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NHMRC

10 OF THE BEST NHMRC RESEARCH PROJECTS

2015

WORKING TO BUILD A HEALTHY AUSTRALIA

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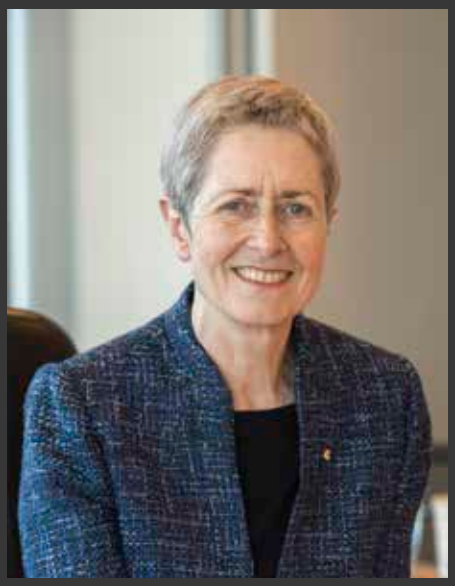
10 OF THE BEST NHMRC RESEARCH PROJECTS

2015

WORKING TO BUILD A HEALTHY AUSTRALIA

CEO FOREWORD



It is a pleasure to introduce NHMRC's *10 of the Best NHMRC Research Projects 2015*. These are projects completed in the previous year that have achieved results of particular significance for the improvement of human health – whether through advancement of knowledge or the prevention, detection or treatment of disease.

Each year when projects are shortlisted for this award, we are struck by the extraordinary quality and diversity of research being undertaken in Australia with NHMRC support. This publication is an opportunity to showcase some of that research and to honour the brilliant researchers who conceived, planned and delivered it.

I congratulate all the researchers and their teams whose work is profiled here.

NHMRC funds a broad range of research and researchers working across the full extent of biomedical, clinical, public health and health services research in universities, medical research institutes, hospitals and primary health care settings. Support is provided in various ways – through scholarships and fellowships for individuals and grants for teams to undertake research in the laboratory, clinic and community using the full range of advanced technologies available today.

The outcomes of this wide-ranging national research effort are extraordinary. In some cases, the benefits are achieved quickly through rapid translation into improved policy and practice. In other cases, the journey is longer and might depend on further investment, clinical trials and regulatory approval, for example for the development of new diagnostics, vaccines and drugs. For others still, such as the discovery of a new biological process, the outcomes might emerge over many years and in unexpected ways as the fundamental mechanisms underlying health and disease are uncovered.

NHMRC has a critical role to play in supporting the breadth of Australia's health and medical research for the improvement of human health, now and in the future. We hope you enjoy learning about some of that research in this celebration of *10 of the Best NHMRC Research Projects 2015*.

Professor Anne Kelso AO
Chief Executive Officer

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DRILLING DOWN: DISCOVERING THE ORIGINS OF DENTAL ANXIETY

Associate Professor Jason Armfield

Associate Professor Jason Armfield set out to explain the origins of dental fear and to understand why fear of the dentist is a serious psychological problem for many Australians. He developed a 'dental anxiety scale' that will help to identify and treat the condition across the world, leading to more people visiting the dentist and better population level oral health.

UNIVERSITY OF ADELAIDE

EARLY CAREER FELLOWSHIP

$336,561

2009-2013

TEAM MEMBERS

Much of this research was conducted solely by Associate Professor Armfield, but several individuals were involved at different times throughout various studies. These people include:

Dr Peter Arrow

Associate Professor Donald Chi

Mr Serge Chrisopoulos

Dr Manon Ketting

Dr Liana Luzzi

Dr Harry Mohan

Dr Vicki Skinner

For most Australians a trip to the dentist is a straightforward, albeit mildly unpleasant, activity. However, for a sizeable minority of people a dental visit can elicit serious anxiety.

Associate Professor Jason Armfield aimed to understand why dental fear is a serious psychological problem for so many.

"Traditionally, it was assumed that dental fear was a simple response to bad experiences at the dentist.

"However, some people who have had bad experiences have no dental anxiety, while others who have had no negative experiences suffer considerable dental anxiety," he explained.

He investigated numerous aspects of the fear, as well as how dentists can identify, manage and treat dental anxiety. He identified that managing dental anxiety is about managing how people perceive a visit to the dentist.

"Specifically, people are more likely to be afraid of going to the dentist if they consider it to be uncontrollable, unpredictable, dangerous and disgusting."

Associate Professor Armfield successfully identified several strategies for tackling dental anxiety and fear. Notably, he developed an adult 'dental anxiety scale' to measure dental anxiety in adults, which allows for a safe and standardised way to identify anxiety.

> High dental fear affects about one in seven Australian adults making it one of the most prevalent anxiety disorders in the country.[1]

1. Armfield JM. The extent and nature of dental fear and phobia in Australia. Australian Dental Journal 2010;55:368-377.

Associate Professor Jason Armfield.

> High levels of dental fear are associated with poorer oral health outcomes such as decayed and missing teeth.

This tool has been translated into almost a dozen languages around the world. A children's scale is currently being developed, which will help to identify and treat the condition in Australia and overseas.

Associate Professor Armfield emphasised that dentists play an important role in identifying both the anxiety and its source. Patients must also take an active role in addressing their own issues.

This valuable research goes beyond understanding the psychological ramifications, but plays a critical role in improving oral health across the community.

"Tackling dental fear from a number of directions will hopefully help us reduce dental anxiety in the community.

"This will lead to more people visiting the dentist and better population level oral health," he concluded.

Next steps:
Having identified and developed robust strategies for adults, Associate Professor Armfield hopes to further explore the causes of dental fear and anxiety in children. Cognisant of aspects such as parental influence and varying child personality characteristics, he hopes to identify and alleviate the problem early. This will reduce the need for expensive, unnecessary and risky options, such as undergoing general anaesthesia for basic dental procedures.

Addressing dental anxiety

In Australia, almost one in three adults with high dental fear has not visited a dentist in 10 or more years. Treating dental anxiety is about managing how people feel about going to the dentist. According to Associate Professor Armfield, there are several elements to be tackled in this regard:

1. Dentists are aware of dental anxiety and its various components. Armfield created a 'dental anxiety scale' to allow reliable and safe self-reporting of dental anxiety.
2. Dentists know how to effectively identify and manage a patient's anxiety, which requires appropriate training and knowledge.
3. An individual understands their own fear and takes an active role to address their anxiety.

DELIVERING AUSTRALIA FROM NEURODEGENERATION

Associate Professor Helen Cooper

Associate Professor Helen Cooper's research aims is to understand the molecular mechanisms controlling the birth of new neurons in the adult brain. In the long-term, it is hoped that these insights will help to design therapeutic approaches to treat neurodegenative diseases.

UNIVERSITY OF QUEENSLAND

PROJECT GRANT

$322,524

2011-2013

TEAM MEMBERS

Dr Conor O'Leary

Dr DanaKai Bradford

Dr Min Chen

Ms Amanda White

Associate Professor Zhi Ping Xu

Professor Perry Bartlett

Getting older unfortunately comes with a higher risk of disease, particularly those affecting the brain. Tackling neurodegenerative conditions such as Alzheimer's, Parkinson's and Huntington's disease is at the forefront of Associate Professor Helen Cooper's research.

"The end goal is to design tangible therapeutic approaches to treat neurodegenerative diseases.

"However, inability to functionally replace damaged brain cells has severely limited the development of effective therapeutics to fully repair the damaged brain," Associate Professor Cooper explained.

The team aimed to identify key molecules that can encourage the silent neural stem cells within the adult brain to reactivate and generate new neurons to replace those damaged by disease, such as stroke or dementia. To achieve this, they set out to understand the molecular mechanisms controlling the birth of new neurons from the adult stem cells.

"Our hypothesis was based on the fact that a newly-discovered protein, Neogenin, plays a key role in producing brain cells in embryos and may therefore play a similar role in the adult brain."

More than 342,800 Australians are living with dementia. This number is expected to rise to 400,000 in less than 10 years.[1]

1. fightdementia.org.au

(L–R) Dr DanaKai Bradford, Dr Conor O'Leary, Associate Professor Helen Cooper, Ms Amanda White.

> A comprehensive understanding of how new brain cells are generated is essential if we are to develop effective strategies to repair the damaged brain.

When the team examined the forebrain of adult mice in which the Neogenin gene had been deleted, they observed a reduction in the number of neurons in these mice.

These valuable insights may lead to strategies to stimulate the production of neurons in parts of the brain that have been damaged by disease or injury.

The team also worked in collaboration with Associate Professor Xu and Professor Bartlett to develop a novel drug delivery system to the brain. The team discovered that very tiny particles, known as Layered Double Hydroxides (LDHs), can carry drugs into damaged neurons.

These tiny particles have the potential to deliver stem-cell activating factors directly to the brain. The team tracked the movement of these 'vehicles' using a fluorescent marker that is visible throughout the brain tissue.

This exciting breakthrough overcomes the limitations of other drug-delivery technology, and provides the ability to successfully transport nanoparticles into the brain without causing undesirable side effects. Previously, this has been extremely difficult to achieve without injecting directly into the brain.

Associate Professor Cooper's research has been made possible by new technologies. Recent advances in the design of highly sensitive microscopes has made identifying, quantifying and tracking these stem cells and nanoparticles in the brain far more accurate.

Next steps:
Associate Professor Cooper and team are now looking to develop a highly effective treatment for these diseases by studying the role of Neogenin in adult brains combined with their new delivery vehicles for delivering targeted therapeutics.

What is neurodegeneration?

Neurodegenerative disease is an umbrella term for a range of conditions that lead to progressive brain damage and neurodegeneration. Examples include stroke, Alzheimer's disease and other dementias, Parkinson's disease, motor neuron diseases and Huntington's disease.

Neurodegenerative diseases are incurable and debilitating and result in progressive deterioration and death of neurons in the human brain. Normally, neural stem cells do not produce enough neurons to adequately repair the damaged brain. This deterioration of neurons gradually causes a loss of nerve structure and function, which can severely impair cognitive abilities, restrict motor skills, and eventually lead to death.

SANGUINE ADVANCES IN DETECTING COLORECTAL CANCER

Associate Professor Leah Cosgrove

Associate Professor Leah Cosgrove and her team have developed a simple blood test to diagnose colorectal cancer. A reliable, non-invasive blood test could augment the National Bowel Cancer Screening Program, either as an adjunct primary screen for those unable to do the stool test, or in triaging positive subjects to colonoscopy. This could help drive a significant reduction in colorectal cancer deaths in Australia.

CSIRO (FOOD AND NUTRITIONAL SCIENCES)

DEVELOPMENT GRANT

$542,260

2011-2013

TEAM MEMBERS

Dr Kim Fung
Dr Tim Adams
Dr Bruce Tabor
Dr Mike Buckley
Ms Ilka Priebe
Dr Leanne Purins
Dr Trevor Lockett
Mr Charles Lindall
Dr Larry LaPointe
Professor Tony Burgess
Professor Ed Nice
Professor Peter Gibbs
Associate Professor Andrew Ruszkiewicz
Mr James Moore
Dr Michelle Thomas
Associate Professor Rajvinder Singh
Associate Professor Paul McMurrick

Associate Professor Leah Cosgrove and her team set out to improve early detection of colorectal cancer (CRC), Australia's second most common internal cancer.

Through their research, the team has developed a blood-based test for CRC as an alternative to the current stool-based tests.

"Blood tests are commonly used in clinical practice, so we believed that a blood-based test may find higher community acceptance than a stool test; a tenet that has been supported by recent research," Associate Professor Cosgrove said.

This is important as the availability of a blood test – in addition to the well-established and validated stool test – could potentially increase the number of people screening and result in a significant reduction in the morbidity and mortality associated with CRC in Australia.

The team identified a specific panel of three protein biomarkers that, when measured together, can accurately identify individuals with colorectal cancer.

Results to date suggest that the test will be able to detect early stage colorectal cancer more efficiently than other screening tests currently available.

"We were able to detect early stage disease and late stage disease with increased sensitivity which is very exciting.

Worldwide, CRC is the third most common cancer and the second leading cause of cancer death.

(L–R) Mr James Moore, Ms Ilka Priebe, Associate Professor Andrew Ruszkiewicz, Associate Professor Leah Cosgrove, Dr Trevor Lockett, Dr Michelle Thomas, Associate Professor Rajvinder Singh.

> This could significantly reduce the morbidity and mortality associated with colorectal cancer in Australia.

"Earlier detection will allow early treatment when surgical removal is most effective, increasing potential for complete cure."

However, Associate Professor Cosgrove also stresses the importance and value of the existing practice of faecal screening.

"The stool test used by the National Bowel Cancer Screening Program saves lives and its benefits are well established.

"Our test could augment this program by providing a screening alternative for people who want to screen but for personal or cultural reasons are unable or unwilling to do the stool test," she explains.

"Earlier detection and early intervention lead not only to higher rates of cure but also reduced health care expenditure."

Associate Professor Cosgrove acknowledges the importance of the NHMRC Development Grant system as a means of translating research into tangible outcomes, with the ultimate aim of commercialisation.

She concludes that this research would not have been possible without the input and dedication from her CSIRO colleagues and other clinical and academic collaborators.

Next steps:
A key future focus for Associate Professor Cosgrove and her team will be to establish whether this improved performance translates across the broader population. To do this, she hopes to undertake a comprehensive, five year study that compares this blood test with others in current use to measure their diagnostic accuracy as well as their ability to monitor or predict post-surgical recurrence of disease to help inform post-surgical patient management.

CRC: facts and stats

Colorectal Cancer (CRC) is the third most common cancer in Australia with 16,640 new cases diagnosed in 2014. CRC is a highly preventable disease and when detected early, cure rates can be as high as 90 per cent. Early detection could significantly reduce the health burden of this disease, which is estimated to cost Australia over $2 billion a year in direct health costs.

The current screening process is underutilised with only 33.5 per cent of the eligible population participating in Australia's National Bowel Cancer Screening Program, which uses a stool-based test. Evidence indicates a robust, blood-based diagnostic tool, if made available as an alternative to the current test, would increase screening participation.

THE SCORPION KING: LIGHTING THE WAY TO DEFEATING BRAIN CANCER

Professor David Craik

Professor David Craik and his team set out to make synthetic derivatives of a naturally occurring peptide, chlorotoxin, from the venom of a scorpion to use for brain tumour imaging. The work was based on a discovery by collaborator, Dr Jim Olson, that through attaching a dye to chlorotoxin it could be used to 'light up' tumours. This allows surgeons to pick up small amounts of cancerous tissue during surgery, reducing the risk of the tumour reoccurring.

UNIVERSITY OF QUEENSLAND

PROJECT GRANT

$511,299

2011-2013

TEAM MEMBERS

Professor Norelle Daly

Dr Jim Olson

Dr Muharrem Akcan

Ms Paola Ojeda

Dr Conan Wang

Dr Richard Clark

Dr Sónia Troeira Henriques

Dr Yen-Hua Huang

In their NHMRC-funded research, Professor David Craik and his team aimed to stabilise peptides and thus unleash their potential as drugs and imaging agents.

Using the venom of a scorpion, the team created synthetic versions of a naturally occurring peptide called chlorotoxin. In turn, these peptides were used to optimise a revolutionary tumour imaging agent for brain surgery operations.

"Peptides have often been regarded as great drug leads, but the pharmaceutical industry has shied away from them because they can be unstable," Professor Craik explained.

"The broad goal of our research is to overcome current limitations on the use of conventional peptides as drugs."

The team stabilised the peptides through cyclisation, a process where the head and tail ends of the protein chain are joined together to make a circular protein that is exceptionally stable.

They developed chemical methods for synthesising chlorotoxin, and tested its ability to bind to tumour cells to use as a diagnostic tumour imaging agent.

"We found that by cyclising the natural chlorotoxin we were able to stabilise it to improve one of its biopharmaceutical properties, that is its stability in serum.

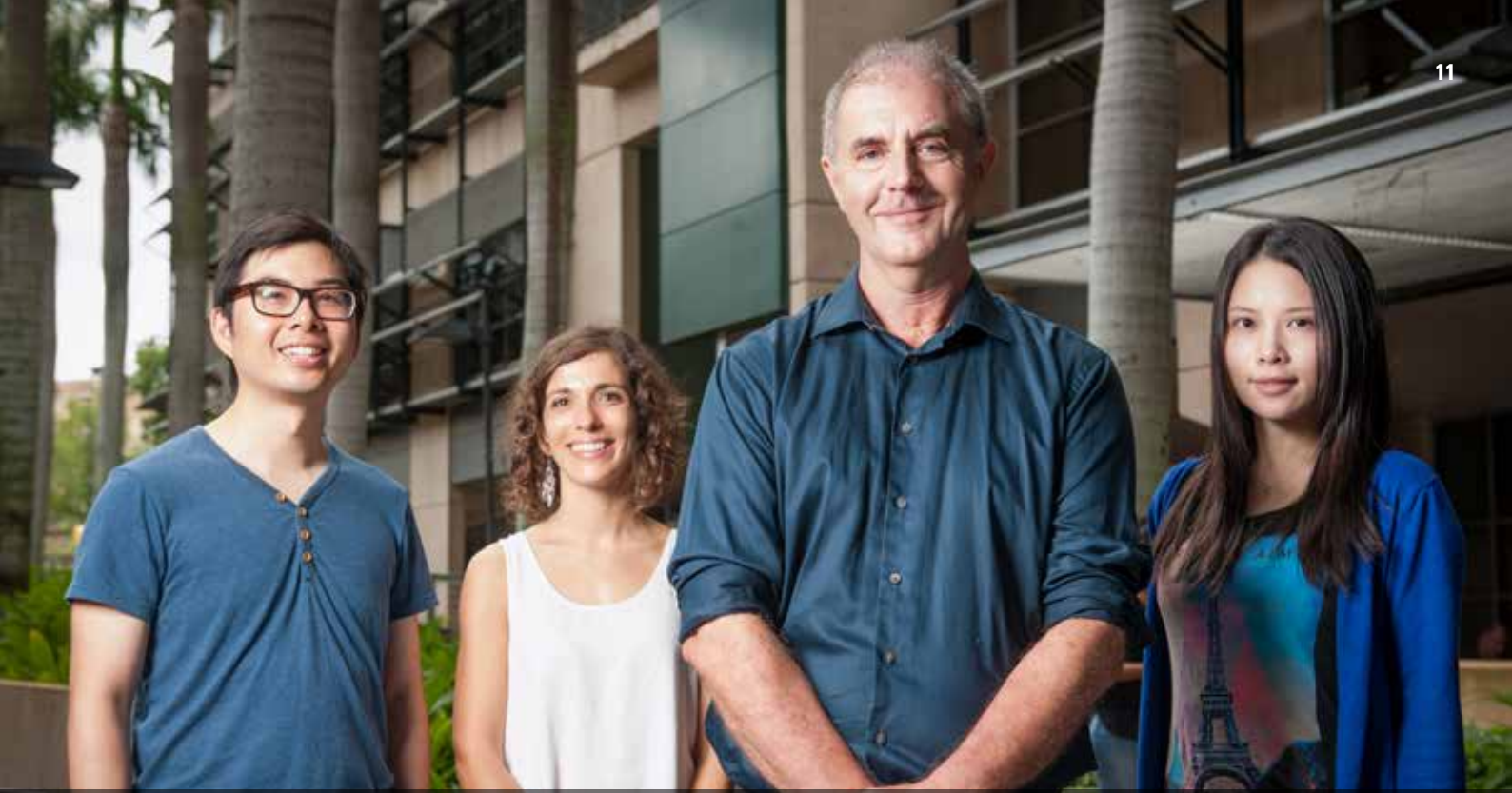
"This process also improved our ability to more specifically label the peptide with a fluorescent dye to be used in tumour imaging."

The ultimate benefit of this work is that surgeons will be able to better define the margins of tumours during brain surgery.

"Using labelled chlorotoxin molecules to 'light up' tumours, surgeons will be able to pick up small amounts of cancerous tissue on the margins of tumours and thereby reduce the possibility of the tumour reoccurring," he adds.

Brain cancer kills more children in Australia than any other disease.[1]

1. ABS (2010 – 2014), 3303.0 Causes of Death, Australia (2009 – 2013), 'Table 1.3: Underlying cause of death, Selected causes by age at death, numbers and rates, Australia, Ages 1 - 14 (2009 – 2013)



(L–R) Dr Conan Wang, Dr Sónia Troeira Henriques, Professor David Craik and Dr Yen-Hua Huang.

> This work will improve the outcomes for brain cancer patients by reducing the risk of tumours reoccurring.

Professor Craik attributes a key collaboration with Dr Jim Olson from the Fred Hutchinson Cancer Research Centre and Seattle Children's Hospital to the success of the project.

Dr Olson had already discovered that coupling a fluorescent dye with chlorotoxin allowed the dye to target brain tumours in order to 'light up' the tumour during surgery.

"He came to my lab to learn peptide synthesis so that we might be able to improve the initial molecule," Professor Craik explained.

Although the molecules made when Dr Olson worked in the Craik lab were not ultimately chosen for the clinical product, relationships built during his Australian visit led to the first clinical trials of BLZ-100 "tumor paint" being conducted in Queensland.

Blaze Bioscience, the company that developed the current clinical investigational agent, set up a subsidiary in Australia and ran the first phase 1 study of BLZ-100 in skin cancer patients. The molecule is now being tested in additional clinical trials, including one more in Australia.

The research paves the way for an exciting future in imaging and combatting the devastating effects of brain tumours.

Next steps:
Professor Craik now seeks to understand exactly how the chlorotoxin peptide targets tumours. Over the years, various theories have been proposed, but so far there is still no definitive information on how exactly this molecule crosses the blood brain barrier to reach tumours. More fundamental work needs to be done to understand this, and Professor Craik is excited to find out.

Brain cancer: the harsh truths

Brain cancer costs more per patient than any other cancer because it is highly debilitating, affects people in their prime and often means family members cannot work if they become carers.[2] On average, approximately 1600 brain cancers are diagnosed each year in Australia; approximately one person diagnosed every five hours.[3] Only two in ten people diagnosed with brain cancer will survive for at least five years.[4]

2. The Cost of Cancer NSW – report by Access Economics, Australia wide, April 2007.
3. AIHW 2015. ACIM (Australian Cancer Incidence and Mortality) Books. AIHW: Canberra. Five year average incidence figure (2007 – 2011) http://www.aihw.gov.au/WorkArea/DownloadAsset.aspx?id=10737422721
4. AIHW 2012. Cancer survival and prevalence in Australia: period estimates from 1982 to 2010. Cancer Series no. 69. Cat. No. CAN 65. Canberra: AIHW pg 42.

PROTEIN: THE KEY TO IMPROVED KIDNEY FUNCTIONALITY

Associate Professor Gordon Doig

Associate Professor Gordon Doig and his team showed that critically ill patients who received better nutrition were less likely to develop kidney injury. These findings represent an important first step towards global practice change and offers the potential to reduce the need for surgery, dialysis and transplantation.

UNIVERSITY OF SYDNEY

PROJECT GRANT

$845,052

2010-2013

TEAM MEMBERS

Dr Fiona Simpson

Ms Elizabeth Sweetman

Ms Philippa Heighes

Ms Jennifer Hannam

Professor Carol Pollock

Dr Douglas Chesher

External collaborators:

Professor Rinaldo Bellomo

Dr Andrew Davies

Associate Professor Michael Reade

Dr Peter Harrigan

Dean John Botha

New onset kidney injury is a very serious complication of critical illness, which can result in a patient needing a kidney transplant or can even cause death. Yet, no treatments have been proven to successfully protect critically ill patients from developing kidney injury.

Associate Professor Gordon Doig has focussed on addressing this issue for quite some time. Since 2003 his primary research goal has been to discover ways that enhanced nutrition may improve survival from critical illness or major trauma.

His team conducted the *Nephro-Protective Trial* to confirm preliminary results reported in their 2008 study, which demonstrated that critically ill patients who received better nutrition might be less likely to develop kidney injury during their critical illness.

"The *Nephro-Protective Trial* was conducted in 474 critically ill patients treated in 16 intensive care units throughout Australia and New Zealand," Associate Professor Doig explained.

"We identified patients with two distinct causes of kidney injury: toxic insult from infection or drugs and shock due to trauma or major surgery.

Almost one in three patients who require treatment in an intensive care unit will develop new onset kidney injury during their illness.[1]

1. Bagshaw SM, George C, Dinu I, Bellomo R. A multi-centre evaluation of the RIFLE criteria for early acute kidney injury in critically ill patients. Nephrol Dial Transplant 2008; 23:1203-10.

(L–R) Professor Carol Pollock, Dr Fiona Simpson, Associate Professor Gordon Doig and Ms Philippa Heighes.

> Kidney injury presents a significant health burden and exacts a considerable toll on social and economic resources.

"We found that a diet with more protein protected against kidney injury caused by shock due to trauma or major surgery.

"In the healthy adult, kidney blood flow and function increases by 25 to 60 per cent for several hours after the consumption of a high protein meal.

"We also found that in patients who do not have any form of kidney injury at the onset of their critical illness, a diet with more protein may reduce the risk of death," he notes.

Associate Professor Doig and his team are thinking big for the outcomes of their research.

"We expect researchers around the world will conduct additional studies to confirm our results and refine our intervention.

"But, the results of this study represent an important first step towards global practice change," he concluded.

Next steps:
Associate Professor Doig and his team received funding from the Heart Research Foundation and the Cardiovascular Research & Education Fund of the Sydney Medical School Foundation to conduct a 72 patient pilot study focusing on patients undergoing major cardiovascular surgery to determine if protein intake during surgery reduces kidney injury. This has garnered interest in Italy and Australia.

Kidney injury: the facts

More than 60,000 patients become critically ill throughout Australia each year and require treatment in an intensive care unit. Up to 30 per cent of these patients will develop new onset kidney injury during their illness.[1] Mild kidney injury results in a longer hospital stay, but for 20 per cent of patients kidney injury is much more severe and may require lifelong dialysis or even result in early death. In fact, ICU patients who develop severe kidney injury that requires dialysis have a six-time increased risk of death.[2]

2. Uchino S, Kellum JA, Bellomo R, et al. Acute renal failure in critically ill patients: a multinational, multicenter study. JAMA 2005;294:813-8.

GLUTEN FOR PUNISHMENT: CHALLENGING NON-COELIAC GLUTEN SENSITIVITY

Professor Peter Gibson

Professor Peter Gibson and his team set out to determine whether gluten causes problems in people who do not suffer from coeliac disease. The team found that short-chain carbohydrates called FODMAPs, not gluten, might be triggering symptoms such as bloating and stomach pain. The results have put some scientifically valid findings in this controversial area.

MONASH UNIVERSITY

PROJECT GRANT

$661,496

2011-2013

TEAM MEMBERS

Dr Jane Muir

Dr Jessica Biesiekierski

Ms Simone Peters

Dr Evan Newnham

Dr Greg Yelland

Dr Jacqueline Barrett

Mrs Ourania Rosella

Non-coeliac gluten sensitivity is an internationally-recognised condition, but remains highly controversial with its prevalence stated to be between 0.6 and 6 per cent of the population across the Western world.[1]

Gastroenterologist Professor Peter Gibson set out to tackle the big issue of whether gluten causes problems in people who do not suffer coeliac disease.

"Many claims were being made by scientists and non-scientists alike without good evidence.

"We performed a 'gold-standard' randomised, blinded cross-over, multi-dose re-challenge study," Professor Gibson explained.

The team developed infrastructure to perform this high-quality dietary study without multiple uncontrolled confounders.

Throughout the study, all meals were provided to 37 participants who had self-diagnosed non-coeliac gluten sensitivity and irritable bowel syndrome.

The participants alternated through gluten-free and low and high gluten diets. To ensure there were no other possible confounders, the diets were all low in FODMAPs (Fermentable Oligosaccharides, Disaccharides, Monosaccharides and Polyols) a type of short-chain, poorly absorbed carbohydrate that can induce abdominal symptoms.

The study provided the first randomised, controlled data in a re-challenge study about whether gluten might indeed be responsible for inducing gut symptoms in people who do not have coeliac disease.

The team found that FODMAPs, not gluten, might be triggering gut irritability.

About 11 per cent of Australian adults follow a gluten-free diet. Less than 0.5 per cent does this for diagnosed coeliac disease.[2]

1. Molina-Infante J, Santolaria S, Sanders DS, Fernández-Bañares F. Systematic review: noncoeliac gluten sensitivity. Aliment Pharmacol Ther. 2015 May;41(9):807-20.

2. Golley S, Corsini N, Topping D, et al. (2015) Motivations for avoiding wheat consumption in Australia: results from a population survey. Public Health Nutr 18, 490-499.

(L–R) Dr Jacqueline Barrett, Dr Greg Yelland, Dr Jane Muir, Professor Peter Gibson, Ms Simone Peters, Dr Evan Newnham & Mrs Ourania Rosella.

> We do hope that our findings dampen enthusiasm for gluten-free diets.

"We demonstrated that gluten, without FODMAPs, did not specifically induce symptoms in patients who believed they were gluten intolerant.

"Indeed, all patients experienced reduced gut symptoms in the run-in period when they, for the first time, restricted all FODMAPs in their diet.

"We found no changes in the physiology of the gut in response to gluten," Professor Gibson remarked.

The research demonstrated how nutritional and dietary studies should be performed if meaningful results are to be obtained.

"Methodological weaknesses and poor data interpretation remain major obstacles to continuing progress in general thought in this area," Professor Gibson noted.

The findings have put some scientifically valid findings in a controversial area and have been pivotal in putting brakes on the gluten-free epidemic that is sweeping the world. Three large studies have since been performed and published with similar results.

Despite the results, most patients continued on a gluten-free diet because 'they felt better'. However, the team hypothesised that this was not because the gut symptoms improved, but because their psyche did. In a pilot blinded, placebo-controlled re-challenge study, they found that gluten was associated with greater feelings of depression, despite not getting more abdominal symptoms.

Next steps:
Professor Gibson and his team will endeavour to understand more about how gluten affects the body, including whether gluten influences cognitive function or psychological health and, if so, whether this affects just susceptible people or if it is an issue across the general population.

Gluten: villain or scapegoat?

Gluten – a sticky protein found in wheat, barley, and other grains – has become a food villain in recent years. It has been blamed for a range of symptoms including bloating and flatulence, anaemia, tiredness and irritability, and joint pain and inflammation. Many people believe that avoiding gluten is essential to a healthy lifestyle and they avoid gluten to alleviate gut symptoms or fatigue. Yet, there is little scientific evidence to support these claims.

Sales of gluten-free foods have skyrocketed, despite often being costed at a premium price. In the USA, sales of gluten-free foods reached approximately $10 billion in 2013,[3] with most of the increased demand for gluten-free foods from those who have not been clinically diagnosed coeliac disease. A rapid growth in the sale of gluten-free foods has also been observed in the UK and Australia.

3. NPD Group (2015) Percentage of U.S. Adults trying to cut down or avoid gluten in their diets reaches new high in 2013, reports NPD.

MENDING A BROKEN HEART: REPAIRING INJURED HEART CELLS

Professor Robert M. Graham

Professor Graham and his team embarked on their research to understand how the heart develops after birth and why heart muscle cells lose their ability to divide and make new cells. Their research markedly shifted the goal post and showed that heart muscle cells actually retain an ability to divide until adolescence. This discovery holds great promise for new approaches to managing a range of heart conditions.

VICTOR CHANG CARDIAC INSTITUTE

PROJECT GRANT

$536,732

2011-2013

TEAM MEMBERS

Dr Siiri Iismaa

Dr Ming Li

Ms Amy Nicks

Dr Jianxin Wu

For more than one hundred years it was thought that the heart, much like the brain, stops being able to make new muscle cells soon after birth, limiting the organ's ability to repair itself after injury.

However, in an exciting discovery with colleagues in the US, Professor Robert Graham and his team discovered for the first time that heart muscle cells can replicate long after birth.

"Surprisingly, we showed that heart muscle cells retain the ability to make new cells until early adolescence.

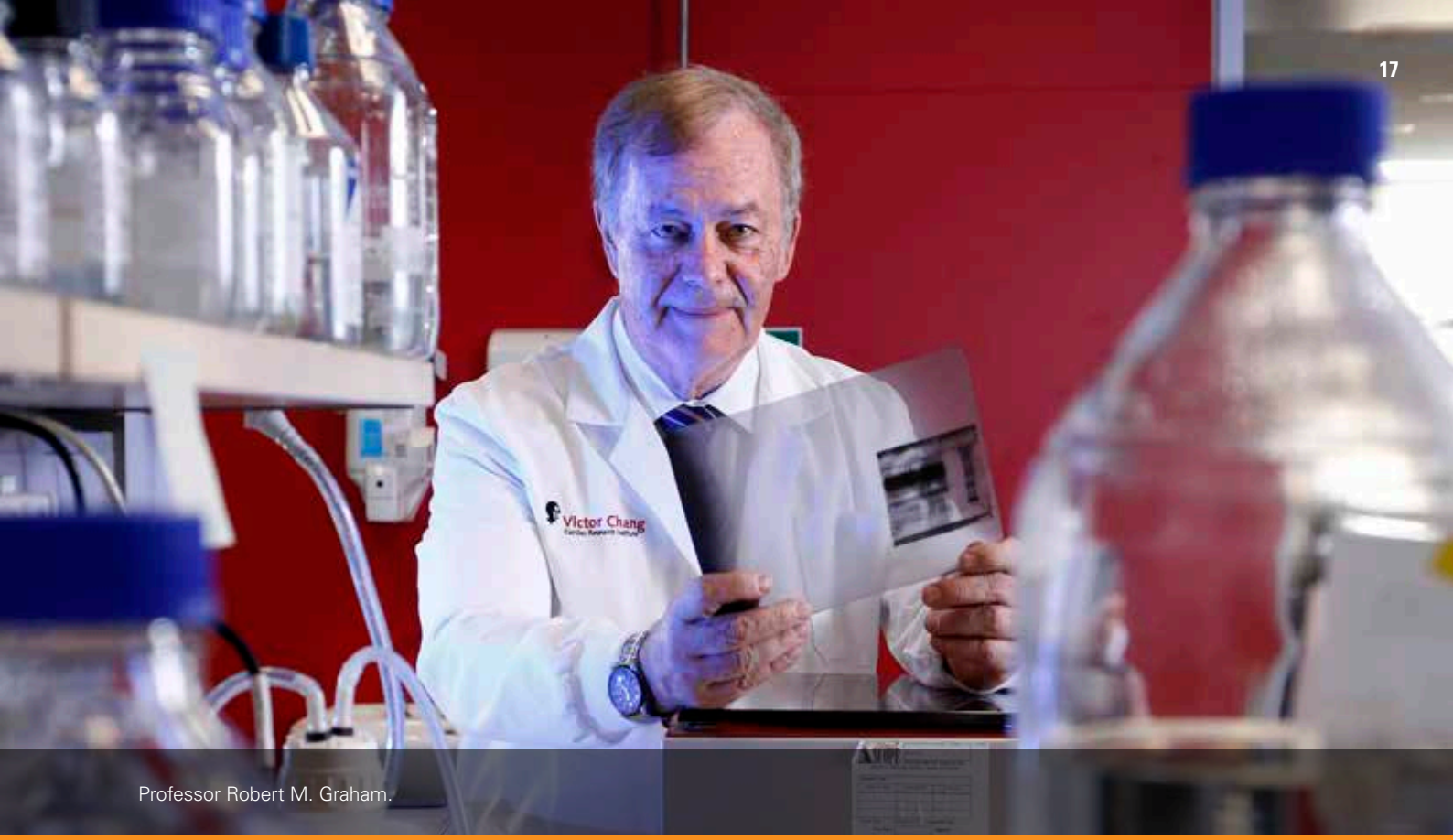
"Our work seeks to understand how the heart develops after birth and, in so doing, understand why heart muscle cells lose their ability to divide and make new cells," Professor Graham explained.

The discovery that the heart can regenerate itself – at least until just before adolescence – holds great promise for new approaches to managing congenital heart disorders in children.

"This opens a window of opportunity to more effectively treat some forms of congenital heart disease in which the heart muscle hasn't developed properly.

In Australia, more than 2000 babies are born with congenital heart conditions each year.[1]

1. AIHW, 2011. *Cardiovascular disease: Australian facts 2011*. Cardiovascular disease series. Cat. no. CVD 53. Canberra: AIHW.



Professor Robert M. Graham.

> This work promises to revolutionise our understanding of postnatal heart development with profound implication for treating a variety of heart conditions.

"By allowing proper healing of the injured or mal-developed heart, we may be able to markedly improve outcomes after heart attacks and prevent the need for major and repeated surgery in children with congenital heart disease," Professor Graham remarked.

The findings challenge traditional thinking about how the adult heart might undergo repair and remodelling after injury, and how scientists may reactivate heart muscle cells damaged after a heart attack in adults.

The research provides new hope that, given the appropriate stimuli, adult heart muscles might be able to divide again to repair damage caused by disease or myocardial infarction in adults.

"It may be possible to reactivate the ability of heart muscle cells to divide and therefore to allow proper healing of the injured heart," Professor Graham concluded.

Next steps:
Now that Professor Graham and his team have shown that heart muscle cells actually retain an ability to divide until adolescence, they are setting out to define the precise molecular mechanism that stimulate their division after birth – insights that may then be applied to stimulate heart muscle cell division at later time.

Cardiovascular disease in Australia

The inability of heart muscle cells to divide and make new cells limits repair of the heart in response to injury, such as some forms of congenital heart disease, a heart attack or high blood pressure. This results in a profound increase in death and disability from these injurious heart conditions. Cardiovascular disease is one of Australia's leading causes of death, leading to 29.5% of all deaths in 2013.[2] However, due to research, the overall death rate from acute cardiovascular disease has dropped by 80% since the 1960s.[3]

2. ABS, 2015, Causes of death 2013. No. 3303.0.

3. AIHW, 2011. Cardiovascular disease: Australian facts 2011. (Cat. no. CVD 53). AIHW: Canberra.

INDIGENOUS HEALTH: UNDERSTANDING THE HEALTH GAP

Professor Louisa Jorm

Across many health indicators, Indigenous Australians remain disadvantaged compared with non-Indigenous Australians. Professor Louisa Jorm linked and scrutinised the vast data held by modern healthcare systems to understand the factors influencing disadvantage for Indigenous Australians. This important research will translate it into better disease prevention and patient care for Indigenous Australians, as well as more effective health care spending.

WESTERN SYDNEY UNIVERSITY AND UNSW AUSTRALIA

PROJECT GRANT

$484,697

2009-2014

TEAM MEMBERS

Ms Deborah Randall

Professor Alastair Leyland

Professor Sandra Eades

Ms Sanja Lujic

Dr Timothy Churches

Associate Professor Mary Haines

Mr Michael Falster

Dr Kathleen Falster

Mr Holger Möller

Dr Aiden O'Loughlin

Professor Rebecca Ivers

Mr Tim Harrold

Ms Tracie Reinten

While there have been improvements in the health and wellbeing of Aboriginal and Torres Strait Islander Australians in recent years, some long-standing challenges remain.

Through the Indigenous Health Outcomes Patient Evaluation (IHOPE) project, Professor Louisa Jorm and her team set out to investigate factors influencing health outcomes for Indigenous Australians.

"Every time you visit a GP, hospital or emergency department, valuable data is generated. Yet, these data are underutilised to inform improvements in health care.

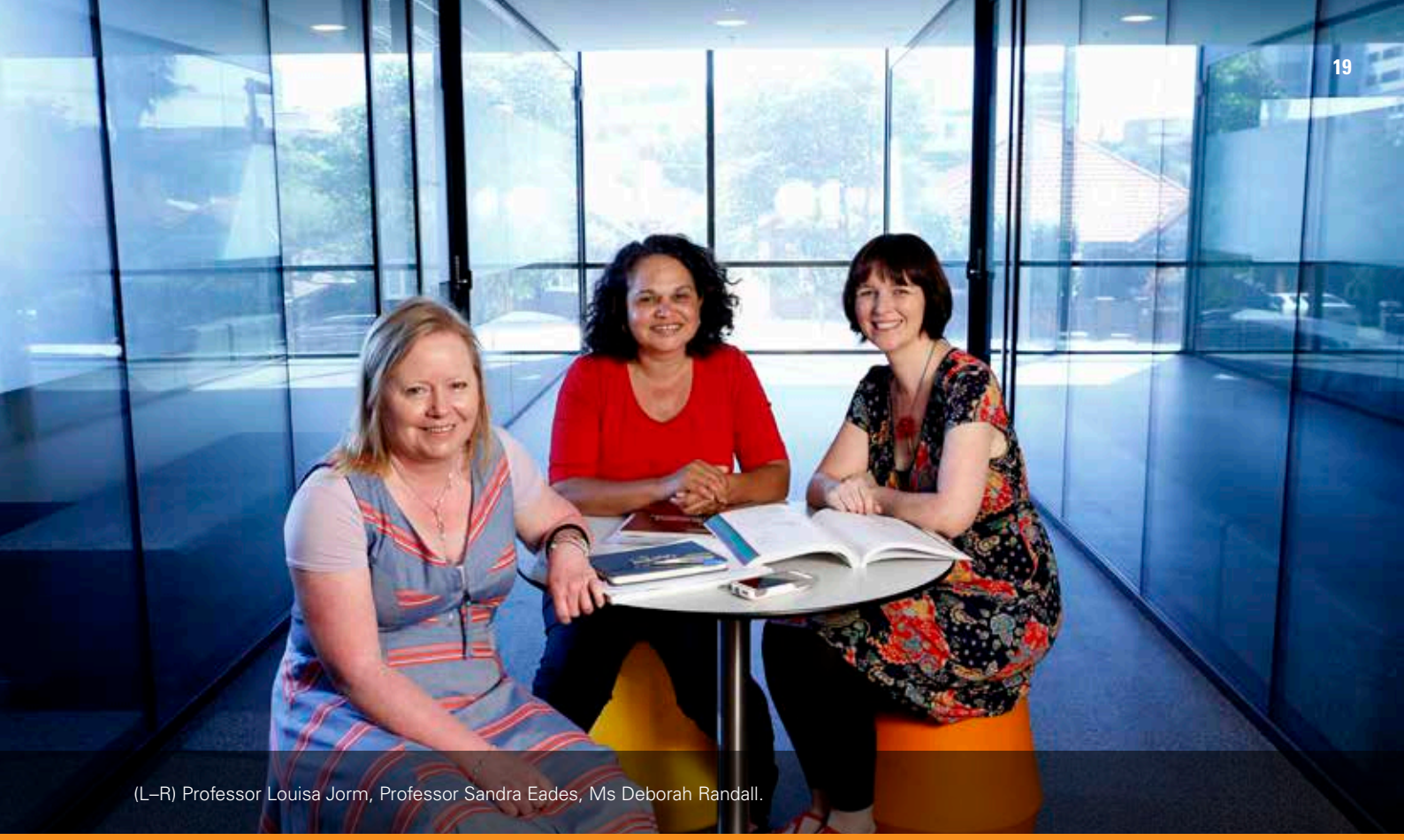
"There is so much crucial health information in data banks that can analysed to understand the best way to deal with major diseases and health issues," Professor Jorm explained.

The team applied advanced statistical modelling techniques to understand how individual, geographic and hospital factors may contribute to disparities in health outcomes for Indigenous people in New South Wales.

By comparing hospital data for Indigenous and non-Indigenous people, the team sought to determine whether these health disparities could be targeted with specific interventions.

Factors investigated throughout this research included socioeconomic status, remoteness, access to hospital and specialist services, and hospital characteristics.

Aboriginal Australians have a life expectancy 11.5 years lower for males and 9.7 years lower for females than non-Indigenous Australians.



(L–R) Professor Louisa Jorm, Professor Sandra Eades, Ms Deborah Randall.

> This research will make a valuable contribution towards improving the underlying disadvantage that Indigenous Australians face in the healthcare system.

"Our research found that crucial issues driving poor outcomes for Aboriginal people included high rates of comorbidities, low levels of private health insurance, use of smaller hospitals with fewer specialist services, and limited access to publically-funded services," Professor Jorm remarked.

The research showed that rates of cataract surgery in Aboriginal people were 30 per cent lower than in non-Indigenous people, despite higher rates of cataract.

This disparity relates to limited access to publically funded eye health services for Indigenous Australians.

"IHOPE research has already helped in planning cardiac, ear and eye health services for Aboriginal people in New South Wales.

"The research has also been used to inform five national and state policy documents."

This will play a vital role in closing the gap and ensuring all Aboriginal and Torres Strait Islander people enjoy the same opportunities as non-indigenous Australians to live a long, healthy and happy life.

Next steps:
With further funding from the NHMRC, the team is now working on a project – using routinely collected data and some of the new methods that were developed for IHOPE – that is investigating the factors that promote successful early childhood development in Aboriginal children.

Research findings

- Rates of hospitalisation for acute myocardial infarction (AMI) in Aboriginal people were 2.1 times those in non-indigenous people, regardless of where they lived.
- Rates of cataract surgery in Aboriginal people were 30 per cent lower than in non-indigenous people, despite higher rates of cataract. This disparity relates to limited access to publically funded eye health services.
- Aboriginal children were around 30 per cent less likely than other children to receive surgery for otitis media, despite higher rates of disease. Again, access to publically-funded services underpinned the disparity.
- Rates of serious road traffic injuries were 1.2 times higher in Indigenous than non-indigenous people. Geography played an important role in driving this disparity.

BREATHING EASY: SUPPORTING LUNG DEVELOPMENT OF PREMATURE BABIES

Associate Professor Jane Pillow

Associate Professor Jane Pillow and her team sought to understand the respiratory problems of premature babies to help the sickest and smallest babies develop their lungs. This research has contributed a great deal to improving both the quality of healthcare available to premature babies at birth as well as their long-term health prospects.

UNIVERSITY OF WESTERN AUSTRALIA

PROJECT GRANT

$395,696

2011-2013

TEAM MEMBERS

Professor Andrew Bassom

Associate Professor David Tingay

Dr Peter Noble

Dr Clare Berry

Professor Bela Suki

Dr David Kaczka

Dr Jane Kee

Dr Alex Wood

Dr Anna Lavizzari

Dr Elroy Zonnerveld

Mr Jake Hermann

Breathing is the most pressing challenge for premature infants at birth, and is the main focus of Associate Professor Jane Pillow's research.

Through their important research, the team is discovering new ways to help premature babies breathe more easily, playing a valuable role in enhancing the immediate and long-term health outcomes for these babies.

Associate Professor Pillow explained that babies with underdeveloped lungs often suffer from severe breathing difficulties.

"Preterm infants often need mechanical ventilation, but their underdeveloped and fragile lungs are very easily damaged by ventilation.

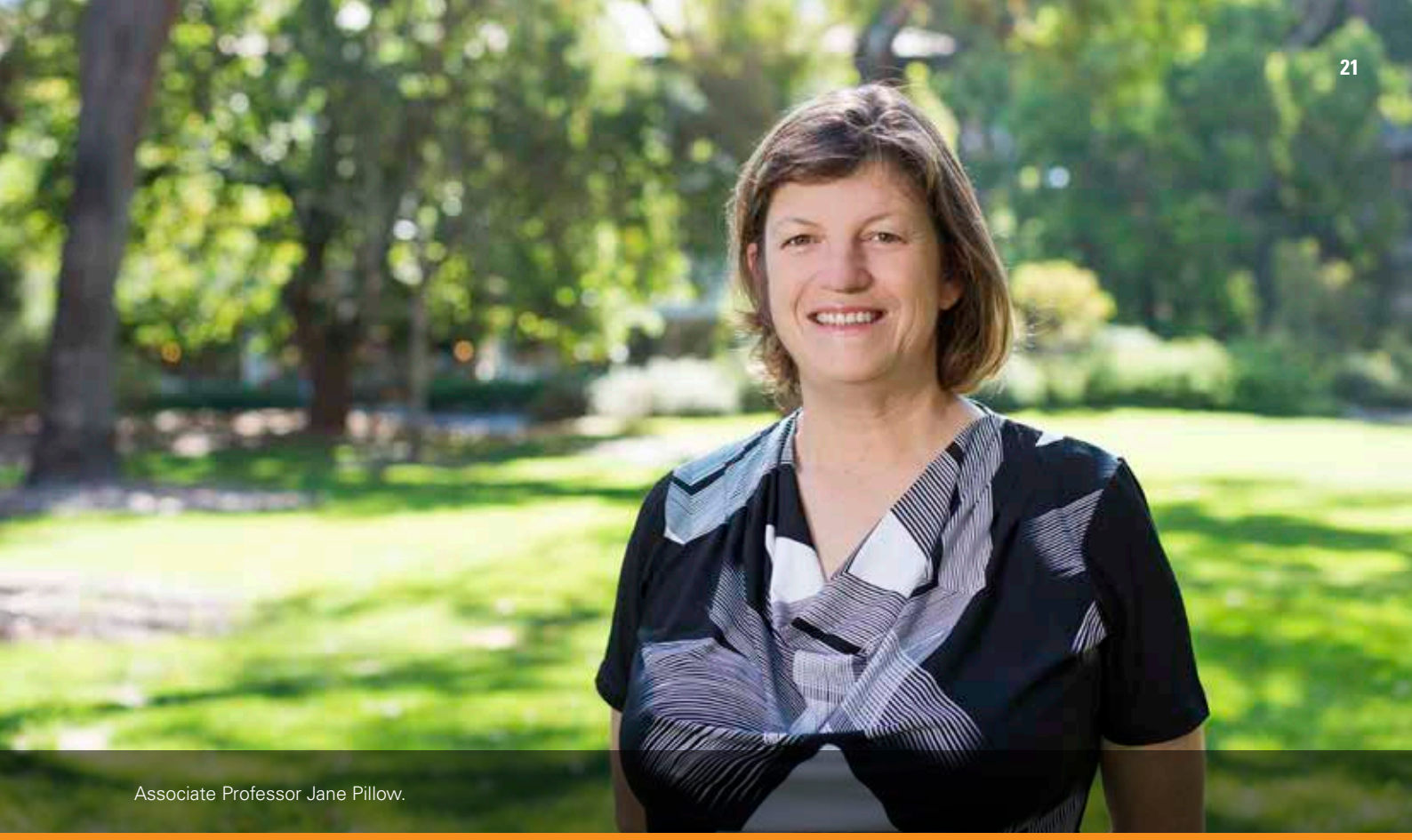
"Our research focuses on finding more gentle and effective ways to assist their breathing.

"We are investigating new treatment strategies to minimise the long-term effects of premature birth on lifelong respiratory health," she explained.

Associate Professor Pillow's team has made some fascinating discoveries about the respiratory systems of premature infants. The most intriguing and exciting observation was identifying new ventilator waveform properties that have distinct advantages for enhanced gas exchange than traditional waveforms.

Using a novel mode of mechanical ventilation called high-frequency oscillatory ventilation, the team examined which components of the ventilator waveform are most beneficial to the airway and lungs of premature babies.

Across the world each year, more than 15 million babies are born prematurely, of which 1 million will die during infancy.



Associate Professor Jane Pillow.

> This research offers the possibility of significantly improving neonatal health and wellbeing at a global level.

"We found that combining multiple different frequencies into the high frequency ventilator waveform resulted in additional benefits for the patient.

"This enables us to ventilate babies using lower pressures and average breath volumes, potentially reducing the injurious effects of mechanical ventilation."

Associate Professor Pillow hopes these findings will contribute to new and improved future treatments.

"Our findings will advance the technologies used to treat premature babies with significant breathing difficulties, whilst reducing the damage inflicted on their lungs by lifesaving artificial respiration.

"Gentle artificial breathing technologies will encourage more normal lung development, reducing the likelihood and severity of long-term lung disease that adversely affects quality of life," she concluded.

Next steps:
In collaboration with international colleagues and industry, Associate Professor Pillow and her team will further develop new ventilator modality and evaluate its application to other respiratory diseases, including acute respiratory distress syndrome in adults.

Premature birth in Australia

Normally, a pregnancy lasts about 40 weeks, but a premature, or preterm, birth is one that occurs before the start of the 37th week of pregnancy. In Australia, around eight per cent of babies are born prematurely, but these babies need vital care in the first weeks and months of their fragile lives. Their short and long-term health outcomes are improved greatly by the care they receive during this time. As premature birth gives the baby less time to develop in the womb, some babies, especially those born earliest, experience complicated medical problems because their organs are too immature to function properly outside the womb.

ECTOPIC PREGNANCY TREATMENT: A SAFER WAY

Professor Stephen Tong

Professor Stephen Tong and the team of investigators are revolutionising the treatment of ectopic pregnancy, meaning most women presenting with the condition could be treated medically, rather than surgically. Not only will this make treating ectopic pregnancies safer, easier and more effective, but it may save many lives across the developing world where surgery is not possible.

MONASH UNIVERSITY

PROJECT GRANT

$228,770

2011-2013

TEAM MEMBERS

Professor Terrance Johns

Dr Monika Skubisz

Professor Andrew Horne

Professor Euan Wallace

Professor Stephen Tong's research is focussed on pursuing scientific discoveries to improve the care of pregnant women. His group (Translational Obstetrics Group, now based at The University of Melbourne) is tackling major complications of pregnancy and searching for better treatments to make pregnancy safer.

Professor Tong's motivation for pursuing translational research stems from his clinical practice as a specialist obstetrician and gynaecologist.

"I continue to manage serious diseases that put women, mothers and babies at risk," he explained.

The team of investigators, lead by Professor Tong, worked to develop novel ways to cure ectopic pregnancies with medication alone, potentially allowing women to avoid surgery and enhance their chance of a future healthy pregnancy.

Currently, most ectopic pregnancies are treated surgically. While the surgery is safe, there are still risks associated with any surgical treatment.

If an ectopic pregnancy is small, a drug called methotrexate can be used to clear the ectopic pregnancy medically.

"Unfortunately, methotrexate is only effective if the ectopic pregnancy is small. Therefore, most ectopic pregnancies still require surgery.

"We have identified a new medication treatment to treat ectopic pregnancies that we hope may be considerably more effective than methotrexate alone," Professor Tong said.

The team is exploring the benefits of combining methotrexate with another drug called gefitinib, which is hoped to treat effectively most cases of ectopic pregnancies.

Ectopic pregnancies complicate one to two per cent of all pregnancies[1] and contribute to three to eight per cent of all pregnancy related deaths.[2]

1. BMJ 2011 342:d2297
2. BJOG 2011;118 [Supp 1]:1-203

(L–R) Professor Terrance Johns, Professor Stephen Tong, Dr Monika Skubisz.

> This would medicalise what is currently regarded as a surgical condition, and may arguably revolutionise the treatment of this important condition.

"We are very hopeful that the combination of methotrexate and gefitinib could be used to improve the treatment of ectopic pregnancy.

"Specifically, we hope it can be used to efficiently resolve larger ectopic pregnancies that currently require surgery.

"Even for smaller ectopic pregnancies, we hope the combination may be able to clear ectopic pregnancies much quicker than methotrexate alone", Professor Tony remarked.

So far, the results are extremely encouraging. The team found the drug combination cured ectopic pregnancies 34 per cent faster than methotrexate alone, reducing risk of fallopian tube rupture and averting the need for surgery.[3]

Importantly, the combination appears safe and a number of women have had subsequent successful pregnancies.

The team has recently completed a clinical trial of women presenting with large ectopic pregnancies (many of these women would have been offered surgery immediately if they presented for routine clinical care). There was an 86 per cent success of all those treated with combination of methotrexate and gefitinib, thus removing the need for surgery.

Next steps:
Professors Tong and Horne have commenced a large a randomised placebo controlled clinical trial, comparing the use of methotrexate alone versus combining methotrexate and gefitinib. It will be rolled out across 25 to 50 hospitals in the United Kingdom this year. If the trial yields positive results, it is hoped this treatment will be widely integrated into clinical care.

What is ectopic pregnancy?

Ectopic pregnancy is a complication where the embryo attaches outside the uterus. It is a life-threatening condition that complicates up to two percent of all pregnancies. Without treatment, ectopic pregnancy can rupture major blood vessels, causing fatal internal bleeding. It is the cause of up to eight per cent of pregnancy-related deaths.

There is an increased risk of an ectopic pregnancy if the fallopian tube is scarred or damaged. Risk factors include pelvic surgery, previous ectopic pregnancy and pelvic inflammatory disease arising from infection. However, for many women diagnosed with an ectopic pregnancy, there is no obvious risk factor.

3. Obstet Gynecol 2013;122:745-51.

EXCELLENCE IN RESEARCH

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