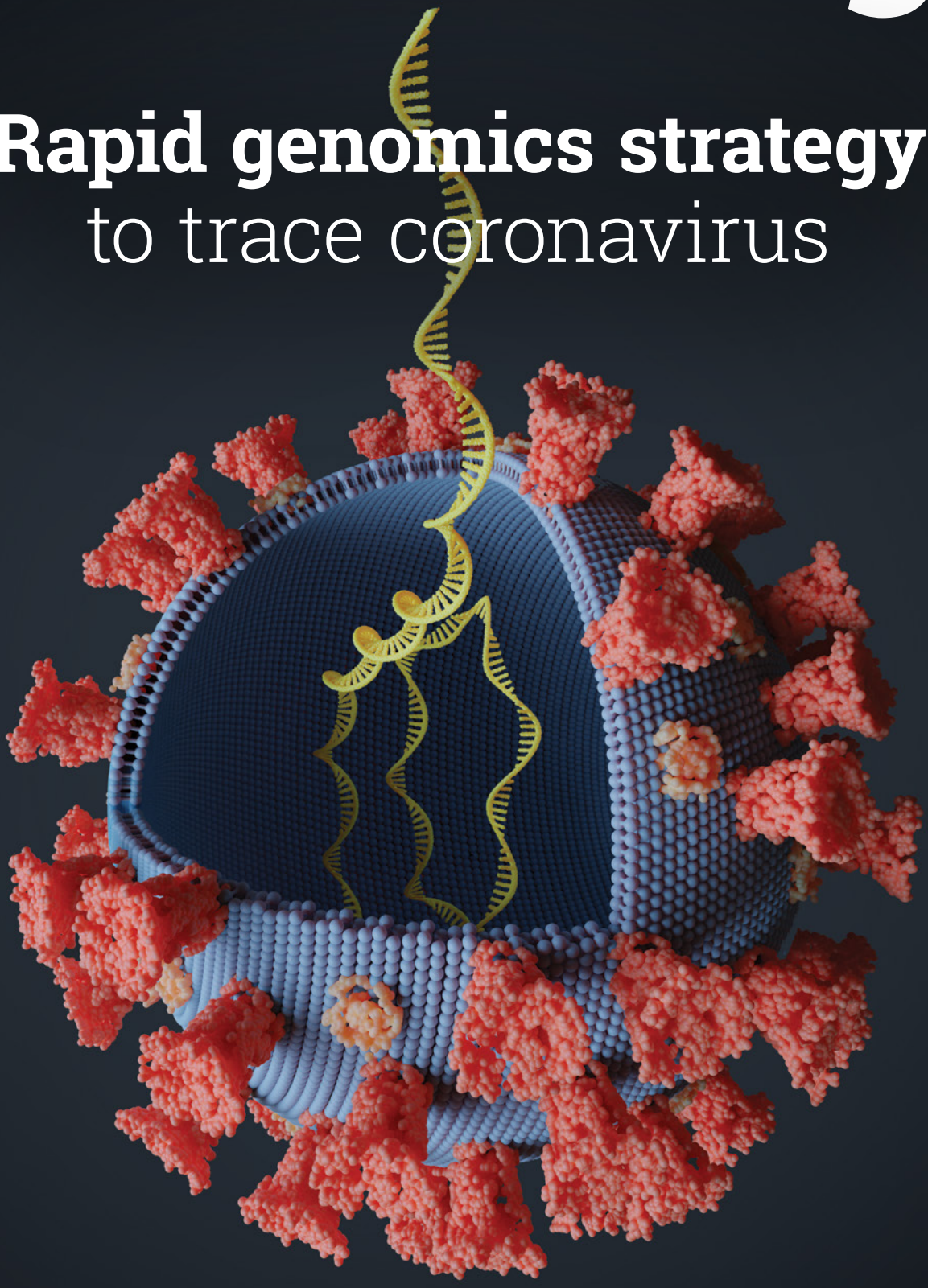
Issue 47

breakthrough

Rapid genomics strategy to trace coronavirus



Also in this issue

A new way to predict bone fracture risk

Introducing the heroes supporting our research

Garvan Institute of Medical Research

Welcome from our Executive Director

Dear Garvan family,

It is a pleasure for me to share with you our first edition of *Breakthrough* for 2021.

I am honoured to be introducing to you 12 incredible heroes (on page 10 and 11) who are living with disease and helping us raise awareness of Garvan's research through our powerful new campaign. We are so grateful to each hero for sharing their story with us so openly and for their belief in the power of medical research.

In the following pages, you'll also meet the Garvan researchers who developed the most rapid coronavirus genome sequencing strategy in Australia to date to assist with contact tracing efforts in NSW; and how a newly developed method will help doctors predict the 'skeletal age' of their patients.

On page 3, you'll also hear from me about the significant benefit of COVID-19 vaccines and the continued importance of public health measures.

Finally, I'd like to acknowledge each and every one of my Garvan colleagues. Despite the obstacles of last year and the challenges and uncertainty we face as a community, Garvan's researchers continue to drive scientific discoveries to improve human health.

Without your support and passion for research as a critical member of the Garvan family, these discoveries simply wouldn't be possible.

Thank you.

Regards,

Professor Chris Goodnow FAA FRS
Executive Director
The Bill and Patricia Ritchie Foundation Chair

RESEARCH NEWS

Random DNA change reversed inherited immune conditions

Researchers have revealed how a rare DNA change rebalanced the immune system of patients with a life-threatening genetic immunodeficiency. Through the Garvan-led CIRCA program, researchers found patients with DOCK8 deficiency had repaired the faulty genes through a rare DNA change known as somatic reversion.

Garvan's Professor Stuart Tangye says "this surprising discovery has implications for future therapies and treatments for the often-fatal disease."

Garvan thanks the John Brown Cook Foundation for their ongoing support of the CIRCA program.

Visit: **garvan.org.au/reversed**

New DNA modification 'signature' discovered in zebrafish

Garvan researchers have uncovered a new form of DNA modification in the genome of zebrafish, a vertebrate animal that shares an evolutionary ancestor with humans ~400 million years ago.

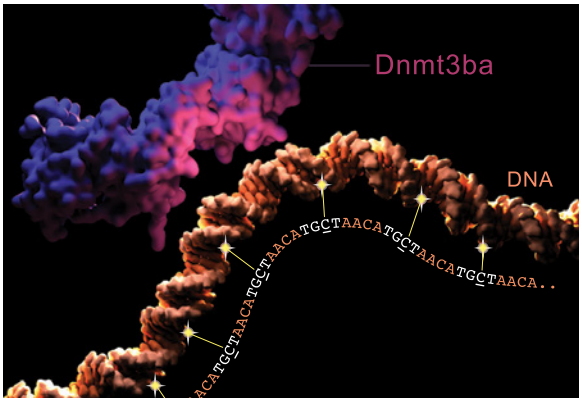


Image credit: Dr Kate Patterson

The study discovered that unusually high levels of DNA repeats of the sequence 'TGCT' in the zebrafish genome undergo a modification called methylation, which may change the shape or activity of the surrounding DNA.

"DNA methylation is vital to cellular function, as it controls which genes are turned on and off," explains first author of the paper, PhD student Sam Ross. "This is why the cells in our body can carry out vastly different functions, despite having almost identical DNA."

This finding has the potential to provide further insight into the molecular mechanisms of neurodevelopmental disorders and could lead to the development of new experimental models for studying how DNA modifications impact human development and disease.

Visit: **garvan.org.au/signature**

Life during the COVID-19 vaccine rollout

Executive Director Professor Chris Goodnow FAA FRS

Communities around Australia have done an admirable job over the last year to contain the novel coronavirus pandemic. Now with the vaccine rollout underway, many of us are rightly looking forward to a return to normality. However, there is still considerable confusion around the implications of the 62 percent and 95 percent efficacy rates, and what that means for us as we begin to receive our first and second doses.

The great news is that published evidence and health authorities in Europe and Australia have repeatedly found that both the Pfizer and AstraZeneca vaccines offer almost complete protection against ending up in hospital with severe COVID-19 caused by the dominant strain of SARS-CoV-2, and have very low risks of harmful side effects such as blood clots.

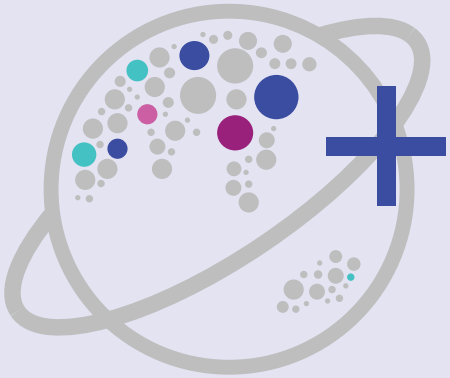
The AstraZeneca vaccine clinical trial results in *The Lancet* on January 9 showed extremely compelling results. Half of the 23,745 participants received both doses of the COVID-19 vaccine while the other half received a meningococcal vaccine as a control. Ten people developed severe COVID-19 requiring hospitalisation, and all 10 were in the control group.

Likewise, results from the Pfizer clinical trial published in *The New England Journal of Medicine* on December 31 show that nine out of 10 people in the trial who ended up in hospital with severe COVID-19 were in the unvaccinated control group. The one hospitalised case that had been vaccinated caught their infection before their immunity had fully developed.

But being vaccinated doesn't mean we can become complacent. Evidence from *The Lancet* paper makes it clear that the AstraZeneca vaccine, which is the vaccination the majority of Australians will be receiving, will not stop you from being infected, and presumably from passing the virus on. This vaccine, and the other mRNA vaccines will not serve as a substitute for the public health measures such as tight international quarantine, rapid contact tracing and physical distancing that has enabled Australia to avoid the worst-case scenarios we have seen play out around the world.

We pulled together well as a community over the past year, and with all we have learnt about where the transmission risks are highest and the advances in rapid contact tracing, we can do so even better throughout this year as vaccination efforts ramp up across the country. As we wait for our turn, we all need to be prepared to keep our guard up so we can get on with life and work in adaptable, COVID-safe ways.

"Being vaccinated doesn't mean we can become complacent. The AstraZeneca vaccine being produced locally will not stop you from being infected, and presumably from passing the virus on." – Professor Chris Goodnow



Professor Chris Goodnow FAA FRS

A family legacy that **continues to inspire**

Garvan *Partner for the Future*

Josie La Spina

"When thinking about my future legacy contributing to new discoveries for treating disease, I feel really hopeful." – Josie La Spina

It was while working for MLC many years ago that Josie La Spina first heard about the Garvan Institute from a colleague. "I worked with a gentleman who was in his 90's and he still looked after the finances and Wills for the last surviving Garvan sisters," says Josie. "He knew them quite well and he told me many stories including how the Garvan Institute was established in 1963 and named in honour of James Patrick Garvan, and about all the wonderful philanthropic work the Garvan family did for the Australian community."

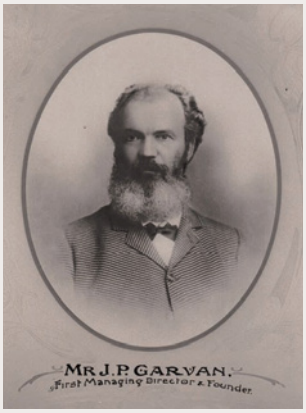
"It was these stories that inspired me to support the Garvan Institute, and go one step further and become a *Partner for the Future* by including a future bequest in my Will to Garvan."

Josie's farsighted generosity and dedication to Garvan is motivated by causes that are close to her heart. Her family has been affected by a wide range of diseases, which has driven home the importance of long-term investment in medical research for her.

"My dad passed away from complications of type 1 diabetes and my mum had dementia. One of my two sisters had bowel cancer – she's all clear now thankfully. My other sister lives with me and I am her full-time carer, she has brain damage, epilepsy and mild type 2 diabetes."

Josie continues, "I decided to leave a gift to the Garvan Institute in my Will because I want to help make a difference for people affected by disease, and for their families as well."

Would you consider this special way of giving to the future of medical research?
To request our *Bequest Giving* brochure or for a no obligation conversation, please contact our Bequest Manager, Donna Mason on (02) 9295 8559 or bequests@garvan.org.au or visit garvan.org.au/bequest



The Garvan Institute of Medical Research was established in 1963 as a small research department of St Vincent's Hospital through funds from the Sisters of Charity's Centenary Appeal. One of the primary donors to the appeal was Mrs Helen Mills, who contributed 100,000 pounds. She requested the Institute be named after her late father, James Patrick Garvan – a distinguished NSW parliamentarian and business leader.

A Pearl with Purpose

This April we celebrate a major milestone with iconic Australian pearl company, Paspaley, raising $1 million in donations to support Garvan's cancer research.

Over five years ago, Paspaley and Garvan formed a partnership supporting our Molecular Screening and Therapeutics (MoST) clinical trials, which focus on accelerating Garvan's pioneering research into rare and less common cancers.

$1 million in donations to support Garvan's cancer research

In September 2020, Paspaley reached the incredible milestone of $1 million in donations to MoST, by donating a percentage of sales from their exclusive Kimberley Bracelet, designed to support Paspaley's generous community and philanthropic initiatives.

Today, over 3,000 people have been enrolled into the MoST program, which provides a novel approach to treating patients with rare and uncommon cancers who have exhausted all other treatment options. The partnership with Paspaley has been fundamental in the continued success of this program.

Paspaley's founder, Nicholas Paspaley arrived from Greece as a young boy in the early 1900s, and went on to establish the Paspaley Pearling Company in the 1950s, setting up his life and business in the Kimberley, Northern West Australia.

With the spirit of a true adventurer, innovator and visionary, Nicholas used his vast pearling experience pioneering the cultivation of South Sea pearl oysters, to produce the world's largest and most valuable cultured pearls in the rich oyster beds of the Kimberley.

The name changed to Paspaley, as the business grew in strength and success. Nicholas however, never forgot his humble beginnings and reinvested his time, resources and finances in his beloved Kimberley, with community philanthropy close to his heart.

"I grew up hearing stories of my grandfather's generosity and dedication to his community. As a company, we share these same values today," says Chris Paspaley, Director of Retail. "I find Garvan's work so inspiring: their leadership, vision and focus on developing a new future for medicine, while treating those who need it the most."

Paspaley is a world-leading luxury brand, and continues to be a family owned and run business. Garvan is very grateful to have the generous support of Paspaley, and the Paspaley family, who are innovative, forward thinking and understand the benefits of long-term investment in medical research.

Visit: **garvan.org.au/paspaley today**

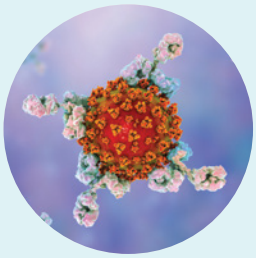
PASPALEY

Research News

How the immune system stays alert to related pathogens

Garvan researchers have revealed the process the body uses to generate a subset of 'early responder' immune cells that recognise threats similar to those they've already seen.

In experimental models, a team led by Professor Rob Brink revealed that the molecule BAFF generates a subset of 'early responder' immune cells that, instead of specialising to produce more effective antibodies, remained dormant and able to recognise close relatives of the pathogen.



Antibodies attacking a virus

This means the immune system ensures it can target foreign antigens that have changed from their original version – a common strategy pathogens such as viruses use to evade immune detection.

Researchers believe the findings carry potential implications for boosting the immune response for a better, broader response to pathogens.

Visit: **garvan.org.au/pathogen-alert**

New discovery in breast cancer treatment

An international study, conducted in collaboration with the University of Adelaide, found new evidence about the positive role of androgens in breast cancer treatment with immediate implications for women with estrogen receptor-driven metastatic disease.

The study looked at the role of androgens – commonly thought of as male sex hormones but also found at lower levels in women – as a potential treatment for estrogen receptor positive breast cancer.

Professor Elgene Lim, a breast oncologist and Head of the Connie Johnson Breast Cancer Research Lab at the Garvan Institute, said: "The new insights from this study should clarify the widespread confusion over the role of the androgen receptor in estrogen receptor driven breast cancer. Given the efficacy of this treatment strategy at multiple stages of disease in our study, we hope to translate these findings into clinical trials as a new class of endocrine therapy for breast cancer."

Visit: **garvan.org.au/bc-treatment**

RAPID GENOMICS STRATEGY **TO TRACE CORONAVIRUS**

Garvan researchers are pioneering the use of a fast genomic sequencing technology to help determine the source of hard-to-trace coronavirus cases.

Thanks to cutting-edge genome sequencing technology, researchers at Garvan and the Kirby Institute at UNSW Sydney have developed the most rapid coronavirus genome sequencing strategy in Australia to date.

The team validated and established best practice guidelines for 'Nanopore' sequencing of coronavirus, a technological advance that has the potential to provide critical, timely clues on how cases of infection are linked. The team hopes their research will enable a greater uptake of the technology by health initiatives in Australia and overseas.

"When a new 'mystery' coronavirus case is identified, every minute counts," says senior author Dr Ira Deveson, Head of the Genomic Technologies Group at Garvan's Kinghorn Centre for Clinical Genomics.

"At Garvan, we have repurposed our genomic sequencing capabilities to enable a rapid analysis of a coronavirus genome in just a few hours."

"When a new 'mystery' coronavirus case is identified, every minute counts." – Dr Ira Deveson

Pioneering rapid genomics

"Every time the SARS-CoV-2 virus passes from person to person, it may make copying errors that change a couple of its 30,000 genetic letters. By identifying this genetic variation, we can establish how different cases of coronavirus are linked – to know where a case was potentially picked up from and who they may have given it to," says co-first author A/Prof Rowena Bull, from UNSW's Kirby Institute.

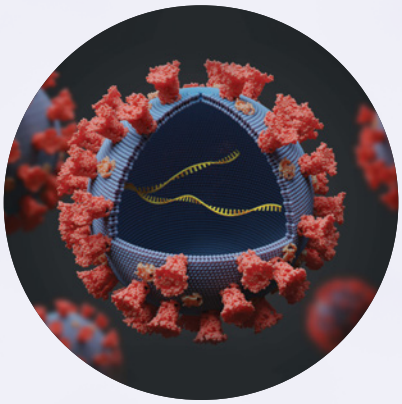
A/Prof Bull says genomic testing is crucial for tracking virus transmission in cases where the source remains unclear from investigating known epidemiological contacts alone.

"By reconstructing the virus's evolutionary history, or 'family tree', we can understand the behaviours that help spread COVID-19 and identify so-called 'super-spreaders'," she says.

Highly accurate emerging technologies

Garvan researchers have fine-tuned the protocols for cutting-edge Oxford Nanopore Technologies to sequence SARS-CoV-2 in less than four hours. Garvan's Kinghorn Centre for Clinical Genomics is the first facility in Australia to establish and apply this Nanopore technology for genomic surveillance of SARS-CoV-2.

The current gold-standard method reads short genetic sequences of just 100-150 genetic letters at a time, whereas Nanopore technologies have no upper limit to the length of DNA fragments that can be sequenced and are able to more rapidly determine the complete sequence of a viral genome.



Virus with RNA molecule inside. 3D rendered illustration.

Garvan's Jillian Hammond loads an Oxford Nanopore GridION flow cell.

Reconstructing the virus's evolutionary history, or 'family tree'

The researchers' analysis revealed the Nanopore sequencing method to be highly accurate, with variants detected with >99% sensitivity and >99% precision in 157 SARS-CoV-2-positive patient specimens.

"Nanopore devices are cheaper, faster, portable and don't require the lab infrastructure needed by current standard pathogen genomics tools," says Dr Deveson. "We hope our validation of this protocol will help other public health teams around the world adopt this technology."

"We've been thrilled to collaborate with the Garvan and Kirby Institutes to develop unparalleled speeds of coronavirus genome testing. Rapid methods such as this provide a way forward, as a potential future option for contact tracing through real time genomic transmission studies," says Prof Bill Rawlinson AM, from UNSW Sydney and NSW Health Pathology Randwick.

"This technical advance is a testament to what's possible when public pathology collaborates with Research Institutes for a common goal," says Prof Sebastiaan van Hal, from NSW Health Pathology – Royal Prince Alfred Hospital.

This method is now in use by NSW Health Pathology laboratories, and public health teams in Victoria and Queensland, with the Garvan team providing ongoing technical support.

Dr Ira Deveson

"This technical advance is a testament to what's possible when public pathology collaborates with Research Institutes for a common goal," says Prof Sebastiaan van Hal, from NSW Health Pathology – Royal Prince Alfred Hospital.

To find out more visit
garvan.org.au/trace

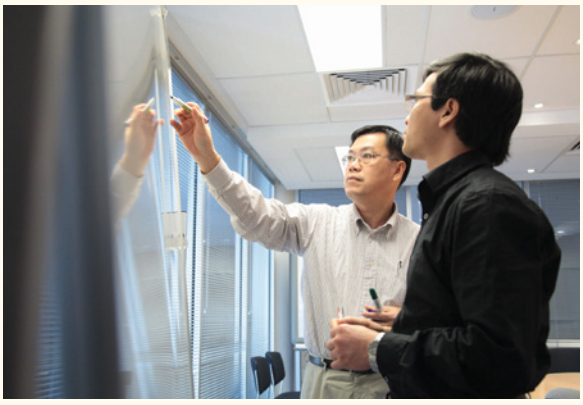
A new way to predict **bone fracture risk**

Garvan researchers have developed a model to predict the biological age of bones, which may improve the management of osteoporotic fractures.

Our scientists have developed a new computational model to calculate 'skeletal age', a personalised estimate of an individual's risk of bone fracture and premature death.

"A fracture shortens life expectancy, even more so in men than in women. But there is a lot of complacency in the community when it comes to bone health – only 20% of those with fragility fractures are taking approved treatments for osteoporosis, which could significantly reduce their risk of further fractures," says the study's senior author Professor Tuan Nguyen, Head of the Genetic Epidemiology of Osteoporosis Lab at Garvan and Professor of Predictive Medicine at the University of Technology Sydney.

"We hope that by calculating skeletal age it will become possible to better identify those at risk of fracture and encourage them to speak to their doctor about how to better manage their condition."



Professor Tuan Nguyen

Predicting fracture risk

Osteoporosis, a disease which reduces bone strength and increases bone fracture risk, is a major national health issue and estimated to affect over 900,000 Australians. From age 50, bone fractures affect one in two women and one in three men. Studies have shown that pre-existing fractures increase the risk of premature death by about 50% in both men and women.

"There are existing models to predict the risk of an initial fracture, such as the Garvan Fracture Risk Calculator that is already available to doctors. But it remains unclear why some individuals do well after an initial fracture, while others go on to sustain further fractures and have a higher risk of mortality," says first author Dr Thao Ho-Le.

To develop their 'skeletal age' calculator, the team led by Professor Nguyen used data from Garvan's Dubbo Osteoporosis Epidemiology Study, which was started in 1989 and is the world's longest-running large-scale study of osteoporosis in men and women. The researchers' model incorporates chronological age, bone density, history of previous fractures and other health conditions.

"We quantified the intricate transitions between fracture, re-fracture and mortality," explains Professor Nguyen. "Using this definition, we for instance estimated that a typical 70 year old man who had sustained a fracture had a skeletal age of 75 years. But when the man had a second fracture his skeletal age rose to 87 years. This means the individual now has the same fracture risk profile as an 87 year old man who has a healthy risk profile."

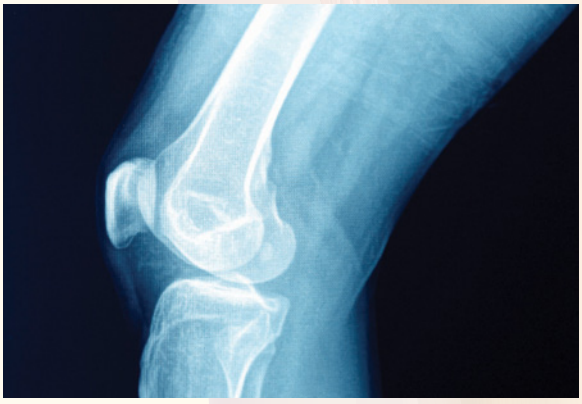
Improving bone health

The team is now developing an online calculator, which doctors will be able to use to calculate their patients' skeletal age.

The researchers hope their new tool will help initiate discussions between health professionals and their patients on how to improve bone health, which may involve medication, exercise, increasing dietary calcium and getting enough vitamin D.

"The key message of this study is that it's never too early to think about your bone health," says Professor Nguyen. "Do not wait until a fracture has occurred to take preventive action. If your skeletal age is higher than your actual age, you should seek medical advice from your doctor on how to manage the higher risk."

This research was published in the journal eLife and was supported by Australia's National Health and Medical Research Council (276413) and the Amgen Competitive Grant Program.



Xray of a knee bone

"The key message of this study is that it's never too early to think about your bone health, do not wait until a fracture has occurred to take preventive action." – Professor Tuan Nguyen.

To find out more visit
garvan.org.au/skeletal-age

OUR GENOMICS RESEARCH CAN HELP

Raising awareness and much needed donations for research at the Garvan Institute.

Have you seen our new campaign, Disease Dilemmas?

It challenges Australians to choose one disease to support over another by asking: Who would you donate to?

Of course, it's an impossible dilemma and a choice we cannot make. Fortunately, you don't need to, because as you know, Garvan's genomic research is focused on improving outcomes for many, many different diseases.

Garvan is incredibly grateful to our 12 heroes – the men and women living with disease who have so graciously shared their stories with us. We sincerely thank them for their bravery and their belief in Garvan and the power of our research.

In a series of 12 portraits, featuring incredible people living with disease, the campaign challenges you to consider an impossible question: Who would you donate to?

Through Disease Dilemmas, we're hoping to increase awareness of Garvan and the breadth of our research, and to inspire others like you to support of our mission 'to harness all the information encoded in our genome to better diagnose, treat, predict and prevent disease'.

Through research, our scientists are making breakthroughs to better predict, diagnose, treat and prevent not just one, but many devastating diseases from the rarest or un-diagnosable and un-treatable to the most common and widespread.

As a not-for-profit, our priority is to support Garvan's cutting edge research. Please join the entire Garvan team in extending our sincere gratitude to BWM Dentsu, the creative agency who worked with us on a pro bono basis to create this campaign. Further, every billboard, bus stop, TV ad (and more) – which you'll see in the community - has been offered to Garvan free of charge with thanks to BWM Dentsu and their generous networks.

Kathren, Candice, George, Andrea, Rosalie, Kieran, Nicole, Brian, Shervin, Hosam, Angela and Ashleigh – thank you for sharing your stories with us.

To hear our heroes stories, visit
diseasedilemmas.org

The Australian newspaper

1 of 6 teaser adverts

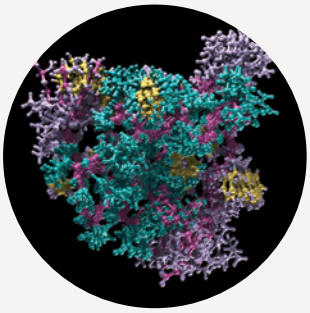

PANCREATIC CANCER
TYPE 1 DIABETES
MULTIPLE SCLEROSIS
OSTEOPOROSIS
KIDNEY DISEASE
IMMUNE DISEASE
BREAST CANCER
PARKINSON'S DISEASE
KIDNEY DISEASE
BRAIN CANCER
TYPE 1 DIABETES
IMMUNE DISEASE

Clinical Trial **Spotlight**

New study aims to improve the way diabetes is classified

Diabetes is the fastest growing chronic condition in Australia, with an estimated 1.8 million Australians living with the condition. While high blood sugar is a common feature of diabetes, how it is treated depends on whether an individual has type 1 (insulin deficiency) or type 2 (insulin resistance and insulin deficiency).

One way by which clinicians diagnose type 1 diabetes is a blood test for 'autoantibodies', antibodies which may degrade the pancreatic tissue that produces the insulin needed for cells to absorb sugar. However, as many as 15% of individuals with type 1 diabetes do not have detectable levels of these autoantibodies, which can potentially result in misdiagnosis.



Insulin molecule

Our new Pan-Autoantibody Negative Diabetes in Adults (PANDA) study aims to investigate how the immune system differs between type 1 diabetes with and without autoantibodies.

We hope to identify unique biomarkers within the immune cell profile of those with autoantibody-negative type 1 diabetes that may help improve future diagnosis of the condition. Further, we aim to reveal insights that may help develop therapy for preserving the pancreatic tissue and its ability to secrete insulin.

We are looking for individuals with type 1 diabetes who are between 18 and 50 years of age and are within 7 years of diagnosis. We are also looking for healthy individuals without diabetes within this age range.

For further information on how to participate please contact: Dr Shivani Patel on pandastudy@garvan.org.au or 0493 085 256 (St Vincent's HREC Ref 2020/ETH00700)

In Memory

Vale Dr Laurie Hammond

Dr Laurie Hammond

Dr Laurie Hammond was ever curious. He had a scientist's appetite for challenge and a thirst for knowledge that was reflected in a professional life that spanned the scientific, business and academic worlds. Laurie's appetite for challenge drove his work as an advisor to governments on research commercialisation, as founder of a venture capital fund and technology incubators, and as a trusted guide to universities on navigating the complex intersection of science and commerce.

On 4 May 2018, Laurie was diagnosed with advanced pancreatic cancer while working as an Adjunct Professor at the Queensland University of Technology where his research focused on scientific policy and funding. So committed to his work, he presented the results of this research to the CRC Association's 2018 Annual conference the same week he started his chemotherapy.

On 4 November that same year, he sadly lost his battle with the disease. In his honour, friends Dr Peter Andrews and Dr Peter Isdale auctioned a portrait of Laurie by Australian artist, and long-term childhood friend, Ian Smith at his 'Celebration of Life', raising $10,000 for pancreatic cancer research.

Generously, Laurie's family and friends donated this money to the Garvan Institute, after Laurie had his genome sequenced and profiled here. He had an enduring belief in the fundamental value of science, scientific research and policy to drive funding for scientific research.

Laurie touched people's lives across Australia. He was a major contributor to the direction of life-saving Australian research into bushfire and other natural disasters as Chairman of the Bushfire and Natural Hazards CRC from its inception in 2013 until his death in November 2018. In 2020, then Chief Scientist of Australia, Dr Alan Finkel AO, delivered the annual Dr Laurie Hammond oration hosted by the Bushfire and Natural Hazards CRC - a tribute to their former chair.

"Laurie was the perpetual scientist with an abiding belief in the fundamental value of scientific research and its contribution to humanity."
– Catherine Hammond, Laurie's wife.

Retrospective portrait of marine biologist Dr. Laurie Hammond, at Ross River, circa 1973 by Ian Smith.

DONATIONS

Made to celebrate a special occasion

Ruth Bell's 70th Birthday
Doreen Cheong's 80th birthday
Jim & Barbara's 60th Wedding Anniversary

Donations made in memory of loved ones

Trevor W Annetts
Maureen Aronson
Ann Atherton
Heather Baillie
Heather Batchelor
Ross Beattie
Vera Bell
Meryl A Bethel
Krista Blunck
Beverley Bolton
John R Bourke
Gordon Bower
Daniel Brand
Lynn Bright
Yvonne Brown
Jane Bryant
Viola Butters
John R Caldon
Georgina Camenzuli
Alan & Greg Connell
Margaret Connellan
Noel Connor
Charles W Cook
Norma & Robert Cook
Rosemary Cooley
Suann Croker
Rosalind J Curran
Thomas S Curran
Raymond Dank
Janelle K Davis
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Brian Gibson
Caeli Glennon
Russel Goldman
Vincent Graham
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Ash Huggett
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Stanley Hunt
Allan Jackson
Evi Joannou
Adele J Johns
Lloyd G Jones
Vanessa Juresic
Carolyn M Kearney
Andrew Kendall
John Kennedy
Karl King
Donald Kingsley
Lindy Kotthoff
Simon Laing
Diana L Larter
Elaine M Lawrence
Daryl L Levy
Paul Lewis
Julia M Linyard
Thomas Lowndes
Tim & Andrew Lynch
Tim Maffey
Michele & Margherita Maldarella
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John E McConkey
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Paul Payne
Robin Pease
Kevin Phillips
Maryanne Pickup
Nick Puopolo
Charles A Reid
Lee Ross
Olga G Salmond
Martin Samociuk
Antonius Sannen
John Sewell
David Sinclair
Andrew Smith
Leslie Smith
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Maria Stefanidis
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