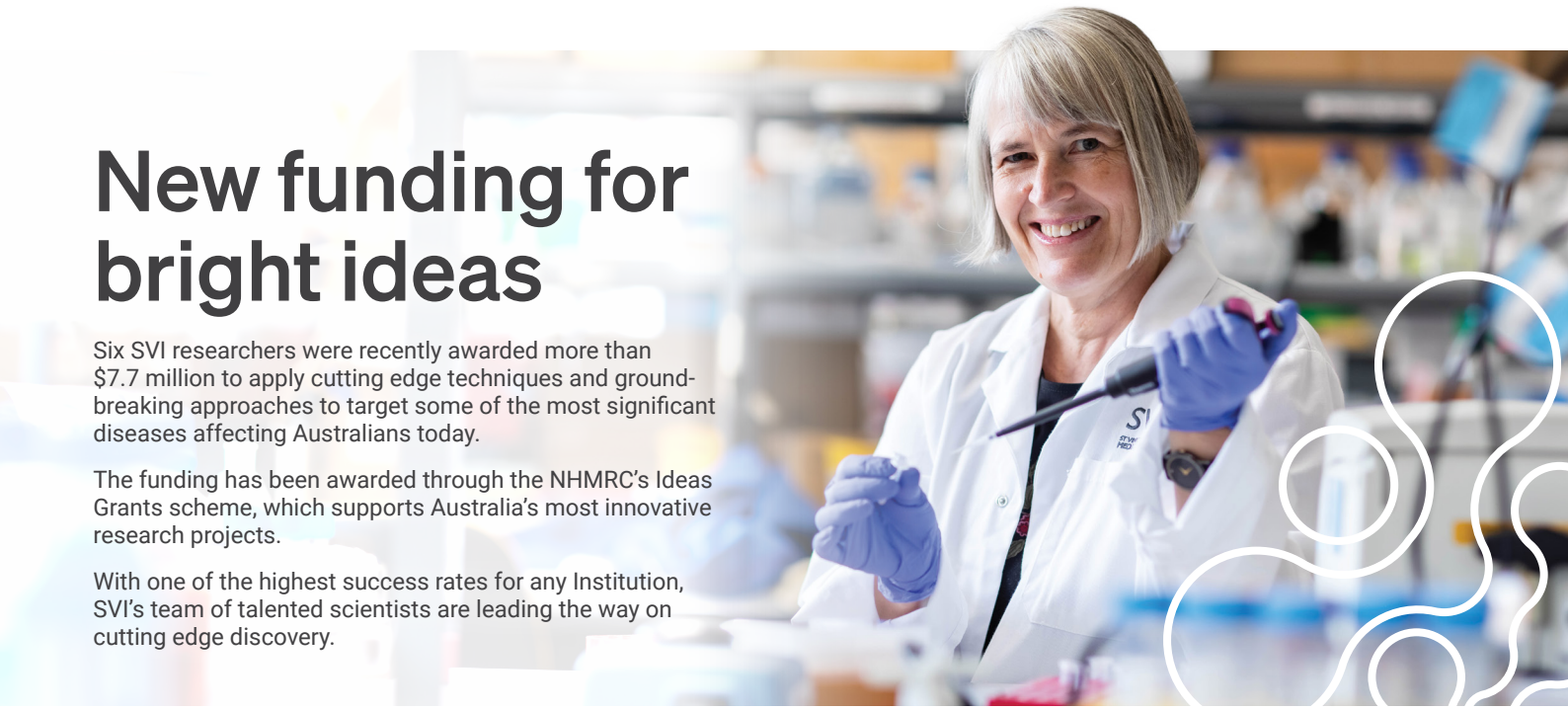
IN focus
AUTUMN 2024
SVI St Vincent's Institute MEDICAL RESEARCH



New funding for bright ideas

Six SVI researchers were recently awarded more than $7.7 million to apply cutting edge techniques and ground-breaking approaches to target some of the most significant diseases affecting Australians today.

The funding has been awarded through the NHMRC's Ideas Grants scheme, which supports Australia's most innovative research projects.

With one of the highest success rates for any Institution, SVI's team of talented scientists are leading the way on cutting edge discovery.

Understanding blood cancer

Professor Louise Purton's outstanding work on blood cells was recognised with two NHMRC Ideas Grants. The grants, worth more than $3.2 million, will allow Louise to unravel the cause of changes in the production of blood-forming cells which can lead to complications including blood cell cancers.

"This funding will allow us to understand how blood cell diseases occur and, in turn, identify better ways to treat patients with different types of blood cell diseases," said Louise.

Tackling drug resistance in ovarian cancer

Associate Professor Elaine Sanij was awarded $761,355 to help better understand drug resistance in ovarian cancer and to test new and emerging treatments. Her work aims to offer hope to the 1800 Australian women diagnosed with ovarian cancer every year.

"Many ovarian cancer treatments used today are virtually unchanged since the 1990s. Better treatments for this cancer are desperately needed," she said.

A new treatment for type 2 diabetes

Dr Kim Loh was awarded $922,820 to investigate whether a newly identified molecule which inhibits insulin release can be targeted as a potential new treatment for type 2 diabetes.

"There is a particular process that happens in the body of people with type 2 diabetes which suppresses the release of insulin. We want to intervene to stop this," says Kim.

Targeting liver disease

Associate Professor Jon Oakhill has been awarded $1.16 million to test a potential new treatment for non-alcoholic fatty liver disease, which is thought to affect up to a third of Australians.

"The enzyme AMPK is the fuel gauge of a cell," says Jon. "It monitors the cell's energy levels and tells it when to store energy and when to use it. We will be using new mRNA technology to precisely modify the activity of AMPK in liver cells in order to find new ways to treat liver disease," says Jon.

Hope for Friedreich ataxia

Dr Jarmon Lees was awarded more than $788,000 to expand his ground-breaking heart organoid research with the goal of identifying new therapies for the devastating genetic condition, Friedreich ataxia.

"Using our 'heart in a dish' - mini-hearts grown in the lab that are derived from stem cells of people affected by Friedreich ataxia - we're investigating two genes that may play a role in its development and progression."

Next generation diagnostics

Associate Professor Wayne Crismani has been awarded $797,705 to improve the diagnosis and management of Fanconi anaemia, a rare genetic disorder that predisposes to early onset cancer and insufficient blood production.

"In this project, we are developing cutting edge diagnostic tools to identify the genetic causes of this serious condition. We are also investigating why some patients' blood production responds well to cheap and safe treatments and others do not, with a view to improving treatment," says Wayne.

Tom says

The beginning of a new year is an opportunity to reflect on what has led us to this point as we look forward to what is yet to come.

Last year was one of the busiest and most successful years SVI has had to date. Our outstanding scientists achieved a remarkable success rate in funding announced by the National Health and Medical Research Council (NHMRC), at the end of 2023.

From ground-breaking heart disease research to being at the forefront of cancer treatments, our work is changing the way Australians meet their health challenges. Our success with NHMRC funding is testament to the extraordinary talent we have at SVI and the outstanding work we are doing.

Last year was also significant for type 1 diabetes research with the publication of our clinical trial results in the *New England Journal of Medicine*.

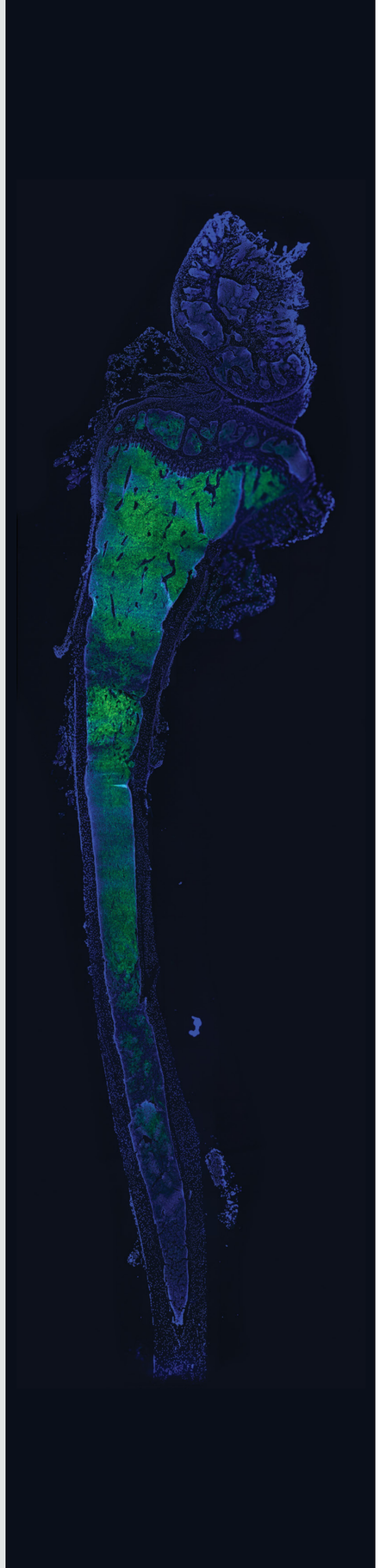
Type 1 diabetes appears to be headed for a watershed moment in which it is treated as an autoimmune disease rather than as a hormone deficiency disorder and SVI is leading the charge.

Of course, this will not be based on one single piece of research but several pathways reaching maturity after decades of work.

One of these pathways is some truly remarkable research by Associate Professor Bala Krishna Murthy, which was recently published in top-tier journal Proceedings of the *National Academy of Sciences of the United States of America* (PNAS).

You can read more about all of the above in this issue of In Focus.

The work we do here on type 1 diabetes, on bone disease, heart disease, cancer, and many other conditions is treading a path no one else ever has. We are at the forefront of scientific discovery and we are grateful to have your support.



Wildely optimistic

In late 2023, Associate Professor Elaine Sanij and SVI's Christine Martin Fellow, Dr Jian Kang, were awarded two grants by The Barrie Dalgleish Centre for Myeloma and Related Blood Cancers.

The Dalgleish Centre is a partnership of academic organisations, including Peter Mac, SVI, and St Vincent's Hospital, formed thanks to a bequest left by psychologist Barrie Dalgleish. The Centre aims to focus the collective talent of cancer researchers across Melbourne on the blood cancer, multiple myeloma.

In multiple myeloma, immune cells in the bone marrow transform into cancerous cells that grow out of control, crowding out normal cells that help fight infection.

Elaine says that symptoms of multiple myeloma vary from person to person. In the early stages of disease, there are often no obvious ones.

"The disease isn't thought to be hereditary and its causes are currently unknown," she says.

It was almost by sheer luck that Karen Wilde was given an accurate diagnosis for a pain in her leg that just wouldn't go away.

"I thought I had injured myself but the pain lingered a bit too long so I went to see a GP," said Karen.

"My doctor suspected it was something a bit more serious than a strained muscle because she had recently diagnosed someone else with multiple myeloma."

"As a physiotherapist, I had always been conscious of staying very fit and healthy. So, when my doctor said that if someone like me could have multiple myeloma, then anyone could, it struck a chord."

Karen's refusal to allow the disease to define her and interest in finding solutions have led her to become involved in clinical trials, raise funds for multiple myeloma research and to forge a connection with Elaine at SVI.

"Understanding the problems of multiple myeloma from the perspective of someone who has first-hand experience really helps us to shape our research program. I have been blown away by Karen's optimistic nature and drive to make a difference," says Elaine.

Elaine and Jian are working to understand how multiple myeloma cells drive the progression of the disease and find ways to evade treatment.

"We are doing this using state-of-the-art technologies that allow us to compare myeloma cells that are sensitive to treatments to ones that have developed resistance. This will help us understand the difference between the two. We are also looking at genes associated with resistance to therapy."

Australia has one of the highest rates of multiple myeloma in the world, with around 22,000 Australians currently living with the disease, and 1100 dying each year from its effects. The disease is generally considered incurable.

Neither Elaine nor Karen are willing to accept this.

"I reject that word, 'incurable'," says Karen. "There is so much work being done by wonderful people like Elaine that I refuse to accept that we won't find a cure."

"It might not be found in my lifetime, but I don't doubt that it will be found."

Image: Karen Wilde with A/Prof Elaine Sanij and PhD student Kezia Gitareja
Image: Cross section of bone with multiple myeloma cells growing in the bone marrow

Type 1 diabetes in focus

New hope for type 1 diabetes

At the end of 2023, the publication of Professors Tom Kay and Helen Thomas' type 1 diabetes clinical trial in the prestigious *New England Journal of Medicine*, drew the world's gaze to the quality research being done at SVI.

Our team's world first trial showed that type 1 diabetes can be prevented from progressing by taking a daily tablet of a widely used rheumatoid arthritis drug called baricitinib.

"It is tremendously exciting for us to have been the first group anywhere in the world to test the efficacy of baricitinib as a potential type 1 diabetes treatment," says Helen.

"It's even more exciting to know that after decades of effort, our work will directly impact the lives of people with type 1 diabetes."

WATCH VIDEO

Exhausting study

As an endocrinologist and immunologist, Associate Professor Bala Krishna Murthy is keenly aware of the problems faced by people with type 1 diabetes. His research at SVI focuses on manipulating the immune system, using insights discovered in other disease areas.

"Cancer cells find ways to evade the body's immune system so that they can continue growing. One way they do this is by 'exhausting' the immune cells through repetitive stimulation, removing their ability to keep the cancer at bay," says Bala.

He explains that new immunotherapy treatments against cancer work by reenergising these exhausted immune cells, allowing them to mount a renewed offence against the offending tumour cells.

In an article published in the prestigious journal *Proceedings of the National Academy of Sciences of the United States of America* (PNAS), Bala turned this concept of immune exhaustion on its head, to stop immune cells from destroying insulin-producing cells in type 1 diabetes.

Bala and his team showed that, while there is some evidence of immune cell exhaustion in mice that develop type 1 diabetes, it is incomplete and not sufficient to stop the disease process.

In fact, the team showed that immune cells appear to recover from exhaustion in part by periodically moving away from the pancreas to elsewhere in the body.

"It's almost as if they are taking a break and regaining their strength," says Bala.

To try to exhaust the immune cells, Bala and his team selected a particular protein found in insulin-producing cells in the pancreas. The immune response to this protein is known to be involved in causing disease in diabetes-prone mice.

They genetically manipulated the mice to expose their immune cells to the protein outside of the pancreas – so that they were not able to take respite from the stimulation.

"As a result, once the cells re-entered the pancreas, they were already exhausted and no longer able to continue destroying the insulin-producing cells. These mice were then protected from developing the disease," he says.

Although in its early days, this research holds great promise.

"Our eventual goal is to develop a short course of treatment that could be deployed in people at risk of type 1 diabetes, which would result in the condition never developing at all."

The study, 'Extraislet expression of islet antigen boosts T cell exhaustion to partially prevent autoimmune diabetes', is published in *PNAS*.

Anna takes action

"I've got it, haven't I?"

That's what then 11-year-old Anna said to the hospital emergency team when she visited following a worrying rise in her blood glucose levels.

The 'it' Anna was referring to was type 1 diabetes.

Anna's oldest brother Max, now 20, had also been diagnosed with type 1 diabetes when he was 11. Their mum, Sarah Jane, said, "When Anna was diagnosed, I experienced sadness, because I see it as a lifelong condition."

Within 100 days of her diagnosis, Anna had put her hand up for SVI's BANDIT trial, because, as she said, "I never want my grandbabies to go through this."

Anna's type 1 diabetes was caught very early on, as Sarah Jane had enrolled Anna and her two brothers in a risk screening study, which led to the discovery that she had antibodies linked to increased risk of developing the condition. While there is a genetic risk of type 1 diabetes, her other brother Harry, who is 18, does not have any of the antibodies.

Sarah Jane describes the BANDIT study as 'intensive' and while they don't know yet if Anna was on the trial drug, baricitinib, or a placebo, she said one benefit of being on the trial was that it provided them with more medical support. "When Max was diagnosed, we felt like a fish out of water," she said.

The trial follow up will continue for the rest of 2024. Anna's 13 now, and on a very low dose of insulin.

"She doesn't have the wide variances in blood glucose levels that her brother had," Sarah Jane said. "Even so, some nights are tough, and she has to have sugar to raise her glucose levels."

Sarah Jane is philosophical about type 1 diabetes research, saying, "I think a treatment and potential cure has been coming for such a long time. I know that it takes money to support type 1 diabetes research, and that if it doesn't affect you, it's not everybody's cup of tea.

"While we wish a treatment to prevent or slow down the progression of the condition was further down the line, we're glad Anna had the opportunity to potentially change someone else's future experience with type 1 diabetes.

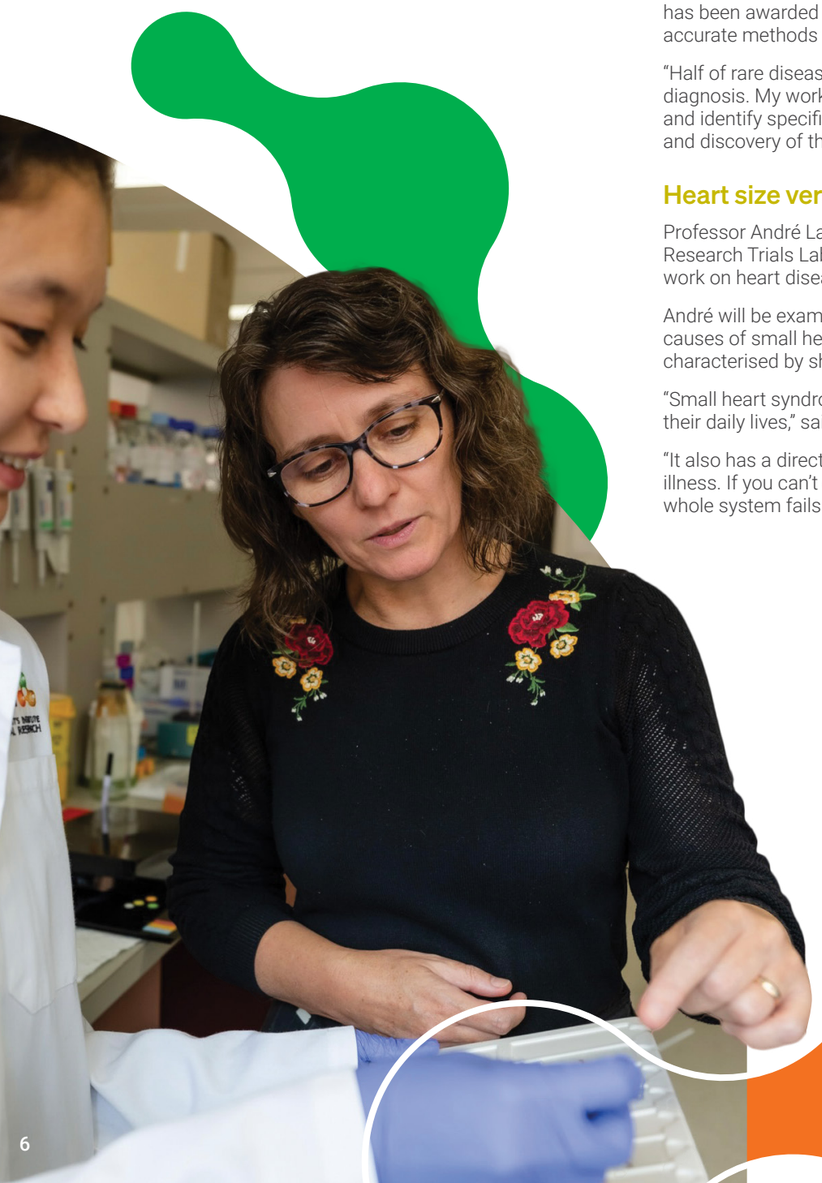
"I'm grateful that SVI's researchers aren't giving up."

Investigating excellence

The NHMRC Investigator Grant scheme is the NHMRC's largest funding scheme and a major investment in Australia's health and medical research workforce.

Awarded to Australia's highest achieving researchers, these grants play a critical role in the Australian health and medical research sector by providing a significant research support package over 5 years.

At the end of 2023, three of SVI's scientists were awarded more than $5M to tackle bone disease, heart disease and rare diseases.



Bone disease in the sights

Professor Natalie Sims, Head of SVI's Bone Biology & Disease Lab was awarded $2.5 million to advance her work on understanding the causes of age-related bone fragility.

"We've known for almost 50 years that cortical bone gets more porous as we age, but we still don't understand how this happens or what drives it," Natalie explains.

"This new knowledge presents tantalising opportunities not only to develop better treatments for osteoporosis, but to improve surgical implants for knee and hip replacements and to engineer better load-bearing materials for manufacturing cars, planes and buildings."

Better diagnosis of rare diseases

Dr Harriet Dashnow, an internationally recognised bioinformatician currently based at the University of Colorado, has been awarded more than $660k to investigate more accurate methods to diagnose rare disease.

"Half of rare disease patients don't receive an adequate diagnosis. My work focuses on developing software to analyse and identify specific genomes in order to improve the diagnosis and discovery of these diseases," says Harriet.

Heart size versus heart health

Professor André La Gerche, Head of SVI's Heart, Exercise, and Research Trials Lab was awarded more than $2.7 million for his work on heart disease diagnosis and treatment.

André will be examining the potential genetic and environmental causes of small heart syndrome, a condition which is characterised by shortness of breath and exercise intolerance.

"Small heart syndrome impairs a person's ability to go about their daily lives," said André.

"It also has a direct impact on their body's ability to cope with illness. If you can't get enough oxygen to your muscles then the whole system fails."

A magical night at The Jade Lantern

Research from SVI's brightest young scientists will be supported in 2024 thanks to the generosity of supporters who attended SVI's For the Love of Science event at the Fitzroy Town Hall in November last year.

The 'Welcome to the Jade Lantern' dinner raised more than $280,000, to support Rising Star Awards at SVI in 2024. This was the fifth For the Love of Science dinner, an initiative that has now raised more than $1million and funded 30 of SVI's brightest young researchers since 2019.

"The evening was truly wonderful – a perfect blend of community spirit and generosity, with like-minded people coming together to have fun, and make a meaningful impact", said Karen Inge, SVI Foundation Board Chair.

SVI extends thanks to everyone involved in the event, and especially to

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Artwork donors: Nellie Castan Projects, Caleb Sheah, Kate Rohde

Stylist extraordinaire: Michael Strownix

Auctioneer: Stephen Smith

Organising committee: Caroline Daniell, Karen Inge, Mem Kirby and Michael Strownix

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THANK YOU

Supporting our next generation

The SVI Support Group has been raising funds for SVI since 1989 – more than half the Institute's lifetime. Over those years, the Group has played an important role in nurturing more than 100 of SVI's brightest young students.

The SVI Support Group dinner is held annually to raise funds for our PhD Top Up Scholarship program. The scholarships allow our emerging scientists to focus fully on their studies and career development, without having to find additional ways to cover the cost of living.

The most recent dinner, held at the Kooyong Tennis Club in October last year contributed towards more than $130,000 raised for the program in 2023. This will support SVI's PhD students to find new treatments for conditions such as osteoporosis, cancer, and inherited diseases.

The success of the program is thanks to the hard work of the SVI Support Group, which has been led by the unstoppable Claire O'Callaghan OAM since its inception. At the dinner, past Top Up Scholarship award recipient, Professor David Ascher, announced that the Institute has established an Award named in her honour – the Claire O'Callaghan Top Up Scholarship.

"SVI's student body have been lifted up by Claire's dedication and enthusiasm. Thank you, Claire, so much for making a difference in the lives of so many students," said David.

THANK YOU

Thank you to our wonderful Support Group Committee:

Claire O'Callaghan OAM (Chair)
Margaret Batrouney
Pam Batrouney
Colleen Bolton
Robyn Brasher
Bernadette Dennis OAM
Angela Griss
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