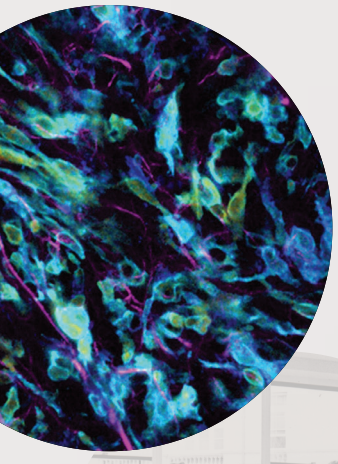
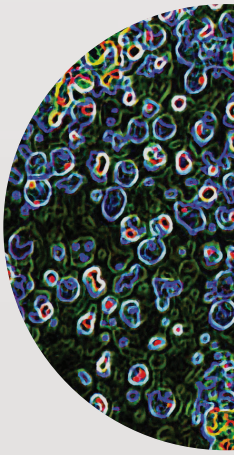
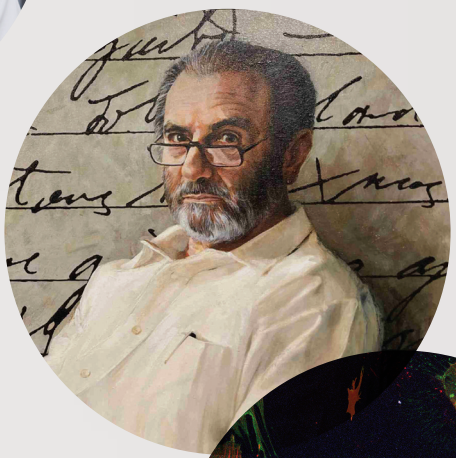
April 2023 | Issue 53

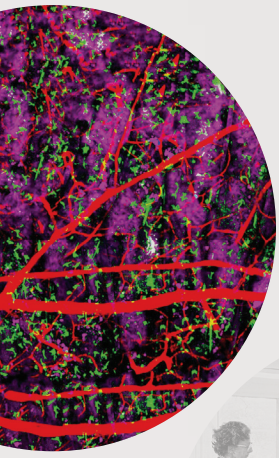
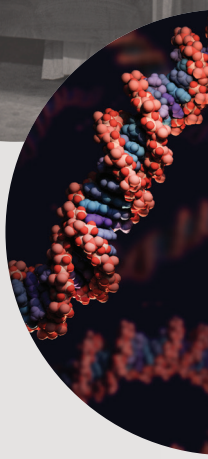
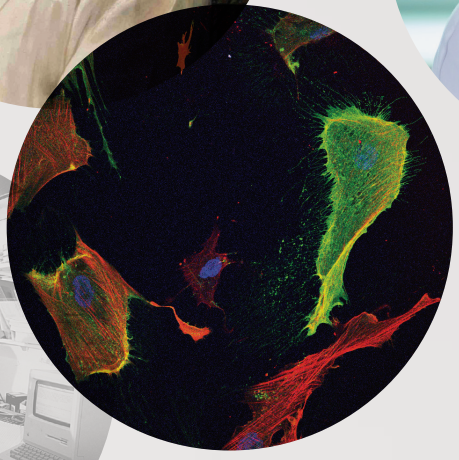
breakthrough

60 YEARS OF DISCOVERY








Garvan Institute of Medical Research

Welcome from the Executive Director (interim)

Dear Garvan family,

This year, we celebrate our 60th anniversary. Founded in 1963 through a noble act of charity, Garvan's establishment was made possible by the unwavering dedication of the Sisters of Charity, who used funds raised from their Centenary Appeal to lay the foundation of what has since become a beacon of hope and progress in medical research. Thanks to your generosity, our researchers have continued to push the boundaries to impact human health by harnessing information encoded in our genome.

In this first edition for 2023, I am excited to share some of our latest news with you. On page 8 and 9, you will read about how children's immune response to coronavirus is fast but doesn't last and what this might mean for the immune system. Garvan scientists are also hard at work developing ways to stop the coronavirus which mutates into new variants over time, from evading vaccines and antiviral medications.

On page 10, you will read about a study uncovering the genes that cause a rare cancer often impacting children. The study has wide implications for people living with sarcoma and their families – allowing earlier detection and potentially improving patient survival.

On page 11, you will hear about the impacts of the undertreatment for fracture prevention of patients with complex medical conditions and high fracture risk.

Finally, on page 12, you will read about a study to examine the effects of a diabetes treatment in slowing cognitive decline to prevent dementia. The clinical trial is already underway, and its success would mean that treatment could be immediately available.

On behalf of everyone here at Garvan, I want to extend my heartfelt gratitude for all your support. Your contributions have been instrumental in driving progress and improving outcomes for patients around the world. I would also like to take this opportunity to welcome Professor Benjamin Kile, Garvan's incoming Executive Director, who will continue to share our journey with you via Breakthrough. We are very honoured to have a respected scientist and research leader join us as we remain committed and focused on achieving impact through our research.

Best wishes,

Professor Peter Croucher
Executive Director (interim)

A DAY IN THE LAB
Researcher profile

Dr Amanda Khoury on epigenetics, motivation and the critical mass of diversity in science.

Dr Amanda Khoury

For me, each day as a medical researcher is a gift, because I'm fascinated by the complexities of the human body. Every little bit we demystify can lead to countless healthier and happier lives.

My work is in the area of epigenetics, which translates to 'above genetics'. We need to go above genetics because not all the answers to how our bodies work can be found in our genetic sequence (i.e. our DNA). Each of the trillions of cells in our bodies contains an exact copy of our DNA, yet somehow this single blueprint gives rise to all our diverse cell types. Epigenetics is the process that instructs different genes to turn 'on' and 'off' to create a certain cell – so the set of genes that are switched on in our skin cells, will be different to the ones in our heart cells.

Like many healthy processes, epigenetics becomes disrupted in cancer – this can lead to tumour-fighting genes being switched off, and/or cancer-causing genes being switched on. My work aims to identify these epigenetic changes in the hope of finding new therapies for cancer.

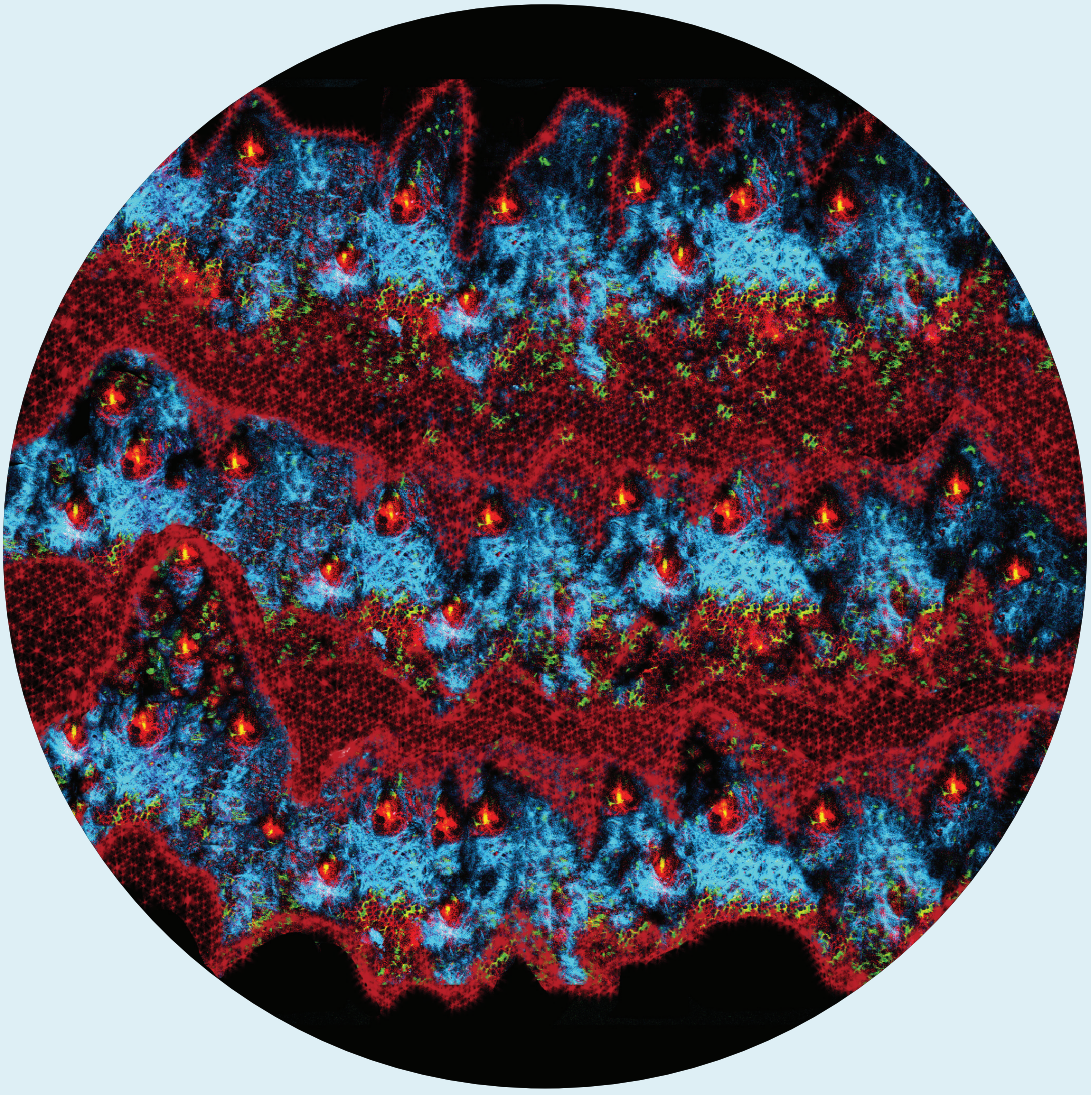
Late last year I was thrilled to find out I'd been selected for the national Superstars of STEM program for 2023-2024. Superstars of STEM aims to boost visibility of women and non-binary people in science, technology, engineering and maths, creating diverse role models for the next generation of young people in these challenging fields.

Why does diverse representation matter? Because scientific research is, at its heart, all about problem solving. The best outcomes are reached when these supposedly intractable problems are approached from a new angle by people with broad perspectives. And when young people see faces that reflect theirs pursuing successful careers in science – making those all-important discoveries that turn into knowledge – it can help to smash stereotypes and break down the barriers to entry.

Visit: **garvan.org.au/superstar-of-stem**

THROUGH THE MICROSCOPE

First prize for scientist's microscopic view inside the body's response to wounds and tumours.



PhD student and microscopy aficionado Arnolda Jakovija has again achieved first place in the Light Microscopy Australia Image Competition, In Vivo category.

Her winning image, titled *Ice and Fire*, shows myeloid immune cells (green) within the connective tissue (blue) and other components (red) inside a mouse's ear.

Being able to visualise the immune cells in different colours, inside living tissue, helps her team in Dr Tatyana Chtanova's Innate and Tumour Immunology Lab study the cellular response to wound healing, as a model for how the body responds to cancerous tumours. These foundational insights could help improve current cancer treatment options.

Despite spending up to 10 hours a day performing 2-photon microscopy in Garvan's ACRF INCITe Centre, Ms Jakovija says she never gets bored of imaging, as it lets her engage her creative side while at the cutting-edge of medical science.

Jennifer and John's Story – Adventure, Travel, Love and Hope

Jennifer continues John's legacy of a fulfilling life through a gift in her Will to Garvan.

John and Jennifer

My husband John and I had a wonderful life together. We sailed all around the world in our own self-built yacht, exploring exciting places and working in ports when the money ran out. We also designed and built our very own wooden house in the country, did 4WD driving and camping trips across Australia, and flew to Europe several times on camping trips, taking our pushbikes and tents as luggage. Later we bought a small van to camp in and explore more places in Europe. John was very talented and at home there was always a boat to be built or always a boat to be sailed, life was never dull. Life was lived in the moment.

One day John was feeling a bit off, which was odd as I don't recall him ever being sick. He had never taken an antibiotic or any other medication in his life. He went to the doctor, who sent him to the hospital and later that same day he was told he had terminal pancreatic cancer. He died four months later. The light went out of my life.

At his funeral, a friend gave me $50 to be put towards cancer research instead of buying flowers. I thought that was such a good idea, so I added another $50 and that is what started my contributions to the Garvan Institute. I have continued my support of Garvan since 2017.

John died just before his 74th birthday. He was lucky in a way that at least he got to live a full and rewarding life; so many others die of terrible diseases early and don't have the chance to experience a life. And for these reasons, I have decided to leave a gift to the Garvan Institute in my Will to support their important work into the future.

"I have decided to leave a gift to the Garvan Institute in my Will to support their important work into the future"

One of John's handcrafted sailing dinghies

Like Jennifer, would you consider this special way of giving to the future of medical research with a gift in your Will?

To request our Bequest Giving brochure or for a no obligation conversation, please contact our friendly Bequest team on **(02) 9295 8559** or email **bequests@garvan.org.au,** or visit **garvan.org.au/bequest**

Tunnelling to success

Recently, we had the pleasure of hosting The Australian Tunnelling Society (ATS) at Garvan for a tour of the Institute and research facilities.

The ATS has been supporting Garvan for over 10 years through its annual Golf Day in memory of the late Peter Watson. Peter was a previous supporter of Garvan and a long-standing ATS member. In recognition of Peter's support for Garvan, the ATS continues to honour his legacy by fundraising and supporting Garvan's research.

"It was such a great day. Along with viewing some of the popular features of the Garvan building and The Kinghorn Cancer Centre, we were taken behind the scenes of genomic medicine research, which was fascinating."

"I learned a lot about the important work they do and am truly proud on behalf of the ATS NSW branch and our supporters, in being able to give so generously. We are already looking forward to the 2023 event and trying to get to $20,000" said Brad Boardman, NSW Chapter of the Australian Tunnelling Society.

Garvan was pleased to celebrate and recognise the Australian Tunnelling Society as a Governor, contributing $100,000 over the past 10 years. We presented the team with a cheque of their donation from their 2022 Golf Day event and added them to Garvan's Honour Board in recognition of their generosity over the last decade.

L to R – Brad Timms, Jake Watson (Front), David Clague (Back), Sarah Watson, Roland Walker, Fatima Watson, Steve Teraki, Brad Boardman.

Without incredible community fundraisers like the ATS we would not be able to fast-track our medical research and help change lives.

You can make a big difference to medical research by fundraising for Garvan. If you're interested in participating in a community fundraising event or to set up your own – we would love to help you.

Visit: **garvan.org.au/support-us/fundraise-for-us**

Australia Day Honours for visionary Garvan supporter

L to R – A/Prof Marina Pajic, Jane Hemstritch and Mara-Jean Tilley.

We are thrilled to share that Jane Hemstritch, a prominent member of Garvan's community, was presented with an Order of Australia for her outstanding contribution through her roles in medical research, the arts and business.

Since losing her husband to pancreatic cancer in 2010, Mrs Hemstritch has dedicated herself to raising funds to support pancreatic cancer research. Her fundraising team, 'Team Phil', was established in 2011 in memory of her late husband, Philip. The team ran marathons in 2011, 2012 and 2013 to raise awareness and support for the Australian Pancreatic Cancer Genome Initiative.

In 2012, Mrs Hemstritch also started the Philip Hemstritch Fellowship in Pancreatic Cancer Research at Garvan. Associate Professor Marina Pajic, at the time an early career scientist, was the recipient and continues to be supported by the Fellowship. She now co-leads Garvan's precision medicine for cancer program and is working on a new targeted treatment for patients with pancreatic cancer.

"We're immensely grateful to have Jane as one of our champions and for her enduring commitment to our team's research in pancreatic cancer," says Associate Professor Pajic.

Visit: **garvan.org.au/aus-day-honours**

RESEARCH NEWS

Rogue killer T cells drive autoimmune disease

Dr Etienne Masle-Farquhar

Garvan scientists have pinpointed rogue immune cells as a major contributor to autoimmune conditions like rheumatoid arthritis and aplastic anaemia.

Dr Etienne Masle-Farquhar's study, led by Professor Chris Goodnow, details how gene variants associated with leukaemia can dysregulate the growth of killer T cells.

The team found that these gene variants can cause rogue killer T cells to grow unchecked, bypassing immune checkpoints to attack the body's own cells. Even 1-2% of a person's T cells going rogue could cause autoimmune disease. Further study is needed to determine whether rogue killer T cells are involved in all autoimmune diseases.

This research identifies pathways that may help target these cells for future treatments. It paves the way for screening technologies clinicians could use to sequence the complete genome of every cell in a blood sample, to identify which cells might turn rogue to cause disease.

Visit: **garvan.org.au/rogue-t-cells**

60 YEARS OF DISCOVERY

On 17 February 2023, Garvan celebrated an incredible milestone: six decades of innovation in medical research.

As Garvan turns 60 we reflect on where it all started, how far we have come and the lives that have been changed through our ground-breaking research.

The Sisters of Charity, who founded St Vincent's Hospital in 1857, used funds raised from their Centenary Appeal to establish the Garvan Institute. One of the primary donors to the appeal was Mrs Helen Mills, who contributed 100,000 pounds. She requested that the Institute be named after her late father, James Patrick Garvan (1843-1896), a distinguished NSW parliamentarian and respected business leader.

Construction of the original Garvan Institute building began in January 1962 and the Institute was officially opened on **17 February 1963** by Bernard Marmaduke Fitzalan-Howard KG, GCVO GBE, the 16th Duke of Norfolk.

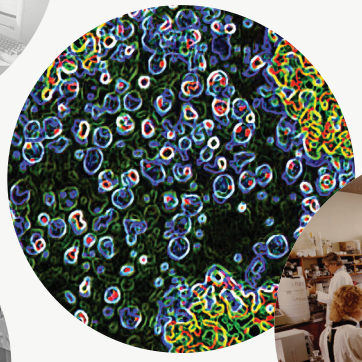
From a small operation, Garvan has grown exponentially to become one of the most respected medical research facilities in Australia. Over the decades, we've launched countless studies and projects that have changed the way we think about and treat disease and we've improved the quality of health care worldwide. We've made significant breakthroughs for diseases including rare cancers and cancers of the breast, prostate and pancreas, immune deficiency and autoimmunity, COVID-19, diabetes and skeletal disease.

Looking back at Garvan's history, it's thanks to the compassionate support of the Garvan community, who have enabled us to translate breakthrough research into meaningful health benefits for those living with disease and their families.

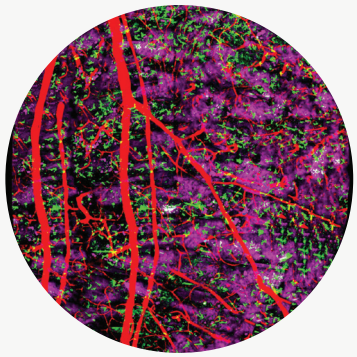
Visit: **garvan.org.au/history**

Please join us in celebrating this progress, thanks to the hard work of a lineage of brilliant researchers, generous donors and visionary leaders. We now look toward the future, as we continue to turn discoveries into impact together.





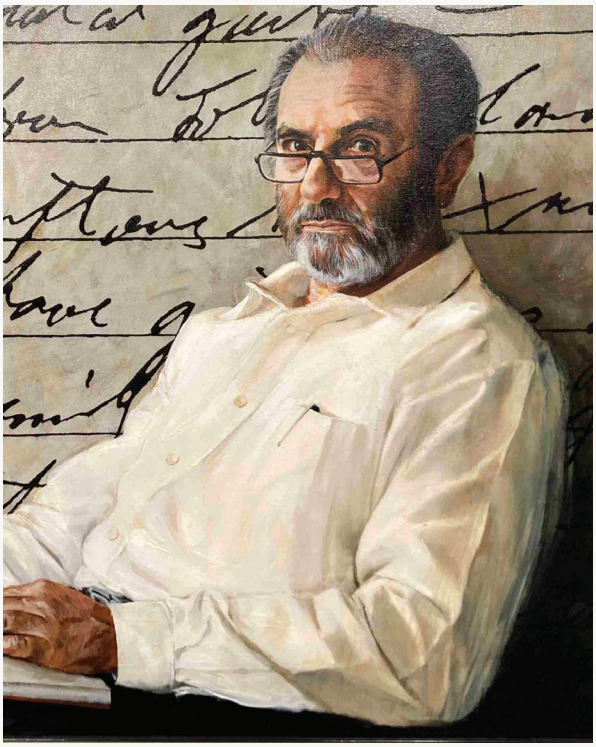




To launch our 60th anniversary celebrations, we hosted our first seminar of the year, 60 Years of Discovery, held in Garvan's Auditorium. Our wonderful speakers were Dr Warren Kidson, Professor John Shine, Professor John Mattick, Professor Sue Clark and Professor Chris Goodnow.

Professor John Shine, Professor John Mattick, Mara-Jean Tilley, Dr Warren Kidson, Professor Susan Clark, Professor Peter Croucher, Professor Chris Goodnow and Professor Edward 'Ted' Kraegen.

Vale Professor Leslie 'Les' Lazarus



Professor Les Lazarus MBBS MRACP FAACB FRACP FRCPA AO, joined Garvan as co-Director in 1963, and went on to become Garvan's first sole Director, holding the position for 20 years, from 1969 until 1990. He was also one of the first trained endocrinologists in Australia. In December 2022, Les sadly passed away at the age of 93.

In his time as Director, he oversaw momentous change, including the establishment and growth of three major research themes (diabetes and endocrinology, osteoporosis and bone, and cancer), the establishment of Garvan as an autonomous research institute and major changes in the funding landscape.

We remember and celebrate Professor Les Lazarus for his exceptional contributions to science and medical research and for his outstanding leadership at Garvan.

To read more about Les and his history, please visit:
garvan.org.au/les-lazarus

Children's immune response to coronavirus: fast but doesn't last

Because children don't develop memory T cells, they are at risk of getting sick when they become reinfected.

Children have largely avoided severe COVID-19 symptoms because they have a strong initial 'innate' immune reaction that quickly defeats the virus.

Research led by scientists at Garvan has now uncovered what this might mean for the immune system. Unlike those of adults, children's immune systems don't remember the virus and don't adapt, so when they're next exposed to SARS-CoV-2, their body still treats it as a new threat, scientists found.

"The price that children pay for being so good at getting rid of the virus in the first place is that they don't have the opportunity to develop 'adaptive' memory to protect them the second time they are exposed to the virus," says lead author Professor Tri Phan, Head of the Intravital Microscopy and Gene Expression (IMAGE) Lab and Co-Lead of the Precision Immunology Program at Garvan.

Because children haven't been exposed to many viruses, their immune system is still 'naïve', Professor Phan adds. "Because they don't develop memory T cells, they are at risk of getting sick when they become reinfected. With each new infectious episode as they get older, there is a risk of their T cells becoming 'exhausted' and ineffective, like the T cells in older people. This is why we think it's important to vaccinate children."

Professor Tri Phan

To find out more please visit:
garvan.org.au/covid-and-children

Two new angles of attack to prevent and treat COVID-19

Researchers are developing a universal mRNA vaccine that will be resistant to emerging variants of the SARS-CoV-2 virus.

As the SARS-CoV-2 virus mutates into new variants over time, it gets better at evading vaccines and antiviral medications.

Garvan scientists are hard at work developing two promising angles of attack for this ongoing problem – both targeting sites on the spike protein that the virus can't easily change.

Researchers are developing a universal mRNA vaccine that will be resistant to emerging variants of the SARS-CoV-2 virus, ending the need to modify booster shot formulas. By preventing new variants of the virus from emerging, this work could bring the COVID-19 pandemic to an end.

Meanwhile, they have found a new class of SARS-CoV-2 antibodies, shown to neutralise multiple variants of the virus with a new mechanism of action.

This discovery could lead to more reliable antiviral therapy for immunocompromised individuals.

This research was generously supported by the NSW Office of Health and Medical Research (NSW OHMR), the Ramaciotti Foundations, Ms Lysia O'Keefe and a philanthropic gift in memory of Dr and Mrs Wing Kan Fok.

To find out more please visit:
garvan.org.au/universal-vaccine

Dr Deborah Burnett

Group Leader – Immunogenomics Lab

Dr Deborah Burnett's contribution to COVID-19 research has been recognised with a Highly Commended in the Griffith University Discovery Award.

The award is one of eight categories of the 19th Annual Health and Medical Research Awards, and acknowledges an early career researcher whose paper, patent or discovery has already demonstrated its importance or impact.

Dr Burnett has pioneered new ways to direct immune responses to generate antibodies to key viral targets. Her research is now being used to generate new vaccines that could help end various disease outbreaks, including the COVID-19 pandemic.

Visit: **garvan.org.au/deborah-burnett-award**

Genes that cause a rare childhood cancer revealed by Australian-led study

The research has wide implications for people living with sarcoma and their families.

Research by Omico, the Garvan Institute of Medical Research and UNSW Sydney has led to the creation of the first genetic map to identify several important genes that cause sarcoma, a rare cancer often impacting children.

The research has wide implications for people living with sarcoma and their families – allowing earlier detection of the cancer and potentially improving survival for patients.

Sarcomas are rare cancers originating in bone, muscle, fat or cartilage. To date, there has been little research into the genetic basis of the disease.

The new study, published in the journal *Science*, found that one in 14 individuals diagnosed with sarcoma carries a clinically important gene that explains why the cancer arose. In addition, the research team identified a previously unrecognised genetic pathway specific to sarcomas.

"The findings uncovered by this research are so important. By understanding how individuals develop sarcomas, we move closer to earlier detection and better treatments," says lead author of the paper, Dr Mandy Ballinger, Group Leader of the Genetic Cancer Risk Group at Garvan.

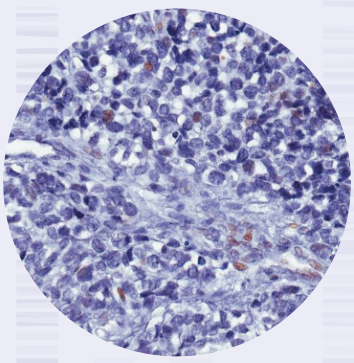
The study was co-led by Professor David Thomas, Head of the Genomic Cancer Medicine Laboratory at Garvan and CEO of Omico, a non-profit nationwide network of genomic cancer research and treatment centres.

"Cancer is fundamentally a genetic disease and genomics is the key to unlocking its secrets. This international collaboration has developed new methods for mapping the genetic basis for cancer and identified new heritable pathways that increase cancer risk. These findings fill important gaps in the missing heritability of cancer."
– Professor David Thomas

The research paves the way for people with a family history of sarcoma to test for their genetic risk of developing the disease.

To find out more please visit:
garvan.org.au/sarcoma

Dr Mandy Ballinger



Sarcoma cells

New study reveals poorer health outcomes for at-risk patients

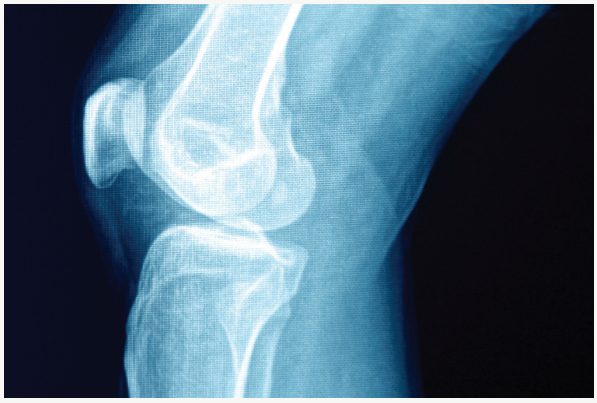
Patients with complex medical conditions at high fracture risk are vastly undertreated for fracture prevention yet at higher risk of further fracture.

According to a new Garvan study, people at high risk of fracture who also have complex or multiple chronic medical conditions are less likely to receive treatment for their underlying osteoporosis and will have poorer health outcomes.

These patients have an increased risk of further fractures, but they are less likely to have the underlying cause of the fracture investigated, compared with those who are at high risk but have no additional chronic conditions.

"No matter the fracture site, we believe fracture is under-prioritised in the clinical setting in a complex patient," says lead author Dr Dana Bliuc, Senior Research Officer in the Clinical Studies and Epidemiology Lab at Garvan.

"People with complex diseases not only fare worse, but they are less likely to receive treatment, which is a double whammy. We think this is because fractures are viewed as less serious than other medical conditions present in patients, and thus not the focus of intervention," says Dr Bliuc. "But fracture itself will affect quality of life and contributes to mortality."



Osteoporosis affects more than 1.2 million Australians

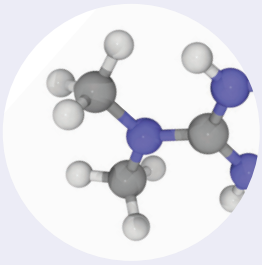
The findings will help inform new guidelines for how fractures in patients with complex medical conditions are investigated and treated by clinicians.

To find out more about the recent study, please visit:
garvan.org.au/fractures

Testing a drug treatment for dementia

A commonly used treatment for diabetes may hold the key to slowing cognitive decline to prevent dementia.

Professor Katherine Samaras



Metformin

A Garvan-led study is seeking participants for a phase 2 clinical trial to test a drug that could slow the process of cognitive decline, a hallmark of the processes that may lead to dementia. The three-year intervention study will examine the effects of metformin – a drug used to safely and cheaply treat diabetes and other metabolic disorders – on cognition, brain anatomy, vascular health and early signs of dementia.

"We are building on promising research on the positive effects of metformin that could have real impact on reducing or stopping the progress of cognitive decline, something for which there is no effective treatment," says lead researcher Professor Katherine Samaras, Head of the Clinical Obesity, Nutrition and Adipose Biology lab at Garvan and endocrinologist at St Vincent's Hospital Sydney.

Success of the randomised-controlled trial, known as MetMemory, would mean that treatment for slowing cognitive decline could be immediately available.

The clinical trial is already underway and requires more volunteers. Participants need to be aged over 60, live in the Greater Sydney region and be experiencing symptoms of mild cognitive impairment like challenges with memory loss and thinking.

To find out more please visit:
garvan.org.au/metmemory

Would you like to help fund life-changing medical research?

Scan to donate online or visit
garvan.org.au/give-now

Call **1300 73 66 77**
(9am - 5pm)

Paspaley's Jewellery with purpose

Paspaley has announced the release of multiple new designs of its beautiful, signature Kimberley bracelet.

Jewellery with Purpose: Paspaley donates 20% from the sale of each Kimberley bracelet to support our Molecular Screening and Therapeutics (MoST) clinical trials programme, which focuses on accelerating Garvan's pioneering research into rare and less common cancers.

Paspaley will continue this charitable programme with the new iteration of the Kimberley collection.

"Paspaley's contribution has supported treatment costs for many people with rare cancers and their funding contributes significantly to the impact and outcomes for these patients. We're thrilled with our ongoing partnership. With Paspaley's support, Garvan is leading the way globally in providing new therapies and hope for cancer patients who have no other treatment options available," says Professor David Thomas, Lab Head – Genomic Cancer Medicine.

First launched in 2016, the collection combines lustrous Australian South Sea Pearls with regional, renewable, aromatic sandalwood for a wearable, timeless style.

Paspaley's new Kimberley Collection designs are available to purchase in-store and online at Paspaley.com from 1 April.

PASPALEY

Clinical Trial **Spotlight**

Join the Personalised Medicine in Prediabetes (PREDICT) study

We're seeking participants aged 20 to 70 years who have prediabetes or newly diagnosed type 2 diabetes but have **not been treated** with a glucose lowering medication for our PREDICT clinical trial.

Led by Associate Professor Dorit Samocha-Bonet, the study aims to identify whether changing the gut microbiota with a personalised diet might increase the effectiveness of a common diabetes drug, metformin.

The goal is to give clinicians and patients the diagnostic tools to deliver more personalised treatments.

To find out more please visit:
garvan.org.au/predict