

# breakthrough

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Garvan Institute  
of Medical Research

# Welcome from our Executive Director



**Dear Garvan family,**

It's my pleasure to share with you the final edition of *Breakthrough* magazine for 2019.

We've had a successful and productive year at the Garvan Institute. Driven in large part by your generosity, our researchers continue to discover the unknown in health and disease through high impact research findings.

In this edition you'll learn about a study, led by Garvan's Professor Katherine Samaras, to assess whether we can help prevent the rapid decline of dementia using a common type 2 diabetes treatment called 'metformin'.

You'll also find a new discovery from our pancreatic cancer researchers. Led by Associate Professor Paul Timpson, the team have shown how targeting the tissue around pancreatic cancer, in addition to the tumour itself, could not only hold the key to stopping the spread of the disease but also improve the results of chemotherapy.

We're running even more free public seminars throughout 2020, as well as regular behind-the-scenes tours of the Institute (page 10). We'd love to see as many of you as possible at our seminars and tours. So please register to attend with your friends, family and community groups. If you're unable to join us in person, our seminars can be viewed on [Facebook.com/garvaninstitute](https://www.facebook.com/garvaninstitute).

Finally, I'd like to offer my sincerest thanks for the support you've provided our research this year. Our incredible researchers simply couldn't investigate better ways to diagnose, treat and ultimately, prevent, diseases without your generosity.

Wishing you all the best for the holiday season.

Yours sincerely,

**Professor Chris Goodnow FAA FRS**

Executive Director

The Bill and Patricia Ritchie Foundation Chair

## NEW RESEARCH

### Gene map of the retina

**Garvan scientists have led the development of the world's most detailed gene map of the human retina, providing new insights which will help future research to prevent and treat blindness.**

The retina, a thin layer of cells at the back of the eye that enables us to see, was mapped as part of the Human Cell Atlas Project. A global project, the Human Cell Atlas aims to create reference maps of all human cells to better understand, diagnose and treat disease.

The study, co-led by Associate Professor Joseph Powell, Head of the Garvan-Weizmann Centre for Cellular Genomics, employed cutting-edge cellular genomics technologies to examine the complex genetic outputs of more than 20,000 cells in order to develop a profile of all major cell types in the retina and the genes they 'express' to function normally.

As a result, researchers can begin to understand the genetic signals that cause retinal cells to stop functioning, leading to vision loss and blindness. The insights that researchers worldwide can gain from this gene map present an entirely new way to approach the treatment and prevention of eye disease.

 Read more at: [garvan.org.au/genetic-code](https://garvan.org.au/genetic-code)

### A big picture microscopic event

**Every time a human cell divides, it has to copy its entire genome accurately – a two-metre, six million letter long instruction manual, through a process called DNA replication.**

The process requires thousands of proteins to work in sync to carry out specialised steps and accuracy is key, as errors in the copy can lead to diseases such as cancer.

To make better sense of the complex process of DNA replication, Garvan's Professor Sean O'Donoghue and his colleagues have illustrated the process in an entirely new way – a step-by-step roadmap of how a cell copies its DNA.

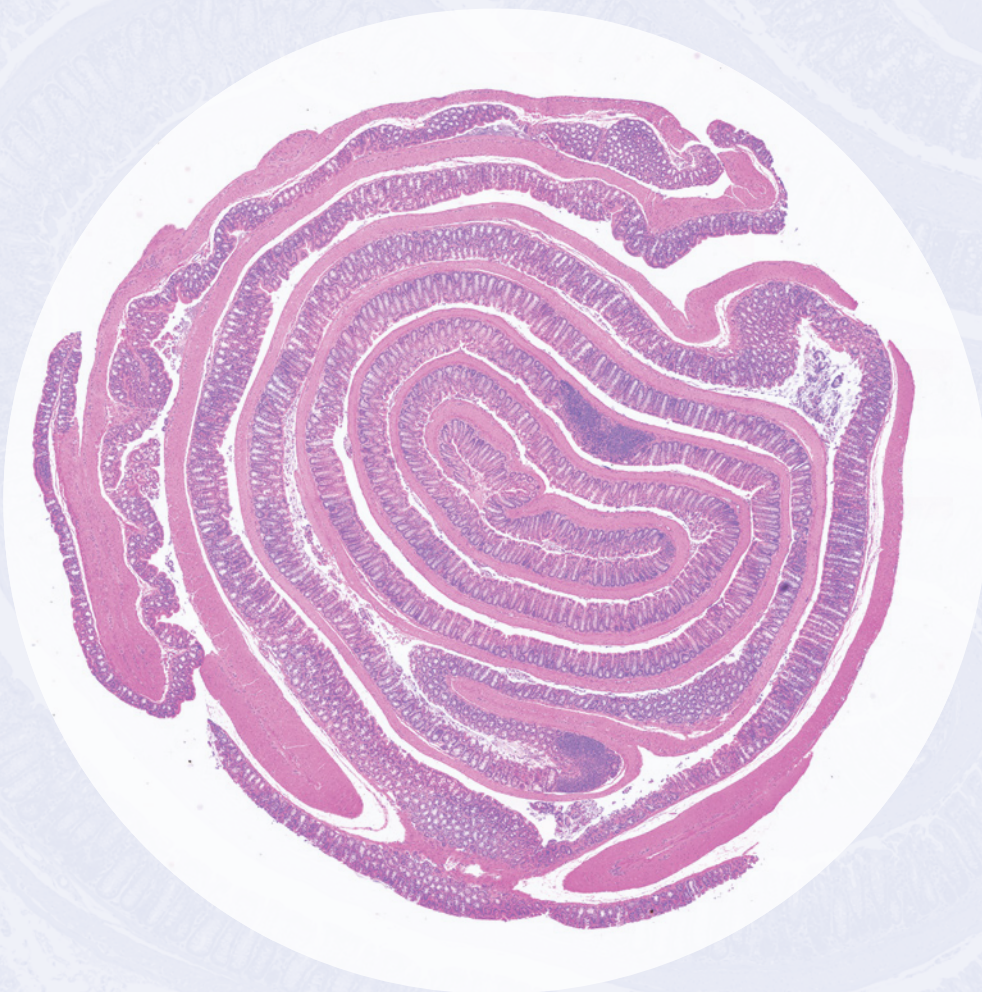
Incorporating the findings from over 280 scientific articles published on the molecular events involved in DNA replication, an interactive graphic marks out, in clockwise sequence, the key events that control how DNA is copied inside a cell.

This roadmap offers researchers an easily understandable glance at the key proteins involved at different stages of the process and, with a single click, allows them to drill down to find out further details, providing a unique perspective that gives researchers a fresh view of existing knowledge.

 Read more at: [garvan.org.au/microscopic](https://garvan.org.au/microscopic)

# THROUGH THE MICROSCOPE

Garvan researchers are uncovering gene variants that shaped the evolution of the human immune system.



**With the likeness of a carefully arranged mosaic, this microscopy image reveals some of the complexities of the digestive system. Such images – this one a cross section of a mouse colon imaged by immunologist Dr Nathan Zammit – help our researchers understand the impact that genetic variants may have on the human gut.**

In a recent study, a Garvan-led research team discovered a gene variant that modern humans acquired from an extinct human population known as the Denisovans. The variant appears to have 'tuned' the human immune system to better adapt to changing pathogens in the environment 50,000 years ago.

By investigating the impact of this Denisovan variant on the mouse colon, the researchers discovered that tuning immunity comes at a cost: a heightened immune response can attack the body's beneficial microbes found in the gut.



*This image graces the cover of the October 2019 issue of the prestigious scientific journal Nature Immunology, in which the research was published.*



Read more at:  
[garvan.org.au/immunity-boost](https://garvan.org.au/immunity-boost)



# A loving legacy to last

A lifetime's desire to help others has led Sid Lewis to become one of Garvan's Partners for the Future.

Sid Lewis has always put others before himself. In 1942 at the age of 16, he joined the army by claiming he was 18 in order to serve his country. After being stationed in Papua New Guinea during World War Two, he joined the Army Reserve and spent 27 years in the 1/15 Lancers.

This desire to help others is what led him to become one of Garvan's *Partners for the Future*, in memory of his beloved wife Kit.

Sid and Kit met on a blind date and were married for over 65 years. When Kit was diagnosed with type 1 diabetes in her 50s, Sid was highly involved in her care, learning all that he could to ensure her condition was properly managed. During his research and Kit's treatments they were introduced to the Garvan Institute, and were highly impressed by the breakthrough work led by our scientists.

Kit and Sid fought hard against her diabetes for many years, including during their travels around Australia. Sid said the importance of medical research for all our community stood out to us during these times visiting remote areas. "I think of the hard conditions the people in remote Australia live in, and then I look at the other side of the coin, and think about the research Garvan does, and the potential that medical research has in helping not only people living in cities, but our people in the outback as well."

Sid and Kit shared a deep love for each other and a love for our land and its people. After the sad passing of Kit in 2015, Sid knew that leaving a bequest to Garvan in his Will was an important way he could honour the memory of his beautiful wife, and provide a future gift back to the land and people they experienced together and loved so much.

"It's a revelation what's occurring in the world of medical research and Aussies have always been unique in wanting to help each other out," says Sid. "If other people are able to leave a bequest to Garvan as well, that legacy will continue on in a very meaningful way for so many people."

**If you would like information about leaving a gift in your Will as a tribute to your loved ones, please contact Donna Mason, Bequest Manager on (02) 9295 8559, email [bequests@garvan.org.au](mailto:bequests@garvan.org.au) or visit [garvan.org.au/bequest](http://garvan.org.au/bequest)**



# The homeland of modern humans

**A landmark study, published in the prestigious journal *Nature*, pinpoints the birthplace of modern humans in southern Africa and suggests how past climate shifts drove their first migration.**

Professor Vanessa Hayes, from Garvan and the University of Sydney, and Garvan's Dr Eva Chan, in collaboration with researchers from Africa combined the disciplines of genetics, geology and climatic physics to determine where anatomically modern humans first emerged and their subsequent migration. This study provides a window into the first 100 thousand years of modern humans' history.

 Read more at: [garvan.org.au/homeland](http://garvan.org.au/homeland)



Prof Vanessa Hayes learning how to make fire with Jul'hoansi hunters in the now dried homeland of the greater Kalahari of Namibia. From left to right: N#amce Sao, |kun N#amce, Vanessa Hayes and |kun |kunta. *Image by Chris Bennett, Evolving Picture.*

# White Butterfly finds its wings

**In October, *White Butterfly* hosted its inaugural fundraising event at the Woolwich Pier Hotel in Sydney, raising almost \$200,000 for Garvan's breast cancer research.**

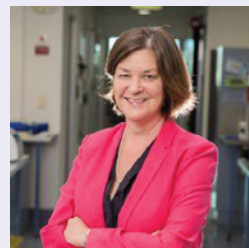
More than 500 people purchased tickets to the White Butterfly Garden Party to raise funds for Garvan in honour of Vanessa Juresic, who tragically lost her life to triple negative breast cancer in May 2018.

Guests were joined by guest speaker, Elle Halliwell, MC, Edwina Bartholomew and Garvan's Associate Professor Alex Swarbrick who explained the current breast cancer research programs underway at the Institute.

We extend our sincere thanks to Sophie and the Juresic family for their support and dedication, as well as the White Butterfly committee, the generous sponsors and entertainment and all who donated to our triple negative breast cancer research.

# Garvan epigenetics leader honoured with NSW Premier's Prize

Only few scientists hold the claim to have pioneered technology that enabled a completely new area in research. Garvan's Professor Susan Clark is one.



**For her pivotal contributions to the field of epigenetics, Professor Clark was awarded the 2019 NSW Premier's Prize for Excellence in Medical Biological Sciences.**

*Prof Susan Clark FAA*

Professor Clark, Genomics & Epigenetics Research Theme Leader at Garvan, witnessed the advent of epigenetics in the 1970s – the discovery that modifications to DNA can control how genes are read. She published one of the first research papers to show the significance of epigenetic silencing in cancer. Professor Clark has pioneered the field of cancer epigenetics ever since.

A Fellow of the Australian Academy of Science and Senior Principal Research Scientist of the NHMRC, Professor Clark has made seminal contributions to a field whose implications are only beginning to be realised. She has also mentored Garvan researchers for 15 years.

"We're still only seeing the tip of the iceberg of how DNA is read and interpreted and it may well take another 30 years until we understand it completely," says Professor Clark. "The legacy I want to leave is to share my passion and to see the amazing individuals I've mentored continue this work – it's like seeing lights coming on all over the world."

 Read more at: [garvan.org.au/premiers-prize](http://garvan.org.au/premiers-prize)



# NEW HOPE

## for dementia

A Garvan-led study will investigate the potential for a safe, commonly prescribed medication for dementia – one of the most devastating conditions affecting elderly individuals today.

**Dementia is a debilitating collection of symptoms caused by disorders affecting the brain, and impacts thinking, behaviour and the ability to perform everyday tasks. In Australia, dementia is the second leading cause of death and affects more than 400,000 individuals.**

Professor Katherine Samaras, Head of the Clinical Obesity, Nutrition and Adipose Biology lab at the Garvan Institute of Medical Research and endocrinologist at St Vincent's Hospital Sydney, is pioneering a new approach to treating the condition.



Prof Katherine Samaras



***“We need better strategies to prevent cognitive decline and dementia, in order to optimise well-being and quality of life, and maintain independence, right into old age. I hope this important study will be life-changing to dementia patients not only in Australia, but worldwide.”***

### **New potential for existing therapy**

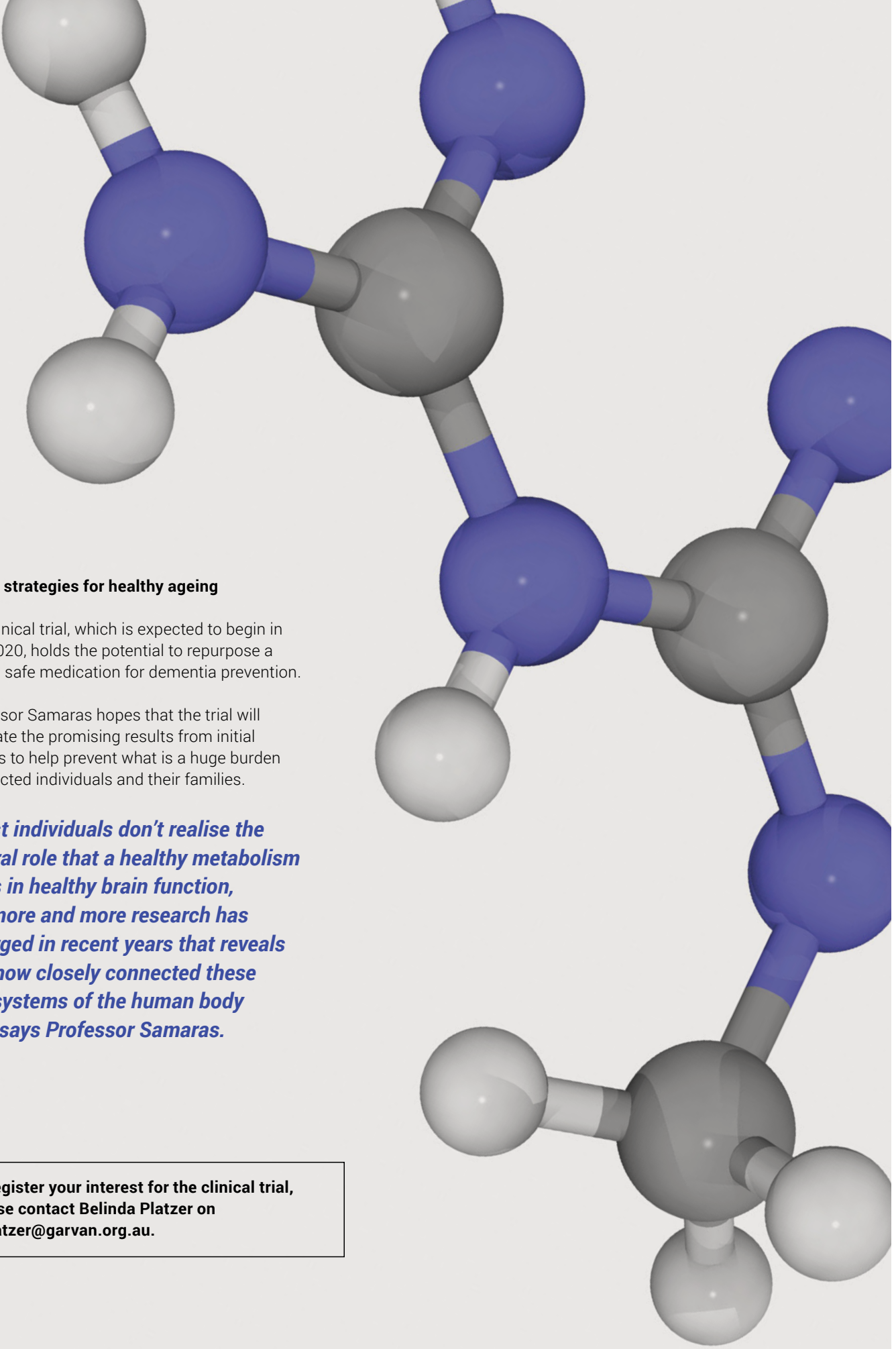
With a team of international collaborators, Professor Samaras will carry out a large-scale clinical trial to assess whether metformin, a common treatment for type 2 diabetes, can help prevent the rapid decline of dementia.

The study has significant potential to help slow or stop cognitive decline and structural brain changes in people at risk of dementia.

Metformin has been used safely to treat type 2 diabetes for 60 years. Studies over the last decade have revealed evidence of metformin's benefits in cancer, heart disease and weight management and recently, it was shown to slow decline in cognition in a small clinical trial.

With collaborators, Professor Samaras will conduct a large, randomised controlled trial of metformin in participants at risk of dementia and assess their cognitive function over three years. The research team comprises an international group of experts, including Australia's leading dementia clinician researchers and experts from metabolism, cardiology, pharmacology and statistics.

The study will also measure biomarkers of cognitive symptoms, conduct brain imaging to evaluate changes to the brain structure, connectivity and blood flow, and will assess health-related quality of life, functional independence and mobility, and psychological health.



### **Better strategies for healthy ageing**

The clinical trial, which is expected to begin in mid-2020, holds the potential to repurpose a cheap, safe medication for dementia prevention.

Professor Samaras hopes that the trial will translate the promising results from initial studies to help prevent what is a huge burden to affected individuals and their families.

***“Most individuals don’t realise the central role that a healthy metabolism plays in healthy brain function, but more and more research has emerged in recent years that reveals just how closely connected these two systems of the human body are,” says Professor Samaras.***

**To register your interest for the clinical trial, please contact Belinda Platzer on [b.platzer@garvan.org.au](mailto:b.platzer@garvan.org.au).**

# S L O W I N G

## the spread of pancreatic cancer

An international team led by Garvan researchers has revealed how aggressive pancreatic cancer cells change their environment to enable easy passage to other parts of the body (or metastasis) – the main cause of pancreatic cancer related death.



A/Prof Paul Timpson  
and Dr Thomas Cox

The researchers discovered that some pancreatic tumours produce more of a molecule called 'perlecan' to remodel the environment around them, which helps cancer cells spread more easily to other parts of the body, and also protects them against chemotherapy.

In a mouse model, the researchers showed that lowering the levels of perlecan resulted in a reduction in the spread of pancreatic cancer and improved response to chemotherapy.

Led by Associate Professor Paul Timpson, Head of the Invasion and Metastasis laboratory, and Dr Thomas Cox, leader of the Matrix and Metastasis group, the research may provide a promising new path to more effective treatment options for individuals with pancreatic cancer, as well as other cancers.

### A spotlight on the tumour matrix

Pancreatic cancer is one of the most lethal forms of cancer, with a five-year survival of ~9% in Australia. In its early stages, pancreatic cancers often show no obvious signs or symptoms and by the time a cancer is diagnosed, it has often begun to spread outside the pancreas.

In their study, the researchers compared the tissue around tumour cells in both metastatic (spreading) and non-metastatic (non-spreading) pancreatic cancers. This tissue – known as the 'matrix' – acts like a glue that holds different cells in an organ or in a tumour together.

Using mouse models, the team extracted fibroblasts – cells that produce most of the matrix – from spreading and non-spreading pancreatic tumours. By mixing these different fibroblasts with cancer cells, the researchers found that remarkably, cancer cells from a non-spreading tumour began to spread when mixed with fibroblasts from a spreading tumour.

Using state-of-the-art mass spectrometry techniques, the researchers discovered several molecules that the fibroblasts from metastatic tumours produced at significantly higher levels than the fibroblasts from non-metastatic tumours.

"What we discovered is a previously unknown set of matrix molecules that aggressive pancreatic cancer cells use to shape the tissue around them, which prevents chemotherapy from working and allows the cancer cells to spread around the body," explains Dr Cox.

### An untapped resource

Using gene-editing techniques, the researchers reduced the levels of one of the molecules called perlecan in mouse models of aggressive metastatic pancreatic cancer. Through advanced live imaging techniques, the researchers tracked individual cancer cells and revealed that lowering the levels of perlecan not only reduced the spread of cancer cells, but that tumours also responded better to chemotherapy.

The researchers hope that specifically targeting aggressive fibroblasts in patients harbouring precise genetic changes will allow them to make pancreatic cancer more susceptible to currently approved treatments.





***“Most cancer therapies today aim to target cancer cells themselves. The environment of tumours is a potential untapped target for cancer therapy and one which we intend to explore further,” says Associate Professor Timpson.***

**If you can, please donate today to support our pancreatic cancer research: [garvan.org.au/donate](https://garvan.org.au/donate)**



# Learning from the best

Several times a year, Garvan hosts free public seminars to share the latest advances in our research with our community.

## Our seminars

Our seminars give you the opportunity to hear from some of the world's leading researchers and learn about medical genomics, epigenetics, and cellular genomics; cancer; diseases of immunity and inflammation; and diseases of ageing affecting bone, brain and metabolism.

Each seminar features presentations from four to six researchers from across the Institute, followed by a Q&A panel session, giving you the opportunity for additional information and to engage with the researchers directly.

All seminars take place in the auditorium at the Garvan Institute of Medical Research, 384 Victoria Street (enter via Burton Street), Darlinghurst, NSW 2010.

Our seminars are free of charge, but registration is essential.

**Please visit [garvan.org.au/public-seminars](https://garvan.org.au/public-seminars)**

## Day seminars

	<b>10am to 11:30am</b>
Lifestyle and disease	25/03/2020
Cancer	24/06/2020
Diseases of the brain and ageing	23/09/2020
Autoimmunity and chronic disease	09/12/2020

## Evening seminars

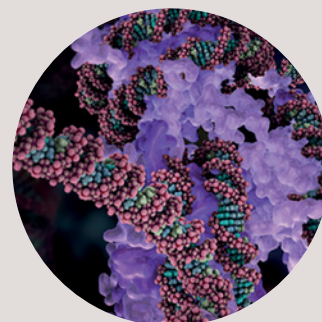
	<b>6pm to 7:30pm</b>
Get into your genes	22/07/2020
The Microbiome - inside your gut	21/10/2020

## Behind the scenes tours

A tour of our site in Darlinghurst, Sydney will give you the chance to see Garvan's state-of-the-art scientific facilities and laboratories first hand, as well as an exclusive opportunity to learn about our research.

Tours start at 10am and run for approximately 1.5 hours. They are held multiple times throughout each month with a recommended group size of 15 people.

**Book a tour here: [garvan.org.au/tours](https://garvan.org.au/tours)**



# PAINTING for Parkinson's

Now a renowned artist, Bernie McGrath, has generously donated the proceeds of a number of his artworks to support Garvan's Parkinson's research.



**Bernie McGrath was diagnosed with early onset Parkinson's disease 20 years ago, at the age of 42. He and his wife Elizabeth had two young children and a thriving real estate business. His diagnosis came as a shock to both himself and his family since Bernie was so young.**

As his condition developed and was more noticeable, he began having trouble doing his buttons up and his writing began to shrink in size. "He was signing contracts and the signatures were getting tiny like a little ant had written it ... as time progressed with his business, I used to have to dress him and then eventually I went to work in his business to help him too, because it was pretty bad," says Elizabeth.

***"It would be wonderful to find a solution or some sort of cure or to be able to manage it a lot better. If you can afford it, it is a tremendous thing to be able to give to medical research," says Bernie.***

In 2008 Bernie underwent deep brain stimulation at the Royal North Shore hospital in Sydney. Following his procedure Bernie began to feel more creative and started playing around with paints, reinventing himself as an artist – "it has given him a whole new lease on life," says Elizabeth.

There are 100,000 Australians living with Parkinson's. The available treatments and interventions, like deep brain stimulation, address only the symptoms of Parkinson's, not the progression of the disease.

Garvan, along with the Shake It Up Australia Foundation, the University of Sydney, the Cure Parkinson's Trust (UK), Michael J Fox Foundation (USA) and Parkinson's Australia, has established the Australian Parkinson's Mission. An innovative research program, the Australian Parkinson's Mission will combine clinical trials with genomics research for people with Parkinson's. The clinical trial component is anticipated to begin in early 2020.

Now a renowned artist, Bernie has generously donated the proceeds of a number of his artworks to support Garvan's Parkinson's research.

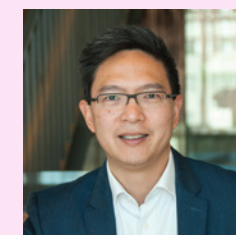


## Clinical Trial Spotlight

**Breast cancer is the most commonly diagnosed cancer in Australia and claims the lives of eight women every day.**

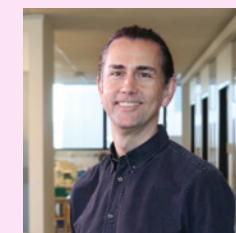
**Thanks to decades of research, the five-year survival rate for women who are diagnosed is now at 91%, but there is still more work to do. With 1 in 7 Australian women diagnosed by the age of 85, and with Australia's increasingly ageing population, it is critical to continue to work towards better treatments.**

In order to undertake novel research, access to human tissue is critical. Project SHARE (Specimens Help All Research Efforts) is a program that encourages people undergoing breast surgery at St Vincent's Hospital to donate tissue to research at the Garvan Institute.



A/Prof Elgene Lim

Led by Garvan's Associate Professors Elgene Lim and Alex Swarbrick, Project SHARE makes the donated tissue samples accessible to breast cancer researchers to underpin their research endeavors.



A/Prof Alex Swarbrick

Garvan is home to one of the largest breast cancer research programs in Australia. Our scientists are conducting cutting-edge research on the progression of breast cancer, and the development of new treatments. Their research focuses on cancer metastasis, resistance to anti-estrogen therapies, finding the 'off-switch' for triple negative breast cancer, cancer metastasis in bone, increasing sensitivity to endocrine therapies and more.

A number of historical breakthroughs, such as the development of a new therapeutic approach that specifically targeted the HER-2 molecular receptor in breast cancer, have only been made possible through the analysis of archival human tissue samples. Today, as healthcare moves increasingly towards precision medicine in part, the need for tissue samples will only increase.

**This research project is supported by Love Your Sister.**

**To find out more, or arrange to donate a tissue sample from your surgery to research, please contact: Claire Gray, Breast Cancer Clinical Research Nurse (Mon-Thur)**

**claire.gray@svha.org.au  
02 9355 5708**

# Be part of progress

Please use this form to make a donation or if you would like further information. We would love to hear from you.

Which scientific areas are you interested in?

Other feedback?

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Please complete this coupon and return it to:

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 Call: 1300 73 66 77 (9am to 5pm)

 Fax: (02) 9295 8136 (you can use this coupon)

 Online: [garvan.org.au/donate](https://garvan.org.au/donate)

## Donations made in memory of loved ones

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Trevor W Annetts  
Jeanette Barrot  
Grace Bird  
Gordon Bower  
Lynn Bright  
Jane Bryant  
Joan Cairns  
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Jarrod Warnes  
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Lynette Watts  
Peter White  
Joan E Willis  
Beryl A Wilmot  
Helen Wong  
Lorna Worgan  
Danuta Zmitrowicz

## Donations made to celebrate a special occasion

### Mr & Mrs André & Jen Piaskowski

were married at the Royal Motor Yacht Club, Newport on 15th September. In lieu of gifts, Mr & Mrs Piaskowski asked for donations to Garvan's research. Thank you, and congratulations!



### Yash and Rosie's Wedding

### Freda Abram's 70th Birthday

### In celebration of Dr James Gnanapragasam

### Nina Leibovitch's 91st Birthday

### Yvonne Meyers' 80th Birthday

### Jen and Andre Piaskowski's Wedding

### Thea Riesel's Birthday

# CLINICAL STUDIES

We offer a range of clinical trials at The Kinghorn Cancer Centre for the treatment of patients with breast cancer. Find the full list at [garvan.org.au/breast-cancer-clinical-trials](https://garvan.org.au/breast-cancer-clinical-trials).

## Personalised therapy for rare and uncommon cancers

We offer the Molecular Screening and Therapeutics (MoST) clinical trials which personalise experimental treatment for patients with rare cancers based on an individual's unique personal and cancer genetic profile.

Find more information at [garvan.org.au/genomic-cancer-medicine-program](https://garvan.org.au/genomic-cancer-medicine-program)

## PREDICT prediabetes clinical trial

We are seeking men and women aged 20-70 years who have pre-diabetes or who have been recently diagnosed with types 2 diabetes and have not yet been treated with a sugar-lowering medication. This study investigates blood sugar response to personalised diet and diabetes medication. HREC Approval: SVH 17/080.

For further information, please contact

**Dr Dorit Samocha-Bonet**

**02 9295 8309**

**[predict@garvan.org.au](mailto:predict@garvan.org.au)**



## The gift that gives back

The Paspaley Kimberley Bracelet reflects the raw beauty of Australia's North-West coast, through a striking combination of pearls, sandalwood and onyx.

Even more beautiful than the bracelet itself is the sentiment behind it. Paspaley donates 25 per cent from each bracelet sold to Garvan's cancer research, helping scientists change the lives of people living with rare and less common cancer.

To give a gift that means more, please visit [garvan.org.au/paspaley](https://garvan.org.au/paspaley) today.