Australian Government

National Health and Medical Research Council

N H M R C

10 of the BEST Research Projects 2009

10 of the BEST Research Projects 2009

ISBN Print: 1864964294

ISBN Online: 1864964235

To obtain information regarding NHMRC publications contact:

Email: nhmrc.publications@nhmrc.gov.au
Phone: Toll free 13 000 NHMRC (13 000 64672)
or call 02 6217 9000
Internet: **http://www.nhmrc.gov.au**

Printed on environmentally sustainable paper

CONTENTS

Why health and medical research is critically important

The Hon Nicola Roxon MP,
Minister for Health and Ageing

In today's world, solutions to health challenges are highly dependent on health and medical research and the people who carry it out.

Health research provides the evidence needed to better understand and tackle health problems, not only in Australia but all over the world. That evidence, in turn, helps us find better ways to prevent ill health and to diagnose and treat disease.

Australia has an outstanding record in health and medical research. We are one of the world's leading Nobel Prize-winning countries per head of population and, of the 10 Nobel Prizes awarded to Australians since 1915, half have been in the field of physiology or medicine.

But our Nobel Laureates are not alone. Across the country, research teams at higher education institutions, public and private sector organisations, and in hospitals, are working on solutions aimed at keeping people healthier for longer.

We need more of these dedicated people. The pace of acquiring new knowledge is moving faster than ever before. Outstanding opportunities are developing out of this knowledge, opportunities to improve the prevention, diagnosis and treatment of disease.

The Australian Government plays a role in this. Through the National Health and Medical Research Council, it invests in the best research ideas by the best researchers.

In these pages you will find descriptions of 10 of the best medical research projects carried out in 2009. They are from among 8,000 vital medical research projects underway in Australia today.

For young people seeking a career direction, I highly recommend the case studies in this book.

The Hon Nicola Roxon MP
Minister for Health and Ageing

What does it take to be a medical researcher?

Professor Warwick Anderson AM,
Chief Executive Officer, NHMRC

What motivates a health and medical researcher? Why do people want to be in this scientific field? Everyone interviewed for this booklet has a few words to say about these questions.

The most common response is that it is incredibly rewarding. Yes, it has its challenges. Yes, it is competitive. No, it is not for the faint hearted. But the reward is that medical research truly can 'make a difference', to contribute to the wellbeing of humanity.

So what qualities does a medical researcher need? Again, the most common response is passion – a passion to solve the mysteries behind disease and relieve human suffering.

Another is perseverance, particularly in the face of setbacks. Many research projects end in the disappointment of a pet theory being disproved. But the resilient researcher takes that as a stepping stone to finding another way to solve the problem. Sometimes the joy is in finding a solution to a problem you did not even set out to solve in the first place.

In my own case there was yet another motivation, one frequently found among medical researchers – a personal connection. As well as being NHMRC's CEO, I am a practising researcher. My interest is hypertension – high blood pressure. My father died from cardiovascular disease and that 'switched me on' to researching this area.

If you have an interest in medical research, or your own 'personal connection', I encourage you to take the advice of those Australian researchers that have walked this path before you.

Professor Warwick Anderson AM
Chief Executive Officer
National Health and Medical Research Council

Malaria warrior

Nicholas Anstey

Project title

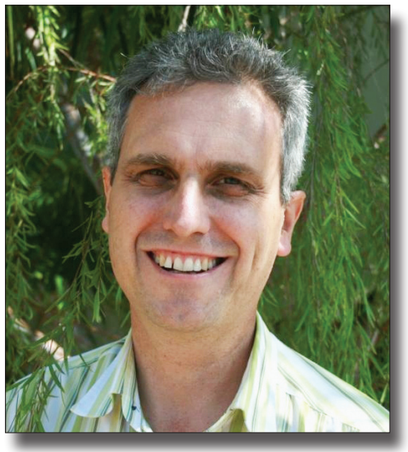
Pathophysiology and treatment of malaria and other tropical infectious diseases in our region

Chief investigator

Professor Nicholas Anstey

Funding

The NHMRC invested $466,025 in this project over five years from 2003



"Strategies to prevent malaria and treat it early are the highest priority, but for people with the severest forms we are identifying better treatments to reduce their risk of dying."

Fighting malaria at the frontline

Malaria claims over a million lives each year, many in the Asia-Pacific where more than 200 million people have the parasitic disease.

Since 2002 a team of researchers at Darwin's Menzies School of Health Research, led by Professor Nick Anstey, have been collaborating with Indonesian counterparts to improve treatments for drug-resistant strains of malaria and identify ways to stop the disease blocking blood supply to vital organs.

As part of a multicentre project across southeast Asia they undertook a clinical trial involving almost 300 patients at Timika in the lowlands of Indonesian Papua. This established for the first time that artesunate, derived from the herb wormwood, is more effective than quinine in saving lives of patients with severe malaria.

The team also proved that cells lining blood vessels in malaria patients are deficient in a protective molecule, nitric oxide, and a related amino acid. Their clinical trials have shown that infusing patients with the amino acid can safely improve their blood vessel function.

Nick recommends taking a medical degree before choosing to enter medical research.

"Studies at the bedside provide invaluable clinical and physiological observations to inform you about causes of disease and why some people develop severe illness," he says.

"There is no better experience to motivate you to solve the mysteries behind any disease and to fuel your creativity to develop and test new treatments to relieve human suffering.

"This is incredibly rewarding."

Genome pioneer
Susan Clark

Project title

Epigenetic variation in early human development

Chief investigator

Professor Susan Clark

Funding

The NHMRC invested $519,000 in this project over three years from 2005

Why genes do what they do

"To be a medical researcher today with the new genome-wide tools at hand is hard to beat- it's like being a space traveller with a new rocket and extra gadgets to explore the universe!"

There are many different types of cells in your body, all with exactly the same DNA. So what makes a muscle cell develop differently to a cell in your retina or your liver?

The trick is that different genes are switched on in different cells to ensure they do the job they are supposed to do. This process is controlled by a number of factors, including DNA methylation, which is a modification of the DNA's chemistry. DNA methylation patterns are set during early development but if perturbed can make us susceptible to diseases and debilating disorders.

The study of methylation is known as epigenetics, a rapidly emerging field in which one of the pioneers is Professor Susan Clark, an NHMRC principal research fellow at Sydney's Garvan Institute of Medical Research.

Her research comparing DNA methylation patterns in pairs of identical and non-identical twins has proved to be a foundation study for the Human Epigenome Project that was launched in 2008.

Susan's team developed a series of new, sensitive tests to monitor DNA methylation at critical DNA sites and found surprisingly high variations between identical twins. They also found that these variations are caused by several factors including the genes themselves, the parent they were inherited from, and sheer luck of the draw.

"Our results are so exciting as they provide a potential mechanism whereby environment and lifestyle can impact on disease susceptibility by changing gene expression," Susan says.

"We now need to unravel the secrets of epigenetic regulation and what factors are deregulated in diseases such as cancer, diabetes, and mental illness."

Sleep shaper
Peter Eastwood

Project title

Obstructive sleep apnoea and general anaesthesia

Chief investigator

Professor Peter Eastwood

Funding

The NHMRC invested $444,500 in this project over five years from 2004

"Like most things worthwhile, medical research has its challenges, but the process of discovery is extremely rewarding."

Breathing easy in sleep and surgery

The nature of a long-suspected relationship between airway collapse during anaesthesia and sleep has been identified by researchers at Perth's Sir Charles Gairdner Hospital and the University of Western Australia.

Led by Professor Peter Eastwood of the WA Sleep Disorders Research Institute and the School of Anatomy and Human Biology, the work is providing insights to identify people at risk of upper airway collapse during sleep and anaesthesia and better understand the role of posture in obstructive sleep apnoea.

A key discovery is that profound decreases in throat muscle activity occur when consciousness is lost during anaesthesia. This is similar to changes at sleep onset, suggesting an "on-off switch" is in play in both cases. The work has also demonstrated how small changes in head position can have marked effects on upper airway stability.

With up to 24% of Australian adults suffering from sleep apnoea - which is associated with increased risk of cardiovascular disease, diabetes and other conditions - this research promises major gains in human wellbeing and reductions in health costs.

The team is currently using this "anaesthesia model" in ongoing NHMRC-funded studies to investigate how subtle head posture change affects airway collapsibility and implications for treatment.

Peter's career has been driven by a keen interest in human physiology and solving diagnostic and treatment dilemmas posed by disease.

His advice to students aiming to work in medical research is "find an area you are passionate about, ask lots of questions, and doggedly pursue the answers".

Cell controller

Karin Eidne

Project title

Dynamic G-protein-coupled receptor-protein complexes in living cells

Chief investigator

Associate Professor Karin Eidne

Funding

The NHMRC invested $685,500 in this project over five years from 2002

Seeing a cell's surface tensions

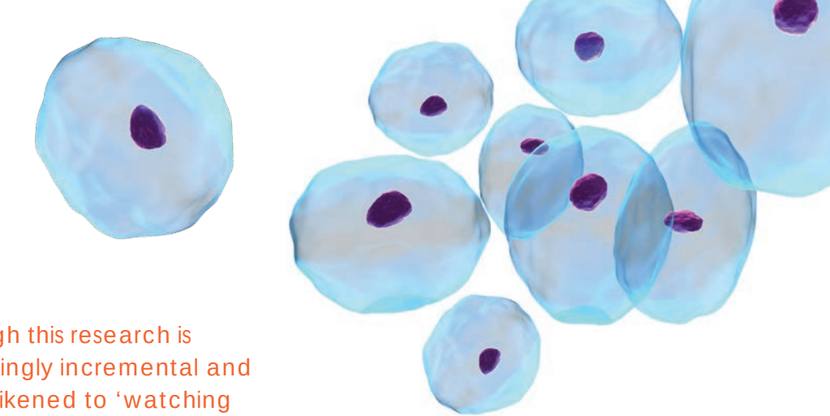
"Although this research is painstakingly incremental and can be likened to 'watching paint dry', chasing the facts to expose precisely what is happening in living systems can generate enormous excitement."

Cells in your body are continually exposed to a multitude of stimuli, from light and odours to hormones and proteins. How cells respond can make the difference between health and illness, which is why almost half of today's pharmaceuticals target molecules known as G-protein coupled receptors (GPCRs) on the surface of cells.

Most people haven't heard of GPCRs but they play a vital role in controlling how their cells behave.

A project led by Professor Karin Eidne of the Western Australian Institute for Medical Research at the University of WA is focused on GPCRs involved in appetite and energy regulation, blood circulation, metabolism and addiction.

"By applying cutting-edge concepts, our findings have increased our fundamental understanding of how these molecules interact with each other, how they switch on and off, and how they activate alternative signaling pathways," Karin says.



"A decade ago I could never have imagined that by pushing the limits of GPCR detection so many new opportunities would become available."

New instruments based on systems developed by her team are being marketed worldwide. A spin-out company has been formed to commercialise the research by designing new treatments to control GPCRs involved in conditions such as heart disease, obesity, and narcolepsy.

Karin recommends a career in medical research where you can work at the frontier of scientific knowledge and contribute to the wellbeing of humanity. Like all experienced and successful researchers, she stresses the importance of patience and persistence.

"Amongst the daily accumulation of failure, the moments of success, the breakthroughs and the triumphs are rare, but all the more rewarding because of that."

Beating diabetes
Len Harrison

Project title

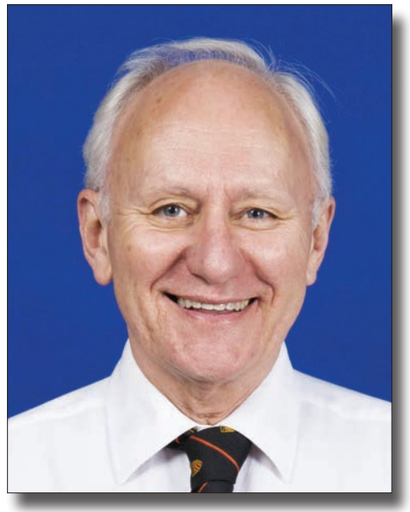
Prevention and cure of type 1 diabetes

Chief investigator

Professor Len Harrison

Funding

The NHMRC invested $5,289,733 in this project over five years from 2004



Making type 1 diabetes history

"My advice to people planning a career in medical research is to be apprenticed to a good mentor, imagine what could be before doing anything, don't believe everything you read, and never give up."

One of the commonest chronic diseases beginning in childhood, type 1 diabetes has doubled in incidence in Australia in the last 20 years.

It is caused by the immune system attacking cells in the pancreas which produce insulin. In most cases symptoms remain unrecognised until the disease takes hold, leaving patients dependent on daily insulin injections to survive.

Research led by Professor Len Harrison at the Walter and Eliza Hall Institute in Melbourne underpins a long-term clinical trial of a treatment with strong promise of effectively vaccinating potential sufferers.

Trial participants, aged 4-30, have a high risk of developing type 1 diabetes because they have relatives with the disease and already have at least two antibodies to the insulin cells in their blood.

Harrison's team made the breakthrough discovery that inhaling an insulin solution can prevent the immune system from switching into attack mode, even if it is already producing antibodies.

Funded by the NHMRC and New York's Juvenile Diabetes Research Foundation, the trial began in 2006 and will track participants for five years. If the treatment proves successful, many of these young Australians will be the first people to be spared from type 1 diabetes by medical science.

"We can now identify individuals many months or years before they develop symptoms and we can prevent the disease in an animal model," Len says.

"I am passionate that by extending our discoveries into the clinic we will eradicate this disease in humans."

Starting equal
Elisabeth Hodson

Project title

Antecedents of renal disease in Aboriginal children: a follow up study

Chief investigator

Dr Elisabeth Hodson

Funding

The NHMRC invested $298,269 in this project over two years from 2006

"Young people aiming for a career in research need a supervisor who motivates, supports and challenges them to keep going despite all setbacks."

Indigenous kids start healthy

Aboriginal Australians are nine times more likely to suffer chronic kidney failure than non-Aboriginal people and up to 10 times more likely to die prematurely of cardiovascular disease.

Many socio-economic and adult lifestyle factors contribute to these sad statistics, but a series of ongoing studies led by Dr Elisabeth Hodson of the Centre for Kidney Research at the Children's Hospital at Westmead in Sydney has found some good news.

"I am passionate about this project because it has provided such important results for Aboriginal people and opened up new opportunities for Aboriginal researchers to work with their own people," Elisabeth says.

Beginning in 2002, more than 1000 Aboriginal children aged 6-12 from a cross-section of New South Wales schools and a matching group of non-Aboriginal children have been tested every two years to assess their risk of contracting these serious health problems. Participation by local communities has been crucial to its success.

Tests taken two years and four years after the first baseline study found no increased risk of persistent markers of chronic kidney disease in Aboriginal children compared with non-Aboriginal children.

And while many risk factors for cardiovascular disease were already common in both groups, they were not more prevalent in Aboriginal children.

"This suggests that a window of opportunity exists to prevent some of these outcomes," Elisabeth says.

"Adolescence and young adulthood are likely to be critical times for preventative strategies so now with further funding from NHMRC we are looking at this older age group."

Smart bombing cancer

Roger Martin

Project title

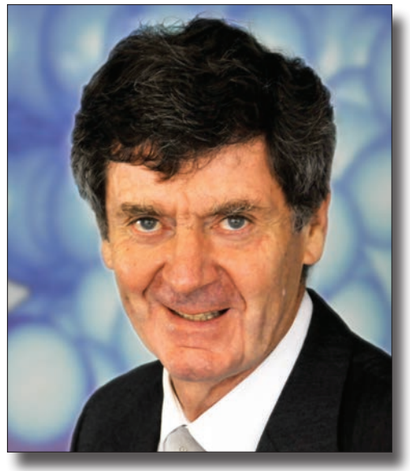
Targeting one – iodine-124 to the DNA of tumours for PET Imaging and Auger-Radiotherapy

Chief investigator

Associate Professor Roger Martin

Funding

The NHMRC invested $787,000 in this project over three years from 2005



Shooting cancers with silver bullets

"The great potential radioactive isotopes offer for targeted cancer therapy is a major ingredient in my passion for the project, another is the elegant simplicity of the science – in a word, it's 'cool'."

Radiotherapy has been used for many decades to treat cancer, but collateral damage caused to healthy tissue is a major problem.

A research team led by Associate Professor Roger Martin of the Peter MacCallum Cancer Centre and the University of Melbourne has developed methods to overcome this by delivering radioactive drugs to tumours without damaging adjacent cells.

Their key discovery was the design of DNA-binding drugs incorporating radioactive atoms called Auger emitters. By attaching these radioactive drugs to proteins which bind selectively to tumour cells, the radiation damage is targeted to the DNA of cancer cells.

Auger emitters are ideal for this application because their nano range of action means damage is focused to molecular dimensions.

One – iodine-124 – also emits positrons, the sub-atomic particles used in positron emission tomography (PET) imaging, creating the potential to monitor tumour targeting during treatment.

Roger was studying to be a science teacher until he attended a lecture at Melbourne University by Melvin Calvin, a co-winner of the 1961 Nobel Prize for Chemistry who discovered the biochemistry of photosynthesis.

"I became fascinated by the potential of chemistry to solve biological problems," he recalls.

He was hooked on a career in medical research, a choice he recommends to others who are prepared for "many trials and few tribulations".

It has led him to oversee a multidisciplinary team which has developed a "smart bomb" for cancer, a patented technology now being developed by the CRC for Biomolecular Imaging Development headed by Professor Rod Hicks.

Birth watcher
Julia Pitcher

Project title

Pre-term birth and long-term physiological and psychosocial outcomes

Chief investigator

Dr Julia Pitcher

Funding

The NHMRC invested $266,500 in this project over four years from 2004

"Every week of gestation is important in ensuring normal brain development, so apart from early identification of at-risk infants and development of new therapies, the findings raise some questions about when we induce births."

When size and timing matters

While medical science has made it possible for more "premmie babies" to survive and live normal lives, research led by Dr Julia Pitcher, an NHMRC Peter Doherty Fellow at the University of Adelaide, has shown that they and other low-birthweight children need special care.

She found that babies born before the optimal gestation period of 40 weeks or below their predicted birthweight show reduced motor system development, which can affect them much longer than previously thought.

A study of 12 year olds born after 24 – 40 weeks of gestation found that for every week of reduced gestation there is a measurable reduction in brain development.

A study of adults of low-birthweight found that altered development of the brain's motor control systems is still evident at age 28 years, most prominently in those born into socio-economically disadvantaged families.

"Underdevelopment of these motor areas appears to have a negative influence on cognitive abilities related to language comprehension and reading," Julia says.

"This is the first physiological evidence that motor and cognitive dysfunction commonly experienced by preterm children when they reach school age probably have common underlying origins in the brain."

The long term aim of the work is to develop early diagnostic and intervention strategies to enable these children to realise their full potential at school and into later life.

"To think we might be able to make a real difference through this research is highly motivating," Julia says.

"I'm passionate about translating research into outcomes that help maximise human wellbeing, a goal every would-be medical researcher should begin with."

Lymph mappers

Steven Stacker and Marc Achen

Project title

The biology and therapeutic manipulation of lymphatic vessels in cancer and lymphedema

Chief investigators

Associate Professor Steven Stacker and Associate Professor Marc Achen

Funding

The NHMRC invested $2,589,100 in this project over five years from 2004

Exploring cancer's secret channels

"Research is an adventure, very much about stepping into the unknown, posing questions, then using your skills to find answers."

Many cancers spread via the lymphatic system but recently it has been shown that cancers alter lymphatic channels to make this possible.

To understand the role it plays in cancer and other diseases, research led by Associate Professors Steven Stacker and Marc Achen at the Ludwig Institute for Cancer Research in Melbourne is delivering fundamental knowledge about how the lymphatic system develops and functions.

The work has identified important protein growth factors in the expansion of the lymphatic system, leading to trials of novel treatments for cancer and other diseases that involve the lymphatic and blood vascular systems.

"It has been very exciting to see the research give rise to new knowledge and potential therapeutic approaches," Steven says.

"Seeing our discoveries translated to the clinic for the benefit of patients is very motivating for our team."

He and Marc entered medical research in the 1980's when molecular biology was making spectacular advances in uncovering genes and understanding how molecules control normal and diseased cells.

With much more knowledge now available, Steven says young people choosing a medical research career have a unique opportunity to work in the field when breakthrough discoveries can be expected to deliver major treatment advances.

"You need to have an enquiring mind, to be passionate about the endeavour, be able to work hard and have the occasional moment of creativity."

"Our Branch Director Tony Burgess also puts it well in saying that to be in research you also need to be a 'robust' individual - it is not a career for the faint-hearted."

Life saver
David Thomas

Project title

Molecular pathogenesis of sarcoma

Chief investigator

Associate Professor David Thomas

Funding

The NHMRC invested $435,500 in this project over five years from 2003

"The most challenging aspects of my work arise from seeing so many young people die from sarcomas. The clear potential of science to achieve better outcomes makes working with these devastating cancers very rewarding."

Saving young lives from sarcoma

The most exhilarating research moment for Associate Professor David Thomas of Melbourne's Peter MacCallum Cancer Centre came when a post-doctoral fellow on his team showed a gene they had identified could be harnessed to slow growth of osteosarcomas.

"After five years of work, this made the fundamental leap from biology to clinical application," he recalls.

Sarcomas are cancers of connective tissue which claim the lives of 40% of sufferers, with particularly high mortality rates amongst adolescent and young adult patients.

Australian sarcoma research was uncoordinated until David established a virtual sarcoma tissue bank involving several research and clinical institutions.

Molecular profiling of many tumours enabled them to identify at least three promising treatment pathways and two genes with potential to suppress sarcoma growth.

This led to the formation of the Australasian Sarcoma Study Group to link clinical research and the Australian Sarcoma Kindred Study, funded by philanthropic support, which focuses on patients and families who inherit an increased risk of developing sarcomas.

When the research also established that adolescents and young adults with sarcomas have a significantly higher mortality rate than children, David established onTrac@PeterMac, which has an international reputation for innovative clinical care of patients who were previously lost within the adult cancer system.

David highly values his opportunity to apply clinical and scientific training in medical research.

"I have been lucky to work as a clinician-scientist when molecular biology is impacting on clinical practice. I strongly encourage all young clinicians to become well-trained cancer biologists, because the future of clinical care will increasingly draw from basic research."

10 of the Best Research Projects

honour roll

The 10 of the Best Research Projects honour roll comprises a list of people, provided by the Chief Investigators, that have made a contribution to the projects featured in this book.

Good teamwork in research projects is essential to success.

Professor Nicholas Anstey

Darwin:

Dr Nick Douglas
Ms Catherine Jones
Dr Jutta Marfurt
Dr Gabi Minigo
Dr Yvette O'Neil
Ms Tania Paul
Ms Kim Piera
Dr Ric Price
Dr Bruce Russell
Dr Rossarin Suwanarusk
Dr Tonia Woodbury
Dr Tsin Wen Yeo

Timika, Papua, Indonesia:

Mr Ferryanto Chalfein
Ms Wendy Fobia
Dr Tajandra Handojo
Ms Natalia Haryanti
Ms Sri Hasmunik
Dr Enny Kenangalem
Dr Daniel Lampah
Yohannes Miramangngi
Pak Prayoga,
Ms Sri Rahayu
Dr Jeanne Rini Poespoprodjo
Ibu Roesmini
Dr Frans Thio
Mr Frans Wabiser
Veronica Yani
Ibu Yoshi

In collaboration with:

Dr Emiliana Tjitra and the National Institute of Health Research and Development, Ministry of Health, Jakarta, Indonesia

Oxford-Mahidol Wellcome Trust Bangkok Unit

NHMRC Program Grant partners at QIMR in Brisbane

Professor Susan Clark

Dr Marcel Coolen
Dr Patrick Dwyer
Professor Nick Martin
Dr Grant Montgomery

In Collaboration with:

Garvan Institute of Medical Research - Sydney
QIMR - Brisbane

Professor Peter Eastwood

Mr Thomas Ansell
Ms Vanessa Baker
Clinical Professor David Hillman
Ms Kathleen Maddison
Dr Peter Platt
Dr Kelly Shepherd
Dr Jennifer Walsh
Dr Jonathan Williamson

Associate Professor Karin Eidne

Mr Matthew Dalrymple
Ms Jasmin Dromey
Mr Werner Jaeger
Dr Martina Kocan
Dr Kevin Pfleger
Mr Ethan See
Ms Ruth Seeber

Professor Len Harrison

Dr Fergus Cameron
Professor Jennifer Couper
Dr Andrew Cotterill
Professor Peter G Colman
Dr Kim Donaghue
Dr Spiros Foulanos
Dr Margo Honeyman
Dr Michelle Jack
Professor Tim Jones
Dr Tony Lafferty
A/Professor Andrew M Lew
Felicity McManus RN
Professor Grant Morahan
Dr Jinny Willis

Dr Elisabeth Hodson

Professor Jonathan Craig
Dr Leigh Haysom
Pamela Lopez-Vargas
Sandra Puckeridge
Rita Williams

Associate Professor Roger Martin

Professor George Clarke
Professor Rodney Hicks
Dr Tom Karagiannis
Dr Brenda Leung
Ms Melissa Leung
Dr Pavel Lobachevsky
Dr Colin Skene
Dr Andrea Smith
Ms Joanne White
A/Professor Jonathan White

In collaboration with:

Peter MacCallum Cancer Centre
School of Chemistry and Bio21 Institute; University of Melbourne
University of Auckland

Dr Julia Pitcher

Assoc. Prof. Nicholas Burns
Dr Richard Cockington
Katie Crocker
John Drysdale
A/Professor Ross Haslam
Ryan Higgins
A/Professor Vivienne Moore
Professor Ted Nettelbeck
Emeritus Prof. Jeffrey Robinson CBE
Alexandra Robertson
Luke Schneider
Ashleigh Smith
Nisan Tuazon

In collaboration with:

Research Centre for the Early Origins of Health and Disease
The Robinson Institute
The University of Adelaide

Associate Professors Steven Stacker and Marc Achen

Katie Ardipradja
Carol Caesar
Natalia Davidova
Rae Farnsworth
Nicole Harris
Tara Kanezis
Sidney Levy
Maria Macheda
Sophie Paquet-Fifield
Sally Roufail
Teruhiko Sato
Ramin Shayan
Richard Williams
Steve Williams
You-Fang Zhang

Associate Professor David Thomas

Sarcoma Genomics and Genetics Lab

Nina Espositos
Dale Garsed
Dr Andrew Holloway
Dr Maya Kansara
Mohamad Sufian
Dr Sally Whyte
Sophie Young

Australasian Sarcoma Study Group (ASSG)

Dr Mandy Ballinger
Kym Boekel
Dr Jayesh Desai
Brianna Hay

onTrac @PeterMac

Elizabeth Ballinger
Pip Barry
Gavin Dyson
Nicole Edwards
Bec Fairchild
Kerryn Fulton
Tina Griffiths
Gayle Jones
Dr Lisa Orme
Felicity Sleeman
Brendan Spence
Kate Thompson

www.nhmrc.gov.au

T +61 2 6217 9000 | F +61 2 6217 9100 | E nhmrc@nhmrc.gov.au

WORKING TO BUILD A HEALTHY AUSTRALIA