at Hudson Institute, Monash University, CSIRO and Monash Health.

OUTSTANDING ACHIEVEMENT – WOMEN IN SCIENCE

Dr Maria Kaparakis-Liaskos was presented with an inaugural veski inspiring women fellowship by The Honourable Linda Dessau AM, Governor of Victoria, at an award ceremony held at Government House in December.

The veski inspiring women fellowship helps outstanding female leaders to continue their research while juggling career and carer commitments. It will enable Dr Kaparakis-Liaskos, from the Centre for Innate Immunity and Infectious Diseases, to continue progressing the upward trajectory of her career while raising her two young children.

Dr Kaparakis-Liaskos' 2015 achievements were outstanding. In addition to the inspiring women fellowship, she has published work in prestigious journals, won Young Investigator Awards and was invited to present her work at international and national conferences, all while caring for her children.

"This fellowship will enable me to continue the momentum of my research, expand my international and national collaborations, and establish a laboratory team while I am returning to work from maternity leave," Dr Kaparakis-Liaskos said.

"My strong collaborators and support network at Hudson Institute and overseas have proven integral to the success of my research and achievements during my career break."

Her research is focused on examining the mechanisms of immune suppression during Helicobacter pylori infection, a bacterium in the stomach affecting more than three billion people worldwide and a cause of gastric cancer and stomach ulcers.

The veski fellowship will support her expanding research program by providing funding for a research assistant and a PhD student while Dr Kaparakis-Liaskos is returning to full-time work.

Photo courtesy veski.org.au

The Honourable Linda Dessau AM, Governor of Victoria, presenting Dr Maria Kaparakis-Liaskos with her award.

"The veski inspiring women fellowship is a visionary fellowship that promotes the advancement of women in science and I am honoured to be part of it. It is vital that female scientists are supported to continue the momentum of their research during essential career breaks," said Dr Kaparakis-Liaskos.

PIONEERING RESEARCH MAY INCREASE IVF SUCCESS RATE

Professor Justin St. John

New research from Professor Justin St. John and his team in the Centre for Genetic Diseases has shown that boosting egg health and development could significantly help a woman to fall pregnant during IVF.

The researchers showed that supplementing the energy-producing mitochondrial DNA in a woman's egg with mitochondrial DNA from another of her eggs, while sperm was being introduced, improved egg quality and increased the chance of fertilisation.

Professor St. John, Head of the Centre for Genetic Diseases, says supplementing the eggs with mitochondrial DNA created better quality eggs which resulted in an increased chance of fertilisation and healthy embryos developing.

"It's becoming clearer that mitochondrial DNA has a bigger role to play in fertilisation outcome and embryo development," Professor St. John said.

A healthy egg normally contains more than 150,000 copies of mitochondrial DNA, which help to provide the 'energy' an egg needs to develop during and after fertilisation.

"Failure to have enough mitochondrial DNA can result in fertilisation failure, embryo arrest and other genetic disorders," he said.

Many women undergoing IVF have poor quality eggs with less than 50,000 copies of mitochondrial DNA – too few for an egg to fertilise or develop into an embryo.

A woman's age, environment (toxins, smoking), and medical issues are some of the factors impacting egg health.

This discovery shows that the health of an egg depends, in part, on the number of mitochondrial DNA copies that exist in an egg cell.

The research was undertaken by Professor St. John in conjunction with first authors Dr Gael Cagnone and Te-Sha Tsai (PhD student) and collaborators Dr Yogeshwar Makanji, Pamela Matthews, Jodee Gould and Dr Matthew McKenzie (all from Hudson Institute) and Dr Kirstin Elgass (Monash Micro Imaging Microscopy Specialist).

If you would like to donate to this important research or support Professor St. John's work in other ways, please contact the Hudson Institute's Head of Philanthropy on +61 3 85722701. All donations are tax deductible and your entire donation will be used to continue his work.

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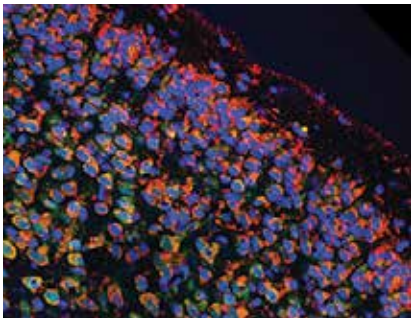
Join - Our Bequest Circle. We are deeply appreciative of the generosity and foresight of those who leave a bequest to support our research. To reflect our appreciation we have established our Bequest Circle.
Please let us know if you have included us in your Will and we will invite you to join with like-minded people at invitation only events with our senior researchers.

To read more about leaving a bequest to the Hudson Institute visit:
www.hudson.org.au/bequests/

For a confidential discussion on how you can support our research through your Will or to receive a copy of our bequest brochure, please contact our Head of Philanthropy on +61 3 85722701.



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