

Australian Government

National Health and Medical Research Council

75 YEARS OF WORKING TO BUILD A HEALTHY AUSTRALIA



















Research Projects 2011



National Health and Medical Research Council

75 YEARS OF WORKING TO BUILD A HEALTHY AUSTRALIA

TEN OF THE BEST

Research Projects 2011



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Paper-based publication

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Health and medical research is an area where Australia shines

The Hon Mark Butler MP

Minister for Mental Health and Ageing

We are renowned internationally for our outstanding contribution to human health, including the development of a rotavirus vaccine to protect children against this gastro killer, the first humidicrib for premature babies and more recently, the cervical cancer vaccine.

Ten of the Best Research Projects 2011 celebrates Australia's best and brightest researchers, highlighting the benefits of their research for Australians of all ages.

Our scientists and medical researchers are working to produce more effective treatments for cancer and reduce the incidence of heart disease – one of this country's biggest killers. They are also working to give our next generations a better start in life by finding solutions to illnesses that affect children and young people.

For our current generation of older Australians, health and medical research has the potential to support them to lead longer, healthier and more independent lives. We are tackling not only the illnesses and conditions that become more prevalent as we age, but also finding ways to improve the wellbeing of carers and their families.

Mental illness can strike at any age, in childhood, adult life or maturity. This is why Australian research aims to unlock the mysteries of conditions such as depression, so we can strengthen our prevention methods, streamline diagnosis and improve care and recovery.

I am pleased the Australian Government is continuing to strengthen Australia's health and medical research capacity through the NHMRC.

By supporting Australian researchers, we can help improve the health of all Australians.

Mark Butter



2011 marks 75 years of NHMRC support for Australian health and medical research

Professor Warwick Anderson AM Chief Executive Officer, NHMRC

In this time, NHMRC has helped bring about groundbreaking discoveries in the fight to improve health outcomes for all Australians.

This year's Ten of the Best features ten research projects that may produce some of our next 75 years of medical breakthroughs and help to address Australia's greatest health challenges. The researchers profiled here have developed a prototype of a simple test for HIV for use in poorer countries and promoted the introduction of folate in flour to reduce birth defects. Another project has shown the benefits of people with depression participating in work, potentially relieving some of the annual \$3 billion cost to the community of depression-related sick leave.

As Australia's single biggest funding agency for health and medical research, NHMRC is proud to support the work of researchers through our grants and fellowships, as well as through our international collaborations. NHMRC is working with researchers to strive for better ways to translate research findings into health practice, to close the gap between bench and bedside.

Progress in health and medical research depends not only on the ongoing dedication of Australia's talented researchers, but also on the support of the community and the involvement of Government, participants, volunteers and advocates.

On this 75th anniversary of the NHMRC, I would like to thank our researchers, the public and the NHMRC Council, committees and staff for the enormous contribution they have made to the wellbeing of all Australians. Together, we will work to improve the health of our future generations.

"Medical research is very competitive so don't go into it unless you are prepared to be highly committed and give it your all—this means long hours and lots of hard work."

Sam Breit's moment of discovery is a perfect example of how smart observation can deliver a medical research breakthrough—after much dogged, clever work beforehand.

It's all about MIC-1/GDF15 – nicknamed MIC-1 – a protein identified by his team at the St Vincent's Centre for Applied Medical Research in Sydney as a marker for several cancers.

They played a leading international role in understanding MIC-1's makeup and function, showing that it dramatically increases in the bloodstream of people with cancers or inflammation caused by disease or physical injury.

This made it a good candidate to enable early diagnosis before a cancer could be detected by imaging technologies. Testing this hypothesis, they grafted into laboratory mice, tumours which produced high levels of MIC-1.

"I noticed that the mice with tumours expressing a large amount of MIC-1 appeared quite happy, but lost a dramatic amount of weight," Sam recalls.

"I realised this was likely to represent mice with anorexia/cachexia."

Anorexia/cachexia is a condition of dramatic weight loss. For cancer patients it worsens their suffering,

limits therapy options, and is responsible for about 25% of cancer deaths.

Sam's team tracked MIC-1 to find it operating deep in the brain, in an area of the hypothalamus which has a major role in regulating appetite. They realised that blocking MIC-1 could be a good way to treat loss of appetite in cancer patients and others with anorexic conditions. For people who eat too much, MIC-1 could be a treatment itself.

Sam's team has identified antibodies to MIC-1 and are working to develop them into a therapy for anorexia/cachexia. They have also licensed pharmaceutical company Novo Nordisk to develop an anti-obesity drug which could help reverse the obesity and diabetes epidemics in rich countries.

This would fulfil Sam's ambition to deliver real health benefits from his research.

rest in ag back nedicine accoming

"I have had a lifelong interest in biomedical research dating back to my teens, I went into medicine with the specific aim of becoming a physician scientist.

"It's very important to me that our studies so far have yielded very important results that have led to practical applications to help patients."

PROJECT TITLE

The mechanism of cachexia induced by the TGF-ß superfamily cytokine, MIC-1

CHIEF INVESTIGATOR

Professor Samuel Breit

FUNDING AMOUNT

\$544,201 (2007–2009)

erver



"A poorly functioning heart leads to a poorly functioning kidney and a poorly functioning kidney makes it harder for the heart to pump—we are looking for new treatments to break that cycle."

Professor Henry Krum is now Director of the Monash Centre of Cardiovascular Research and Education in Therapeutics, but like many medical researchers he began his career treating patients.

"As a clinician coming through the ranks of hospital medicine, I wanted to know a lot more about why we do the things we do," he says.

Working in clinical pharmacology he found that around 50% of the drugs at his disposal were for cardiovascular conditions, so that's where he headed as a researcher.

"That's where the action is and hopefully where you can make a difference."

His team is developing new pharmaceutical treatments for heart conditions, looking at how nerve function in the kidney may affect the heart, and investigating potential stem cell therapies.

The team is also evaluating whether diseases such as diabetes alter the efficiency of existing therapies. They have patented several experimental

heart treatments, while a recent discovery has opened the way to a new use for an existing drug.

"Failing kidneys produce toxins, but nobody has really looked at how these toxins affect the heart; we have and we've found that one does indeed affect the heart," Henry says.

In 2012, they plan to start human trials of a kidney medication to prove that it can benefit heart function. If that is successful, it will mean it can be used to treat patients much faster than a new drug which would require more stringent testing. Either way, Henry knows that success doesn't come easy.

"The best word to describe a career in research is 'persistence'. It's like a marathon where you keep getting tripped over and knocked down, but you've just gotta get up."

The rewards are seeing patients living longer and healthier lives, earning the respect of the international research community, and working with a motivated team.

"One thing that is really gratifying is seeing a junior researcher flourish and develop and become independent. It is all about the team - other investigators and PhD students with ideas – it's shared defeat and shared victory."





dio decoder

reduce the burden of chronic heart failure

CHIEF INVESTIGATOR

Professor Henry Krum

FUNDING AMOUNT

\$4,928,323 (2005–2009)

Left to right: Alison Cox, Dr Andrew Kompa, Dr Yuan Zhang, Dr Alice Owen, Professor Chris Reid, Professor Henry Krum, Professor Darren Kelly, Louise Shiel, Associate Professor Robyn Langham, Dr Bing Wang

"I was an anguished clinician, I decided I had to prevent disease rather than going on treating it."

Like many medical researchers, Fiona Stanley set out to be a doctor.

"I never finished my paediatric training because I got very anxious about the shocking things that kids got.

"I thought there has got to be another way of doing medicine, then I discovered public health, maternal and child health, and disease prevention."

As the founding Director of the Telethon Institute for Child Health Research at the University of Western Australia, she has established a multidisciplinary team whose mission is to research illnesses afflicting children and young people, and provide solutions.

Despite Australia's increasing prosperity, the incidence of low birthweight, behavioural and mental health problems, autism and obesity have been steadily increasing, while many Indigenous children face much higher rates of illness than their contemporaries.

"These problems weren't going away in adulthood so we saw that they could have a huge negative impact on Australian society," Fiona says.

"We passionately felt that we had to find the best ways to prevent and interrupt these problems."

The team of expert researchers is focused on establishing rationales for early intervention in the development of disease and disorders.

Their research has led to the mandatory inclusion of folate in flour, lowering the risk that a mother's diet could cause her child to be born with spina bifida.

It has reduced the numbers of Indigenous children needing antibiotics or hospitalisation for pneumonia, gastroenteritis and other infections, and initiated vaccination programs which caused declines in childhood pneumococcal disease and meningitis.

They showed that the recorded increase in autism is mainly due to changes in diagnostic practices, instigated the establishment of a national approach to cerebral palsy research and treatment, and provided the platform for the introduction of the Australian Early Development Index.

"We are the first country in the world to have a true measure of child development – like a GDP," Fiona says.

As she prepares to retire at the end of 2011 she knows that this work will continue, providing lasting satisfaction after a career in the best job in the world.

"I can't think of a career that is more exciting, nor

more respected in the community.

"You are totally engaged intellectually, which

interv

is so much fun, travel the world meeting all sorts of amazing people, and know you can make a real difference.

"How about that? Forget all the pain of writing grant applications and getting rejected and all that, just go for it."



Early entionist

Determinants of child health and development: populations, partnerships, pathways and prevention

CHIEF INVESTIGATOR
Professor Fiona Stanley

FUNDING AMOUNT \$8,214,334 (2005–2009)

Left to right: Clinical Associate Professor Deborah Lehmann, Professor Carol Bower, Professor Nick de Klerk,
Professor Fiona Stanley, Professor Steve Zubrick, Clinical Associate Professor Helen Leonard

Absent on the day: Professor Sven Silburn

"I've always had a keen interest in marine bioactives."

It sounds like Nemo meets Terminator, and it's happening in the waters of the Great Barrier Reef.

Many species of cone snail stab at prey with a venomous barb on the end of a long stalk known as a proboscis. Within seconds of being hit, fish can be immobilised by toxins that cause nerve paralysis. Slower acting toxins often follow up by paralysing the muscles.

Identifying the potent blocking agents in cone snail venom and working out how to apply them to relieve pain in humans is the work of the research group Richard Lewis leads at the University of Queensland's Institute for Molecular Bioscience.

"Many types of pain, especially chronic pain associated with diseases like cancer and diabetes, remain poorly treated," Richard says.

"New drugs are required that produce fewer dose-limiting side effects or target pain pathways more effectively.

"Cone snails produce venom peptides that act very selectively across a diverse range of neurological targets associated with pain pathways, presenting a unique opportunity to develop new pain therapies."

Building on work he did for his PhD at the University of Queensland, Richard's group is also looking at ways to use ciguatera toxins produced by plankton which live on algae in coral reefs. Small fish eat the algae and

bigger fish eat them, the toxins accumulate along the food chain and can cause neurological illness in people who eat fish at the top of the chain.

His team collaborates with other groups in Australia, Japan, the US and UK, China and Germany and their work has led to three patents which offer promise of new pain treatments without side effects associated with existing drugs.

Brisbane-based biopharmaceutical start-up Xenome has progressed one of the group's findings through to clinical trials of a treatment for patients who gain no relief from traditional morphine-based treatments. For Richard and his team, that is what it's all about.

"A career in medical research is both challenging and highly rewarding," he says.

"You have to be passionate about your research and make the most of opportunities to better understand diseases and their treatments."

Toxin nat ge of pathways, par new taster

Front Row: Nikita Abraham, Mriga Dutt, Professor Richard Lewis, Josh Wingerd. Back Row: Dr Lotten Ragnarsson, Prerna Jha, Simon Sattler, Marco Inserra, Dr Irina Vetter, Silmara Rodrigues de Sousa Absent on the day: Dr Sebastien Dutertre. Dr Ching-I Wang



"Working in a hospital where I see patients every day is my motivation to keep striving for a cure for the diseases that afflict our society."

Everyone knows about T cells. They are the warriors of our immune system, marching to sites of infection to protect us, defeating the enemy, and remembering how to fight different aliens when they attack again.

Shame it isn't so simple. Jane Oliaro's research is a great example of how the more we discover in medical science, the more mysteries and complexity we find.

Like 'asymmetric cell division'. A cell splitting to form two clones is a fundamental process of life, but Jane's team at the Peter MacCallum Cancer Centre in Melbourne has contributed to a discovery that when some T cells divide following an infection, the new cells are different from each other.

Differences in the protein makeup of the new daughter cells have led to the theory that one becomes a warrior cell and the other a memory cell. The report of this discovery was ranked in *Science's* Top Ten Discoveries of 2007, and testing the theory is a focus for Jane's research.

"Understanding how memory is generated during an immune response will help us develop better immunisation strategies," Jane says. Nor are T cells invincible. All warriors have chinks in their armour. For T cells, one is a protein receptor on their surface called CD46. Attackers like the measles virus latch onto CD46 to disable T cells.

"Our research showed that signals generated when the CD46 is activated on T cells prevent normal responses to an infection," Jane says.

"This represents a critical step forward in understanding how pathogens can suppress immune function."

Achieving this kind of progress is what motivated Jane to follow a career in immunology, because improving our understanding of how the immune system works

improves our ability to relieve suffering. She says working in medical research is challenging but can be incredibly rewarding when new knowledge leads to new treatments.



"Undertaking research in a hospital environment provides a strong translational aspect, where researchers work closely with clinicians, thereby accelerating the 'bench to the bedside' path.

"Ultimately, I hope my research will allow the development of more effective treatments for both infectious disease and cancer."

PROJECT TITLE

Competition for polarity influences lymphocyte signaling and function

CHIEF INVESTIGATOR

Dr Jane Oliaro

FUNDING AMOUNT

\$500,460 (2007-2009)

unity novator



"Never underestimate the value of lateral thinking – the world is full of unmet medical needs, and they won't all be solved by the people who are looking the hardest, straight at them."

David Anderson and his team at the Burnet Institute in Melbourne had a problem. Their research to create a simple blood test for HIV patients in poor countries was being hampered by interference from cells which they didn't need to target. At a team meeting, he proposed sidelining those cells with a cocktail of antibodies, knowing that could take years to develop.

"Simone van de Waarsenburg, a research assistant on the project, realised that what I had described already existed as a commercial product for a different purpose," he recalls. "Around two weeks later, she was able to show us a working prototype."

Which goes to show the value of teamwork in medical research, and every now and again you get a lucky break.

Partly funded by the Bill and Melinda Gates Foundation as well as NHMRC, David's team was looking for a better way to measure levels of specific white blood cells – CD4+ T-cells – in the blood of HIV patients. Patients under a certain CD4+ threshold should start taking antiviral drugs, but current blood

tests require skilled staff and expensive instruments, which are not widely available in the poor countries where most of the world's 33 million HIV patients live.

"We can remember what it was like for HIV-infected patients in developed countries before the advent of highly effective combination therapies in 1996 – and it is intolerable that 15 years later this situation has not improved for most patients in the developing world," David says.

They devised a solution – measuring levels of a protein associated with CD4+ cells – and turned it into a simple test that is currently being trialled in the US to ensure its accuracy before wider trials in developing countries.

HIV test

To see his research improve the wellbeing of millions of poor patients will be the best reward for David who as a PhD student worked alongside researchers studying vaccines for hepatitis viruses.

"The practical side of the work, such as delivering the new hepatitis B vaccine to babies in developing countries where it was most needed, provided a lasting inspiration to focus on translational research and improved equity in health worldwide."



"I quickly realised that a career in research would allow me to influence the wellbeing of potentially hundreds of thousands of people rather than the hundreds I could individually help as a clinician."

It's uncool to go to work or school if you've got an infectious disease like the flu. But what if you suffer from an illness that is not infectious, like depression?

The Mental Health Council of Australia estimates that each year a million Australian adults and 100,000 young people cope with depression. The majority have jobs and careers. Should they front up to work when the black dog of depression bites, or stay home until they feel able to put in a good day's work?

Kristy Sanderson's team decided to find the answer. They developed epidemiological and economic models to evaluate the health outcomes and economic costs of both scenarios over a year, five years, and a lifetime.

"This is the first analysis of its type in the world for a chronic disease in the workplace," says Kristy, a Senior Research Fellow with the Menzies Research Institute Tasmania at the University of Tasmania.

For individual workers, they found no significant differences in health outcomes. But absenteeism incurred higher economic costs than presenteeism across all time periods. Mostly borne by employers, this could amount to \$3 billion a year nationally in

lost productivity according to a separate study which Kristy co-authored.

She says the study gives people with depression guidance that "working through it" may be advisable.

"There can be benefits to keeping on working when you are sick, not just in terms of earning an income and keeping your job, but also the mental health benefits from continuing with the routine and social support of working.

"This is the first time such a recommendation has been made with evidence behind it."

The study also indicates that presenteeism would be less costly for employers, but each case has to be assessed individually.

"We need to work out how to reach a balance between what is best for the employee and what is best for the employer, and that is what this study aimed to do," says Kristy, who began her career with a degree in psychology.

"The desire to help the mental health of populations rather than individuals led to my specialisation in psychiatric epidemiology."



Left to right: Fiona Cocker, Dr Kristy Sanderson

"When I had a go at research, to see what it's really like, I had a revelation — it was a fantastic experience and I was completely hooked."

Benjamin Kile got hooked on medical research during his Honours year at the Murdoch Childrens Research Institute after gaining a Science/Law degree at Monash University. A little over a decade later he won the 2010 Science Minister's Prize for Life Scientist of the Year. In between, he had spent three years at Baylor College of Medicine in Texas, a world leader in research into the genetics of health and sickness.

"We were searching for novel disease genes and I became the blood guy, looking for genes playing a role in blood cell development."

That opportunity set him on track to a discovery that contributed to him earning the 2010 award – the genetic basis for the short lives of the billions of blood platelets that a human body generates every hour.

"We demonstrated that each platelet contains a molecular clock and that we can slow it down or speed it up in mice. The goal now is to do the same thing to extend the lifespan of blood bank platelets." With colleagues at Melbourne's Walter and Eliza Hall Institute, his team has also discovered that a gene involved in cancer cell proliferation also regulates the ability of stem cells to keep renewing our blood supply. Now they are working to understand exactly how this critical factor exerts its effects, with the aim of identifying new targets in cancer therapy.

"I enjoy having the freedom to get up in the morning and pursue things that are interesting, not being completely beholden to what the boss wants, but being able to chase those little slivers of excitement that may represent the start of something really profound," Ben says.

"Underlying what we do is the belief that research holds the key to improvements in human health. It's exciting to be part of that broader endeavour, nationally and internationally.



"Even if you don't personally make the critical discovery, international research is moving ahead on many fronts and it's exciting to be part of that.

"If you are passionate about making a difference and you find the lure of discovery irresistible, then a career in medical research is for you."

PROJECT TITLE

The genetic control of platelet production and function

CHIEF INVESTIGATOR

Dr Benjamin Kile

FUNDING AMOUNT

\$558,920 (2007-2009)

blood guy



"Probably our greatest knowledge gap is in the area of effective intervention to prevent diabetes, kidney and heart disease in Indigenous young people."

One of the most challenging undertakings in medical research is a long-term study. Testing people over extended periods can provide deep insights into changes in their health and the reasons for those changes.

By gathering and analysing data over 10-20 years, Kerin O'Dea and other Chief Investigators, with strong support throughout from NHMRC, have conducted a series of the longest and most comprehensive studies of health and chronic disease profiles in remote Indigenous communities.

As Director of the Sansom Institute for Health Research at the University of South Australia, Kerin is a leader in research into the health of Indigenous Australians. Other projects in the Homelands Program included research into the high risk of kidney disease, which involved biopsy and post mortem examinations, a trial of targeted medication to see if the onset of diabetes, high blood pressure and kidney disease can be delayed in susceptible populations, and a demonstration that a 40% lower mortality in a community living on their traditional lands was likely related to a sense of control over their lives, access to bush foods, and an excellent primary health care service.

By serving as a director of Outback Stores, an organisation committed to providing healthy

and affordable food in more than 20 remote northern communities, Kerin is fulfilling her commitment to translate research findings into better health policy and service provision.

"One of the things that characterises a lot of public health research is that we describe how bad things are but we don't do enough intervention," she says.

"While it is very important to document bad health outcomes and describe what factors contribute, we must not stop there.

"What we've been interested in doing is looking at how things could change."

One change she welcomes is the growing number of Indigenous people progressing through PhD and postdoctoral training to take up roles as health research project leaders in Indigenous health and other areas.

"Why become a health researcher? Because

you have the possibility to spend your life working on questions that fascinate you – and what a privilege that is," she says.

"I am passionately interested in the therapeutic potential of traditional diets and lifestyles of numerous populations, including Indigenous Australians – there is still so much we do not know."

PROJECT TITLE

Health outcomes, monitoring and evaluation: learning about activity, nutrition, diet and social factors

CHIEF INVESTIGATOR

Professor Kerin O'Dea

FUNDING AMOUNT

\$7,518,100 (2005–2009)

ck vocate



"The exciting part about leukaemias is that with current therapies many patients can achieve sustained remission, some can even be cured."

More than 3000 Australians are diagnosed with leukaemia each year. For those with chronic myeloid leukaemia, where white blood cells survive beyond their use-by date to clog up the bloodstream and organs, a drug called imatinib is a lifesaver.

Before imatinib was introduced in 2002 only 50% of patients survived longer than 5 years, now 90% can expect to live at least that long. But for around 25% of them, imatinib is ineffective, a problem Tim Hughes and his team at SA Pathology and the University of Adelaide set out to solve.

Like most medical research projects, it caused them frustration and puzzlement. After devising a way to measure the amount of imatinib in the leukaemic cells of individual patients, they found that this did not correlate with the effectiveness of the treatment. Eventually, they discovered that the key to the puzzle was measuring the imatinib actively pumped into the cells by a surface protein called OCT-1.

"With this knowledge, we were able to show a remarkably strong linkage between low OCT-1 activity and failing to respond to imatinib," Tim says.

"This provides clinicians with a test to identify patients who are not likely to respond to imatinib and treat them with new-generation drugs which are more potent but have a shorter track record."

Tim chose to specialise in haematology because it is a field where scientific discoveries are delivering real improvements in diagnosis and treatment.

"My memories of the 1990s when I would watch my patients gradually decline and lose their battle with leukemia are in such contrast to my recent experience, where most of my patients enjoy near normal quality of life and have excellent long-term prospects.

"Powerful new technologies are giving us abundant information about every patient, so the prospect that we can deliver truly personalised medicine is very real."

He warns that medical research requires commitment and passion, especially in the early years when hours are long and there is little job security.

"However it can be exciting and very rewarding, if you are focused and work hard, you can actually make a difference."

PROJECT TITLE

The role of intracellular uptake and retention of Abl kinase inhibitors in modifying clinical response in chronic myeloid leukemia

CHIFF INVESTIGATOR

Professor Timothy Hughes

FUNDING AMOUNT

\$465,210 (2007–2009)

aemia racker



purpose revelation

Honour Roll

Professor Samuel Breit

Professor Herbert Herzog

Associate Professor Amanda Sainsbury-Salis

Dr Heiko Johnen

Dr Shu Lin

Tamara Kuffner

Dr Vicky Tsai

Dr David Brown

Ten of the Best Research Projects 2011

Professor Henry Krum

Alison Cox

Associate Professor Robyn Langham

Professor Darren Kelly

Dr Andrew Kompa

Dr Alice Owen

Professor Chris Reid

Louise Shiel

Dr Bing Wang

Dr Yuan Zhang

Professor Fiona Stanley

Clinical Associate Professor Deborah Lehmann

Professor Carol Bower

Professor Nick de Klerk

Professor Steve Zubrick

Clinical Associate Professor Helen Leonard

Professor Sven Silburn

ose revelation

Honour Roll

Professor Richard Lewis

Nikita Abraham

Asa Andersson

Dr Sebastien Dutertre

Mriga Dutt

Marco Inserra

Prerna Jha

Dr Marion Loughnan

Dr Lotten Ragnarsson

Silmara Rodrigues de Sousa

Simon Sattler

Dr Christina Schroeder

Dr Iain Sharpe

Dr Irina Vetter

Dr Ching-I Wang

Josh Wingerd

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Anupama Pasam

Kim Pham

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Associate Professor Sarah Russell

Professor Mark Smyth

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Associate Professor David Anderson

Nadine Barnes

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Serina Cucuzza

Professor Thomas Denny

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Mary Garcia

Professor Alan Landay

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Robyn Lloyd

Dr Pat Mottram

Simone van de Waarsenburg

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Professor Jan Nicholson

Professor Brian Oldenburg

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Professor Harshal Nandurkar

Professor Kerin O'Dea

Professor James Best

Dr Julie Brimblecombe

Associate Professor Zhiqiang Wang

Dr Alex Brown

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Dr Louise Maple-Brown

Dr Kevin Rowley

Dr Sue Sayers

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