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10

OF THE BEST
RESEARCH
PROJECTS 2014



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L to R: Associate Professor Michael Kershaw, Ms Carmen Yong, Ms Melissa Henderson, Associate Professor Phil Darcy, Mr Alex Davenport, Ms Connie Duong, Dr Paul Neeson, Dr Paul Beavis.

REMOVING CANCER'S CAMOUFLAGE

ASSOCIATE PROFESSOR PHILLIP DARCY

KEY FACTS:

IN AUSTRALIA IN 2009, 1 IN 2 MEN AND 1 IN 3 WOMEN UNDER THE AGE OF 85 WERE DIAGNOSED WITH CANCER¹.

AN ESTIMATED 128,000 NEW CASES OF CANCER WILL BE DIAGNOSED IN AUSTRALIA THIS YEAR, WITH THAT NUMBER SET TO RISE TO 150,000 BY 2020².

THE SURVIVAL RATE FOR MANY COMMON CANCERS HAS INCREASED BY 30% IN THE PAST TWO DECADES³.

1 <http://www.aihw.gov.au/cancer>

2,3 <http://www.cancer.org.au/about-cancer/what-is-cancer/facts-and-figures.html>

AFFILIATION

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TEAM MEMBERS

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Associate Professor

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Ms Connie Duong

GRANT TYPE

Career Development
Fellowship

FUNDING AMOUNT

\$428,603 (2009-2012)

White blood cells are the first line of defence in the human body, identifying viruses and bacteria and fighting them off. It's thanks to our white blood cells that sore throats mend and viral infections like the flu are cleared.

Unfortunately, when it comes to detecting the threat of cancer, our white blood cells are often blind.

To patrol for diseases, white blood cells constantly search for antigens, which can trigger the cells to attack. But cancer cells are sneaky and some hide their antigens, slipping past the ever watchful white blood cells and wreaking havoc on other cells without resistance.

To counter this, Associate Professor Phillip Darcy from the University of Melbourne has found a way to train white blood cells to better patrol for cancer antigens and attack when the cells emerge.

"The focus of this project has been to develop a novel approach to enable white blood cells to better recognise cancer cells," Associate Professor Darcy said.

To do this, he genetically modifies white blood cells by adding chimeric antigen receptors, which can specifically recognise antigens on cancer cells.

The receptors also have a binding agent which means that when the white blood cells find a cancer cell, they latch on and are triggered to attack.

Research into these 'genetically modified killer white blood cells', has shown them to be highly effective in mice bearing established breast, sarcoma and colon cancer cells.

"We found that the killer cells are able to specifically recognise cancer cells and can effectively eradicate these rogue cells in mice without causing any harm to normal tissues."

"The potential benefit of this study is the development of a novel and effective treatment for cancer patients which does not cause toxicity," he said.

Most current treatments for cancer, such as radiotherapy and chemotherapy, attack cancer by killing growing cells indiscriminately – attacking both cancerous and healthy cells.

Associate Professor Darcy's work, which harnesses his expertise in immunology, is ground breaking for its ability to target cancer cells specifically.

"We were very excited to see our approach working effectively in our mouse models, and it is even more exciting now that this therapy has been translated into human patients."

Associate Professor Darcy's results are currently being tested in a phase I clinical trial at the Peter MacCallum Cancer Centre.

"This trial is the first of its kind in Australia. Results so far have shown that our approach was well tolerated in all patients, that the transferred cells can persist for up to 10 months and that they home specifically to the site of the cancer to mediate anti-tumor activity."

If Associate Professor Darcy's research continues its path of success, we could well have a new cancer therapy that treats patients with few side-effects. And that would be great news for millions of Australians and people worldwide.

NEXT STEPS:

Associate Professor Darcy expects his work will move to a phase II clinical trial in future. The expected future outcome is the development of a safe and effective option for patients which have not responded to first line conventional treatments, such as radiotherapy and chemotherapy.



L to R: Ms Nada Cvijanovic, Ms Sina Ullrich, Mr Scott Standfield, Ms Nicole Isaacs, Professor Christine Feinle-Bisset, Dr Gudrun Schober, Ms Penelope Fitzgerald.

FATTY ACIDS COMBAT OBESITY

PROFESSOR CHRISTINE FEINLE-BISSET

KEY FACTS:

OBESITY HAS NEARLY
DOUBLED WORLDWIDE
SINCE 1980¹.

IT IS PROJECTED THAT BY 2025,
APPROXIMATELY ONE THIRD OF
AUSTRALIAN ADULTS WILL BE
CLASSIFIED AS OBESE².

LAURIC ACID IS THE MOST
ABUNDANT FATTY ACID IN
COCONUT OIL, AND HUMAN
BREAST MILK IS ALSO RICH IN
LAURIC ACID³.

1 <http://www.who.int/mediacentre/factsheets/fs311/en>

2 <http://www.abs.gov.au/ausstats/abs@.nsf/Lookup/by%20Subject/4338.0~2011-13~Main%20Features~Overweight%20and%20obesity~10007>

3 <http://www.ncbi.nlm.nih.gov/pubmed/19665786>

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 Ms Nicole Isaacs
 Mr Scott Standfield
 Professor Michael Horowitz
 Professor Thomas Rades

GRANT TYPE

Project Grant

FUNDING AMOUNT

\$744,646 (2009-2012)

In most people, becoming overweight or obese is a simple equation: it's a balance of calories consumed versus calories burned off. If your intake of energy is more than what you expend, you will inevitably gain weight.

While this is widely accepted, an increasing number of people are struggling to resist their food cravings and limit their portion sizes.

Over the years various treatments have emerged to help people manage their weight; the most effective so far being surgery to limit stomach size. Pharmacological treatments are also available but they often have severe side effects. However, a new non-invasive and side-effect free treatment lies on the horizon.

Professor Christine Feinle-Bisset is a Chief Investigator in a NHMRC-funded Centre of Research Excellence in Translating Nutritional Science to Good Health with the University of Adelaide's School of Medicine. A few years ago, she and her research team discovered a fatty acid that can trigger the body's natural physiological mechanisms to suppress appetite and help reduce energy intake.

This fatty acid was lauric acid. In a major research program funded through a NHMRC Project Grant, Professor Feinle-Bisset and her team administered lauric acid directly into the small intestine where fatty acid-sensing receptors are located. In doing so, they were able to evaluate the effects of lauric acid on the gastrointestinal tract and learn how they could enhance the release of gut hormones to control appetite.

With this established, the team set about determining whether the observed effects could be replicated when lauric acid was ingested orally.

Here they met a number of challenges. Because lauric acid doesn't dissolve well in water, it's very difficult to deliver in liquid form into the gastrointestinal tract, even in small amounts. What's more, it has a very unpleasant taste.

Working with Professor Thomas Rades from the University of Copenhagen, they developed novel delivery solutions that overcame these obstacles and managed to replicate their earlier results. Critically, they found that oral ingestion of lauric acid suppressed appetite and reduced energy intake by up to 18% compared with placebo.

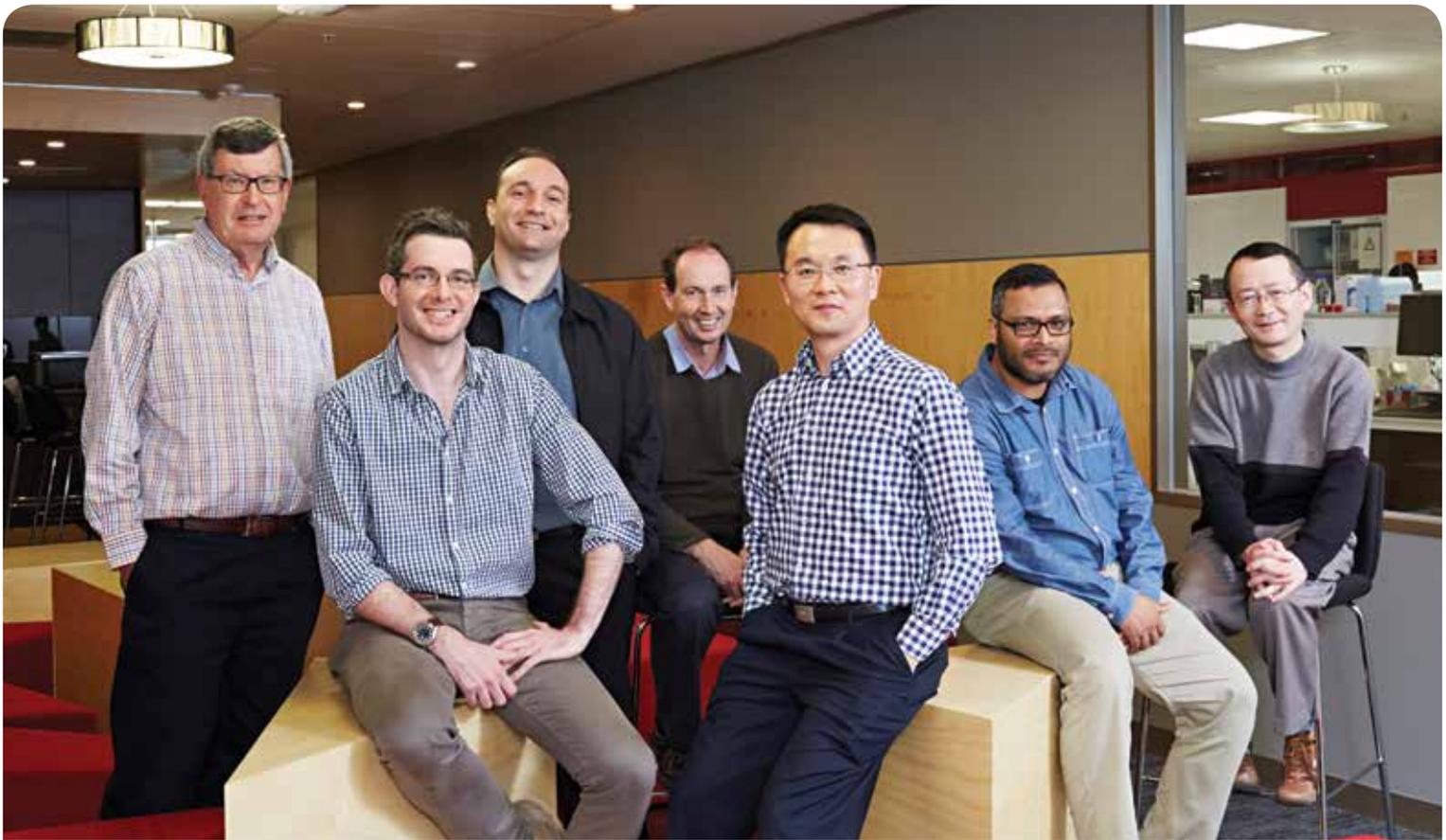
Professor Feinle-Bisset adds, "Importantly, these effects occurred at very low caloric loads, so consuming lauric acid does not contribute significantly to overall energy intake."

What this means is that the number of calories someone would consume in taking lauric acid would be more than made up for by the resulting weight loss.

Having made these findings, Professor Feinle-Bisset is now collaborating with industry partners in Australia and overseas to develop their discoveries into novel, nutrient-based options for the management and treatment of obesity.

NEXT STEPS:

Professor Feinle-Bisset and her team are currently working on a number of other projects that they hope will lead to obesity treatment options that can complement lauric acid. This work involves understanding how other nutrients might reduce energy intake and regulate blood glucose.



L to R: Professor Roger Nation, Dr Kade Roberts, Dr Tony Velkov, Associate Professor Phillip Thompson, Professor Jian Li, Dr Mohammad Azad, Dr Jiping Wang.

RESISTING ANTIBIOTIC RESISTANCE

PROFESSOR JIAN LI

KEY FACTS:

BETWEEN 5 AND 10% OF PATIENTS ADMITTED TO HOSPITAL IN AUSTRALIA ACQUIRE AN INFECTION DURING THEIR STAY – ABOUT 200,000 EACH YEAR¹.

IT IS ESTIMATED THAT ANTIBIOTIC RESISTANCE COSTS THE AUSTRALIAN ECONOMY MORE THAN \$1 BILLION A YEAR IN DIRECT HEALTH CARE EXPENDITURE².

ONLY TWO NOVEL ANTIBIOTICS WERE APPROVED BY THE FOOD AND DRUG ADMINISTRATION (IN THE UNITED STATES) BETWEEN 2008 AND 2012, COMPARED TO 16 APPROVED BETWEEN 1983 AND 1987³.

1 <http://www.abc.net.au/news/2012-11-05/cooper-is-australia-doing-enough-to-stop-superbugs/4353816>

2 <http://cainz.org/files/2014/04/Digest-E6.pdf>

3 www.idsociety.org/AntibioticResistanceFactSheet-April2013.pdf

AFFILIATION

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TEAM MEMBERS

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Associate Professor

Philip E. Thompson

Dr Kade D. Roberts

Dr Jiping Wang

Dr Heeji Lee

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Ms Heidi H. Yu

Mr Jovan Jacob

Ms Anima Poudyal

Mr Mohammad Azad

GRANT TYPE

Project Grant

FUNDING AMOUNT

\$661,070 (2010-2012)

Antibiotic resistance has been identified by the World Health Organisation as one of the greatest threats facing human health globally.

Professor Li from Monash University explains, "Since the 1990s there has been a marked decline in discovery of new antibiotics. The world is now facing an enormous and growing threat from the emergence of bacteria that are resistant to almost all available antibiotics."

"The situation is especially worrying with multidrug-resistant (MDR) Gram-negative pathogens, notably *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and *Klebsiella pneumoniae* against which no new antibiotics discovered by pharmaceutical companies will be available for many years to come."

As a result, health practitioners need to use 'old' antibiotics such as polymyxins as a last-line defence against these three difficult-to-treat 'superbugs'. But polymyxin resistance is increasingly reported in many countries, and the clock is ticking.

Professor Li and his colleagues understand the urgency of this issue and have dedicated themselves to developing new-generation polymyxins.

"Our NHMRC project discovered novel polymyxin-like antibiotics that act against Gram-negative 'superbugs'. These new compounds were identified using a novel model defining the relationship between the chemical structures of polymyxins and their biological activity, as well as the extensive pharmacological knowledge we have obtained over the last decade," Professor Li says.

"More than 120 novel polymyxin-like compounds were designed and synthesised, using our efficient chemical synthesis platform, for in vitro and in vivo pharmacological evaluations."

In going about this project, Professor Li's team faced the major challenge of designing compounds which have both superior effectiveness and minimal toxicity. Currently available polymyxin antibiotics have been associated with significant kidney toxicity, compromising the benefits they bring. In this project, Professor Li and his team had their work cut out for them, creating novel compounds that have a much lower toxicity profile but comparable or higher antibacterial activity.

They conquered this obstacle and excitingly, Professor Li's NHMRC project led to a partnership with an international pharmaceutical company. He and his team also won a large 5-year grant in 2012 through the US National Institutes of Health (NIH) worth \$4.48 million to develop the novel compounds into new antibiotics.

"When President Barack Obama welcomed Prime Minister Tony Abbott to the White House in June 2014, our program was highlighted as one of the six key examples of successful collaborations between the United States and Australia," Professor Li says proudly.

With more hard work, it is very likely that these novel polymyxins will be able to be added to our armoury in the near future in our ongoing battle against Gram-negative 'superbugs'.

NEXT STEPS:

Professor Li and his team will identify one particularly promising compound, based on comprehensive safety evaluations, for an Investigational New Drug application. If it is approved by the US Food and Drug Administration – paving the way for the compound to be tested in humans – the compound will progress to a phase 1 clinical trial.



L to R: Ms Kavitha Iyer, Dr Hongjun Shi, Dr Duncan Sparrow, Professor Sally Dunwoodie, Dr Julie Moreau, Ms Victoria O'Reilly, Ms Joeline Major, Dr Gavin Chapman.

PUTTING THE PIECES TOGETHER: UNDERSTANDING BIRTH DEFECTS

PROFESSOR SALLY DUNWOODIE

KEY FACTS:

BIRTH DEFECTS AFFECT AN ESTIMATED 1 IN 33 INFANTS AND RESULT IN APPROXIMATELY 3.2 MILLION BIRTH DEFECT-RELATED DISABILITIES WORLDWIDE EVERY YEAR¹.

AN ESTIMATED 270 000 NEWBORNS DIE DURING THE FIRST 28 DAYS OF LIFE EVERY YEAR FROM BIRTH DEFECTS WORLDWIDE².

THE MOST COMMON SEVERE BIRTH DEFECTS ARE HEART DEFECTS, NEURAL TUBE DEFECTS AND DOWN SYNDROME³.

AFFILIATION

Victor Chang Cardiac
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TEAM MEMBERS

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Dr Stanley Artap
Ms Kavitha Iyer
Dr Alex James
Dr Kylie Lopes Floro
Ms Joeline Major
Mr Zamil Mattar
Dr Julie Moreau
Ms Victoria O'Reilly
Dr Sharon Pursglove
Dr Hongjun Shi
Professor Kenro Kusumi
Professor David Sillence
Dr Lesley McGregor

GRANT TYPE

Research Fellowship

FUNDING AMOUNT

\$630,275 (2008-2012)

Given the intricacies of creating life, it's no wonder the birth of a healthy baby is often referred to as a miracle. The process of molecules, genes and cells coming together to form an embryo and then grow into a human is incredibly complex, and just one error along the way can result in death, or defects that affect the baby for the rest of its life.

It is this process that has continued to amaze and fascinate Professor Sally Dunwoodie for more than 20 years of research. This curiosity, combined with a belief that every child has the right to a healthy start to life, led her to study why birth defects occur.

"We only understand what caused birth defects in about 20% of cases. For the vast majority, defects are considered sporadic and questions concerning why they occurred remain unanswered."

Professor Dunwoodie and her team at the Victor Chang Cardiac Research Institute set out to explain the nature of such sporadic birth defects by studying mice to determine how the vertebrae developed in the embryo.

At the same time, they hunted for genes that could be responsible for vertebral defects. Then, they put their discoveries to test.

The team had two hunches of what might cause vertebral defects – one was genetic and the other was low oxygen levels (hypoxia) in embryo cells.

When they studied each factor on its own, they found each had little effect on the formation of the vertebral column. But when combined, they caused defects in a significant number of embryos.

Importantly, they showed how the defects happened. In all mice, short exposure to hypoxia was enough to disrupt the transmission of two signals that are key to developing vertebral tissue. In the embryos

that developed defects, they found that they were also carrying genetic mutations that were responsible for the signals getting through to the tissues.

"We therefore demonstrated how an interaction between genetic predisposition to disease and an environmental factor, combined to disrupt a developmental process and cause a defect."

"Understanding that gene-environment interaction can cause developmental defects in mice alerts us that this is a likely cause of some cases of sporadic birth defects in humans."

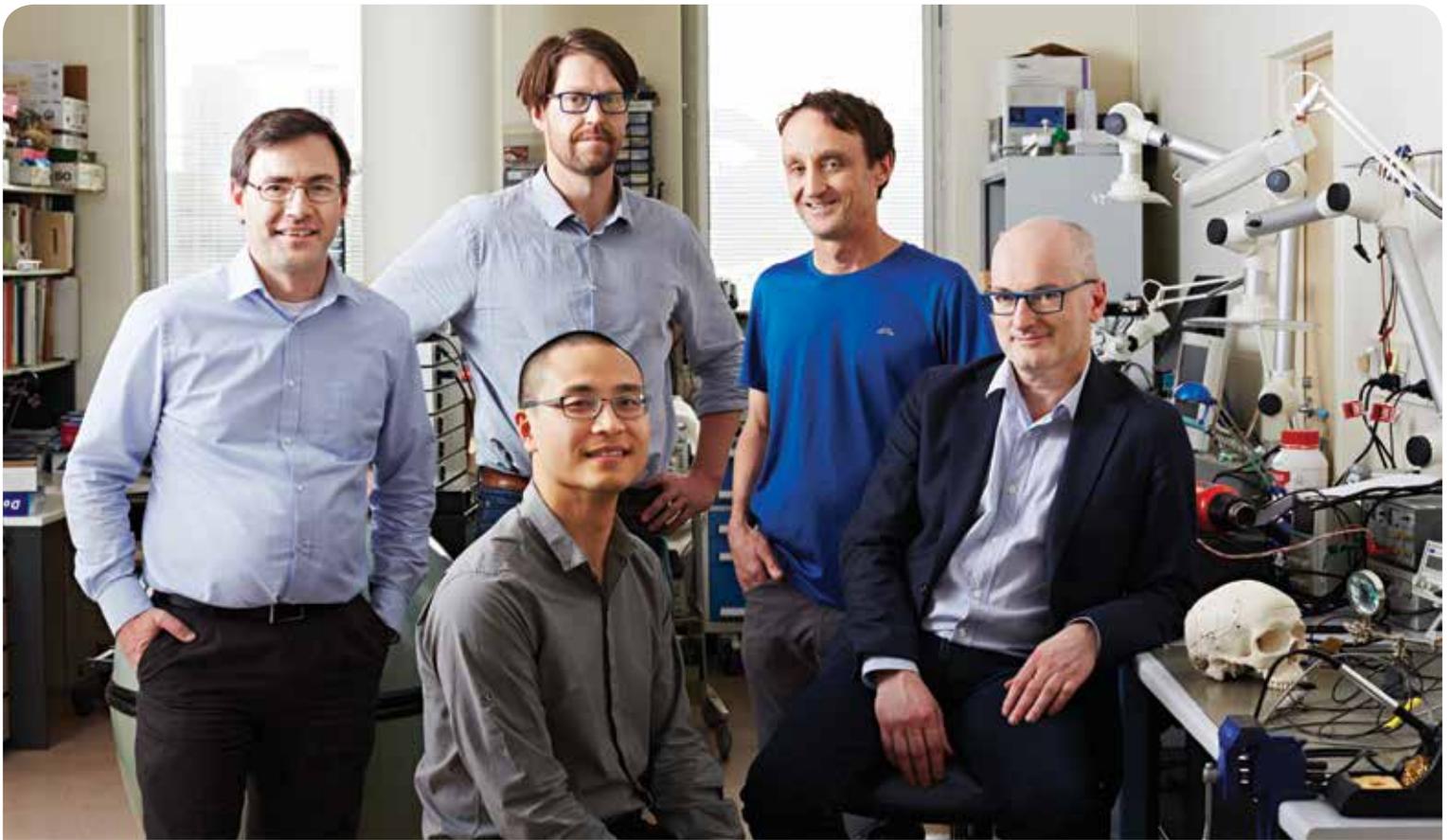
Human diagnostic tests for the genes they identified have since been developed, and their research has shed much light on the role of hypoxia in human birth defects.

"Hypoxia may have a number of triggers such as high altitude, hyperglycaemia, placental insufficiency and the effects of some prescription medications."

"Our research highlights the fact that things other than smoking might affect embryonic development. Women of child bearing age should be mindful of these, especially if they have a history of birth defects in their family."

NEXT STEPS:

Professor Dunwoodie will extend her research to investigate other types of birth defects that might be susceptible to gene-environment interaction. She is now looking at congenital heart disease, which affects the structure of the heart and its vessels. Congenital heart disease is the most common type of birth defect, but the cause is unknown in about 80% of cases.



L to R: Associate Professor David Grayden, Dr Dean Freestone, Dr Alan Lai, Associate Professor Chris Williams, Professor Mark Cook.

STIMULATING EPILEPSY TREATMENT

PROFESSOR MARK COOK

KEY FACTS:

EPILEPSY IS THE WORLD'S MOST COMMON SERIOUS BRAIN DISORDER, AND THREE TIMES MORE PREVALENT THAN MULTIPLE SCLEROSIS, PARKINSON'S DISEASE AND CEREBRAL PALSY¹.

APPROX 3% TO 3.5% OF AUSTRALIANS WILL EXPERIENCE EPILEPSY AT SOME POINT IN THEIR LIVES².

AROUND 49% OF PEOPLE WITH EPILEPSY AND THEIR FAMILIES ARE LIVING BELOW THE POVERTY LINE³.

1 http://www.who.int/mental_health/neurology/epilepsy/en

2 <http://www.epilepsy.org.au/resources/for-media/facts-statistics-about-epilepsy>

3 http://www.epilepsyaustralia.net/Current_Issues/Reports/Reports.aspx

AFFILIATION

University of Melbourne
St Vincent's Hospital

TEAM MEMBERS

Dr Alan Lai
Mr Tim Nelson
Associate Professor
Chris Williams
Professor Anthony Burkitt
Associate Professor
David Grayden
Professor Peter Blamey
Dr Dean Freestone

GRANT TYPE

Development Grant

FUNDING AMOUNT

\$419,240 (2010-2012)

Everyone experiences what could be called 'life's little interruptions', but for people with epilepsy, this phrase takes on a whole new meaning.

As with many conditions, epilepsy ranges from mild to serious. Even for mild cases, however, epilepsy impacts a person's quality of life; in 1993, the World Development Report assessed the burden of living with epilepsy as being equivalent to having breast cancer for women or lung cancer for men.

The main characteristic of epilepsy is persistent seizures. Apart from the unpleasant experience itself, people with epilepsy are unable to predict when their seizures will happen. This makes it difficult for sufferers to lead a normal life, hinders their ability to attain a driver's license, and makes activities that the rest of us take for granted – like swimming, cooking or simply crossing a street – potentially dangerous.

Currently, epilepsy treatments include medications, brain surgery or other techniques. None of these, however, have shown to work for all people treated with these methods. And all entail their share of risks, complications and side effects.

Enter Professor Mark Cook who, together with his team at the University of Melbourne and St. Vincent's Hospital, have made significant advances in developing an epilepsy treatment that could be more effective than existing therapies and potentially help more people.

The concept underlying their research was to predict when a seizure was going to occur and then preventing it from actually happening.

Professor Cook explains, "Our research involved the design and construction of a system that could detect seizure activity and rapidly respond with a counter-stimulation to prevent the seizure progressing."

They had previously created a system that could do this, but to further validate their system, they needed to create a smaller, more portable system that could be used in different clinical settings. They achieved this through the support of their NHMRC Development Grant.

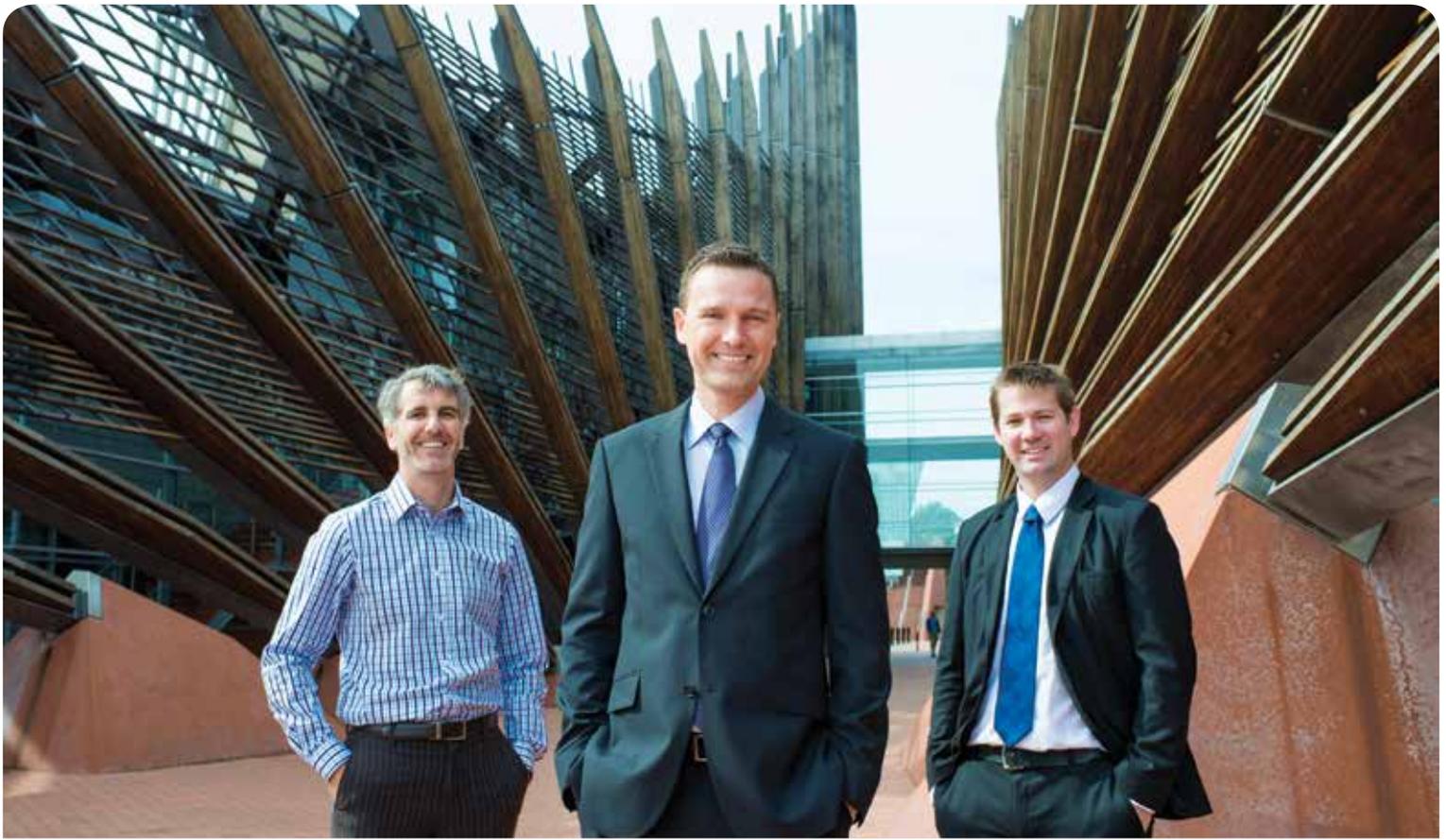
"We successfully built the system and have used it in a clinical setting to show that seizure activity can be effectively treated with direct brain stimulation," he says.

"We are now able to engage larger groups of collaborators to help study the best patterns of stimulation, and where to optimally place the electrodes."

Professor Cook and his team's ultimate goal is to create a portable device that can be implanted in people with epilepsy and prevent them from having seizures. For the more than 225,000 people in Australia who have epilepsy – and millions more worldwide – this could be revolutionary. They could live more active, independent lives and be free of epilepsy drugs. In short: it would give them their lives back.

NEXT STEPS:

Professor Cook and his colleagues are now working with other groups around the country and internationally to improve their brain stimulation techniques to suppress seizures more effectively. To do this, they may incorporate predictive algorithms and real-time seizure trajectory modelling.



L to R: Mr Steve Pratt, Associate Professor Owen Carter, Mr Brennen Mills.

RETHINKING JUNK FOOD: TRANSLATING KILOJOULES INTO WALKING TIME

ASSOCIATE PROFESSOR OWEN CARTER

KEY FACTS:

63% OF AUSTRALIAN ADULTS
AND 25% OF AUSTRALIAN
CHILDREN ARE CURRENTLY
OVERWEIGHT OR OBESE¹.

OVERWEIGHT PEOPLE ARE
TWICE AS LIKELY TO DEVELOP
HEART DISEASE, ARE THREE
TIMES MORE LIKELY TO
DEVELOP DIABETES AND
FIVE TIMES MORE LIKELY TO
DEVELOP BOWEL CANCER².

ENERGY-DENSE BUT NUTRIENT-
POOR FOODS (LIKE SOFT
DRINKS AND CHOCOLATES)
MAKE UP 36% OF AUSTRALIAN
ADULTS' AVERAGE DAILY
ENERGY INTAKE³.

1 <http://www.abs.gov.au/ausstats/abs@.nsf/Lookup/4364.0.55.001Chapter1002011-12>

2 Giovannucci E, Ascherio A, Rimm EB, Colditz GA, Stampfer MJ, Willett WC. Physical Activity, Obesity, and Risk for Colon Cancer and Adenoma in Men. *Ann Intern Med.* 1995;122(5):327-334.

3 Rangan AM, Schindeler S, Hector D, Gill TP, Webb KL. Consumption of 'extra' foods by Australian adults: types, quantities and contribution to energy and nutrient intakes. *European Journal of Clinical Nutrition.* 2009;63:865-871.

AFFILIATION

Edith Cowan University

TEAM MEMBERS

Mr Brennen Mills

Mr Steve Pratt

GRANT TYPE

Project Grant

FUNDING AMOUNT

\$77,758 (2011-2012)

Walking is the most popular recreational exercise in Australia. Other than improving your mental health and fitness, it also helps keep our body weight down. But how much walking is needed to compensate for all the little 'extras' we eat during the day?

Few people have the answer, according to Associate Professor Owen Carter.

"The average Australian gets about a third of his or her kilojoules from snacks throughout the day but doesn't do nearly enough exercise to burn this off," he says.

And Australian adults seem to be struggling to get the balance right: currently, over 60% are classified as overweight or obese.

Enter the Daily Intake Guide (DIG), a voluntary nutrition labelling system which lists the amount of energy, fats, sugars and sodium in a single serve of a product, plus the percentage of recommended daily intake each amount represents.

Over 7200 Australian packaged foods and drinks currently feature the DIG, which should be good news. However, in an audit of seven supermarkets, Associate Professor Carter and his team from Edith Cowan University noticed that in most cases junk foods only featured the 'energy' component of the DIG and didn't display fat, sugar and salt content.

"For instance, one 500ml energy drink had a single label '16% daily intake of energy', which doesn't sound too bad. It's only when you read the little nutrition panel on the back that you learn it also contains 93% of your daily intake of sugar, which is really bad."

Through focus groups and a large online survey, the team found Australians don't understand how to interpret the 'energy alone' DIG label.

"People looking at new foods with the DIG 'energy alone' label were more likely to base their judgement of its nutrition value on the pictures and packaging colours rather than the DIG energy alone label itself."

Associate Professor Carter and his team set about testing a simple label that described in practical terms how much energy a product contains. Their solution: translate the number of kilojoules in a product into the number of minutes it would take an average person to walk off those kilojoules. They termed their label 'equivalent walking time'.

"Our participants loved it. Although they were often shocked by the amount of exercise required to burn off many foods and drinks, they felt it told them exactly what they needed to know," he says.

"When people were presented with a can of soft drink and told it would take 40 minutes' walking to burn off, all of a sudden a bottle of water with no kilojoules looked much more attractive."

The team hope to one day see 'equivalent walking time' labels on junk foods to help people make more informed choices – and in turn, reduce the number of obese and overweight Australians.

NEXT STEPS:

Associate Professor Carter and his team are currently investigating whether 'equivalent walking time' labels would make a difference to purchasing and consumption behaviours. While they have the ambition of replicating their results overseas, they plan to use their current findings to advocate for greater government regulation of the nutrition labelling of junk foods.



Dr Noel Faux.

WRITTEN IN BLOOD: BIOMARKERS FOR ALZHEIMER'S DISEASE

DR NOEL FAUX

KEY FACTS:

DEMENTIA IS THE THIRD LEADING CAUSE OF DEATH IN AUSTRALIA AND CURRENTLY THERE IS NO CURE FOR THE DISEASE¹.

BIOLOGICAL INDICATORS OF ALZHEIMER'S DISEASE OCCUR UP TO 15 YEARS BEFORE CLINICAL SYMPTOMS SHOW².

BY 2060, SPENDING ON DEMENTIA IS SET TO OUTSTRIP THAT OF ANY OTHER HEALTH CONDITION AND WILL REPRESENT AROUND 11% OF HEALTH AND RESIDENTIAL AGED CARE SECTOR SPENDING³.

1,3 <https://fightdementia.org.au/about-dementia-and-memory-loss/statistics>

2 <http://www.mind.uci.edu/alzheimers-disease/articles-of-interest/behaviors-mindfulness-biomarkers-stem-cells-other-dementia/biomarkers-alzheimers-disease>

AFFILIATION

The Florey Department of Neuroscience and Mental Health – University of Melbourne

Australian Biomarker Imaging and Lifestyle (AIBL) study of ageing

CSIRO

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Professor Ralph Martins

Dr Justin Bedo

Dr Samantha Burnham

Dr James Doecke

Dr Simon Laws

Dr Kathryn Ellis

Dr Alan Rembach

AIBL research team

GRANT TYPE

Early Career Fellowship

FUNDING AMOUNT

\$292,639 (2009-2012)

Dementia. It's a collection of diseases that strike fear into the hearts of many, but we've barely scratched the surface to understanding it.

Our methods for staving off and treating dementia have been gaining in number very slowly despite intense international focus. But according to Dr Noel Faux from the Florey Institute of Neuroscience and Mental Health, one of the main issues with dementia is that by the time a clinical diagnosis is made, a huge amount of brain damage has already occurred. And the damage caused by this progressive disease is not reversible.

The race is on to develop an inexpensive test that will enable far earlier diagnoses of dementia. As with most diseases, the earlier the diagnosis the sooner treatment can begin and the better the chance of a good outcome. Making the test affordable is also important as it will allow greater numbers of people to access it and act on the results.

Dr Faux is in the thick of this race and is using data from the ongoing Australian Imaging Biomarker and Lifestyle Study (AIBL), which began in 2006, to support his research into the most common form of dementia, Alzheimer's disease.

"AIBL is a large scale population-based observational study with over 700 cognitively healthy participants, over 100 participants with mild cognitive impairment and over 200 participants with Alzheimer's disease," Dr Faux explains.

"Using blood-based measurements from AIBL, we were able to identify two useful signatures. One was able to distinguish people with Alzheimer's disease from cognitively healthy individuals. The other signature was able to distinguish people who have a biomarker identifiable through brain imaging from those who do not."

Analysing blood avoids the need for expensive imaging and cerebrospinal fluid analyses, which are currently used. Potential distress and pain are also minimised using this method.

Other researchers have adapted the research approach Dr Faux used to identify blood-based signatures for several other diseases and conditions such as schizophrenia and Parkinson's disease.

Looking back, it's apparent that Dr Faux was well-placed for his line of research with his background in computer science and PhD in bioinformatics.

"During my PhD studies, I became very interested in neuroscience and how I could apply my bioinformatics knowledge to help understand neurodegenerative diseases and, in the instance of Alzheimer's disease, how we could identify people at high risk of developing Alzheimer's disease before clinical symptoms show," he says.

With nearly 1 million Australians expected to be diagnosed with dementia by 2050, Dr Faux's research could not have come at a better time. Needless to say, the hopes of the nation hang on significant breakthroughs in dementia – and Dr Faux could be just the person to deliver one of them.

NEXT STEPS:

Having designed two useful blood biomarkers through his research, Dr Faux's next steps will be to validate these results with the AIBL cohort, international volunteers and those with other neurodegenerative diseases (to ensure disease specificity). From there, Dr Faux and his colleagues will develop a prototype test that will be administered in a healthcare setting.



L to R: Dr Glen Boyle, Dr Jacinta Simmons, Ms Jenny Johns, Dr Catherine Barnett, Dr Jason Cullen, Ms Natasa Korica, Professor Peter Parsons.

SOWING SEEDS OF HOPE FOR CANCER PATIENTS

PROFESSOR PETER PARSONS

KEY FACTS:

IN 2010, THE FIVE MOST COMMONLY DIAGNOSED CANCERS IN AUSTRALIA WERE PROSTATE CANCER, BOWEL CANCER, BREAST CANCER, MELANOMA AND LUNG CANCER¹.

AROUND 19,000 MORE PEOPLE DIE EACH YEAR FROM CANCER THAN 30 YEARS AGO, DUE MAINLY TO POPULATION GROWTH AND AGEING. HOWEVER, THE DEATH RATE HAS FALLEN BY MORE THAN 16%².

FOR 2006 – 2010, FIVE-YEAR RELATIVE SURVIVAL FOR ALL CANCERS COMBINED IN AUSTRALIA WAS 66.1%³.

1,3 <http://canceraustralia.gov.au/affected-cancer/what-cancer/cancer-australia-statistics>

2 <http://www.cancer.org.au/about-cancer/what-is-cancer/facts-and-figures.html>

AFFILIATION

QIMR Berghofer Medical Research Institute and QBiotech Ltd

TEAM MEMBERS**Chief Investigators**

Dr Glen Boyle

Dr Paul Reddell

Associates

Dr Victoria Gordon

Dr Craig Williams

Dr Andrei Savchenko

Dr Steven Ogbourne

NHMRC support

Dr Lidiya Maslovskaya

Ms Jenny Johns

Ms Carly Pierce

GRANT TYPE

Development Grant

FUNDING AMOUNT

\$260,669 (2011-2012)

Northern Queensland is known for many things: the Great Barrier Reef, sugarcane, cyclones. And soon, it may be able to add to that list: home of a new and significant cancer drug, EBC-46.

EBC-46 is derived from the seeds of the blushwood shrub, which is native to rainforests west of Cairns. First discovered by Queensland researchers Drs Victoria Gordon and Paul Reddell, the chemical has been put through its paces and found to destroy or significantly shrink tumours in large animals as well as in mouse models when injected directly into their tumours.

Professor Peter Parsons has been working with QBiotech Ltd (established by Drs Gordon and Reddell) on EBC-46 for the past seven years and has helped to reveal EBC-46's amazing potential.

Through his NHMRC Development Grant, Professor Parsons and his team at QIMR Berghofer Medical Research Institute developed a pre-clinical profile of EBC-46. This comprised a range of achievements, from determining the extent of the chemical's impact on cultured cells, its success at killing tumours in animals, to identifying safe dosage levels. They also managed to devise a method for isolating EBC-46 from the blushwood fruit seeds so that the chemical can be produced on a commercial scale.

As EBC-46 continued to obliterate tumours with few side effects, Professor Parsons and his team worked rapidly to try to understand how it was doing this.

"We found that EBC-46 is a potent activator of protein kinase C, an enzyme involved in numerous signalling pathways in normal and tumor cells," he says.

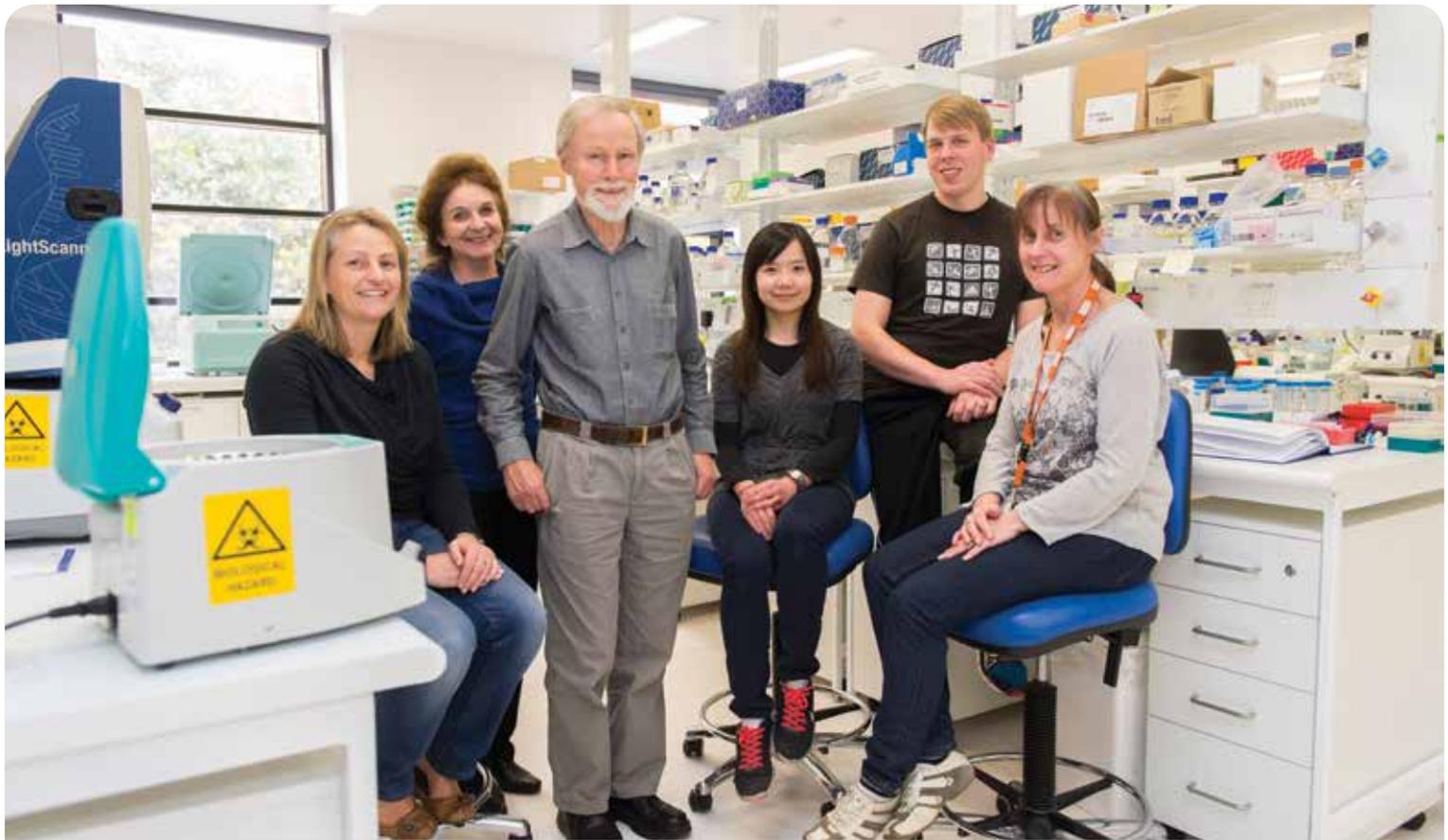
"Details of the anticancer mechanism are still being worked out, but the host response appears to be an important factor in the destruction of the tumor."

Hopes are high for this potential cancer drug, which is proving to be simple to administer, fast-acting and largely effective in animals. Professor Parsons believes that EBC-46 might be able to treat a range of tumour types (such as melanomas, head and neck cancers, and breast cancers) and avoid drug resistance, serving as a complement to surgery and radiation for the local treatment of tumours in humans.

If this happens, it'll put northern Queensland on the map for one more thing – saving cancer patients.

NEXT STEPS:

QBiotech, the major funding partner for this project, has received ethics approval to conduct a phase I clinical trial of EBC-46 in human cancers. From a research perspective, Professor Parsons and his team will next seek to identify the factors that are key to the efficacy of EBC-46. They may also expand to testing EBC-46 on internal tumours.



L to R: Ms Sarah Popp, Dr Charmaine Simeonovic, Professor Chris Parish, Dr Fui Jiun Choong, Mr Peter Hamilton, Ms Debra Brown.

THE SWEETEST THING: HALTING THE PROGRESS OF TYPE 1 DIABETES

PROFESSOR CHRISTOPHER PARISH

KEY FACTS:

TYPE 1 DIABETES AFFECTS OVER 122,000 AUSTRALIANS, WITH OVER 1800 AUSTRALIANS BEING DIAGNOSED EACH YEAR¹.

TYPE 1 DIABETES IS ONE OF THE MOST COMMON CHRONIC DISEASES IN CHILDREN, OCCURRING MORE FREQUENTLY THAN CANCER².

THE CURRENT TREATMENT OF TYPE 1 DIABETES INVOLVES THE FREQUENT INJECTION OF INSULIN WITH ASSOCIATED LIFE THREATENING RISKS OF HYPO- AND HYPER-GLYCAEMIA AND MANY LONG-TERM COMPLICATIONS³.

AFFILIATION

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TEAM MEMBERS

Dr Charmaine Simeonovic

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Dr Gerard Hoyne

Dr Andrew Ziolkowski

Dr Zuopeng Wu

Ms Sarah Popp

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Mr Peter Hamilton

Ms Debra Brown

GRANT TYPE

Diabetes Collaborative Research Grant

FUNDING AMOUNT

\$3,242,772 (2008-2013)

Most people find needles unpleasant and are relieved to be able to go months, even years, without needing to get an injection or blood test. But for those with type 1 diabetes, needles are a part of daily life, with some people requiring up to four injections a day to survive.

Scientists have long understood what happens in the bodies of people who have type 1 diabetes: the immune system attacks and destroys cells that produce insulin in the pancreas.

Without insulin, the body struggles to draw glucose from blood and switches to burning fatty acids instead, in a process called diabetic ketoacidosis. This can lead to deadly levels of ketone bodies in the blood with life-threatening consequences.

To avoid this complication and ensure their bodies are in balance, people with type 1 diabetes must test their blood glucose levels several times a day and inject themselves with insulin if levels fall too low.

To date, there is no method for preventing diabetes, but research led by Professor Chris Parish from the Australian National University has shed new light on how to protect insulin-producing cells – a finding which may lead to a new therapy that is an improvement on existing treatments.

“While insulin treatment keeps diabetics reasonably healthy, serious complications can develop in the long term. There is a critical need for better treatments for type 1 diabetes, which is where our research is headed.”

Like many scientific breakthroughs, it all began with a little luck.

Unexpectedly, Professor Parish and his team discovered that the pancreatic cells that produce insulin contain extraordinarily high levels of a special carbohydrate: heparan sulphate.

“This finding was incredible because heparan sulphate normally only exists outside cells, not within them. It was totally unexpected and required an explanation.”

Letting this discovery guide them, further studies revealed that heparan sulphate is essential for insulin-producing cell survival and a protein called heparanase, produced by the immune system, is responsible for destroying the heparan sulphate inside the cells, ultimately stopping the body from producing the insulin it so desperately needs.

This finding was the foundation for the development of a new treatment that is showing promise in stopping type 1 diabetes in its tracks.

The team injected an inhibitor into mice with early-stage diabetes to stop heparanase from attacking the insulin-producing cells. The inhibitor prevented the depletion of heparan sulphate inside the cells, and ultimately prevented the onset of type 1 diabetes.

“Collectively, our research has revealed a new understanding of how type 1 diabetes develops as well as identifying a new therapeutic strategy for preventing the progression of type 1 diabetes and associated complications.”

With plans already underway to develop their findings into a new treatment for humans, Professor Parish hopes that the treatment will allow diabetics to manage their disease more reliably and safely.

NEXT STEPS:

Professor Parish and his team are currently working on identifying the best heparanase-inhibiting drug for clinical development, and have already established a start-up biotech company, Beta Therapeutics, to help move things along.



L to R: Dr Yu Gao, Professor Lesley Barclay, Professor Sue Kildea.

THE MOTHER OF ALL PROBLEMS: IMPROVING MATERNAL AND INFANT HEALTH

PROFESSOR LESLEY BARCLAY

KEY FACTS:

THE NORTHERN TERRITORY HAS THE HIGHEST RATES OF INFANT AND YOUNG CHILD MORTALITY IN AUSTRALIA AT 9.2 DEATHS PER 1,000 LIVE BIRTHS¹.

THERE ARE ONLY 60 ABORIGINAL AND/OR TORRES STRAIT ISLANDER WORKING MIDWIVES IN AUSTRALIA².

THE PERCENTAGE OF ABORIGINAL AND TORRES STRAIT ISLANDER BABIES BORN WITH A LOW BIRTH WEIGHT IS 11% (2007-2011) COMPARED TO THE REST OF AUSTRALIA AT 4.8% (2009-2011)³.

1 <http://www.nhpa.gov.au/internet/nhpa/publishing.nsf/Content/Media-Release-Areas-with-highest-rates-of-child-deaths-and-pregnant-smokers-revealed>

2 Australian Institute of Health and Welfare. Nursing and Midwifery Workforce 2011. National Health Workforce Series No.2 Cat. no. 482102. [Online] 2011.

3 National Health Performance Authority. Healthy Communities: Child and maternal health in 2009 – 2014. Sydney : National Health Performance Authority, 2014.

AFFILIATION

Charles Darwin University and the University of Sydney

TEAM MEMBERS**Chief Investigators**

Professor Jonathan Carapetis
 Professor Sue Kildea
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 Dr Joanne Curry
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 Ms Molly Wardaguga

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Dr Robyn Thompson
 Dr Steve Guthridge
 Dr Suzanne Belton
 Dr Ngaire Brown
 Dr Jacqueline Boyle
 Associate Professor Terry Dunbar

PhD students

Ms Sarah Bar-Zeev
 Ms Malinda Steenkamp
 Ms Cath Josif

GRANT TYPE

Strategic Award

FUNDING AMOUNT

\$587,272 (2007-2012)

We all want our children to have the best possible start in life. But not all Australian mothers are afforded this opportunity equally.

While most Australian mothers in urban centres can access high quality maternity and infant care, those living in rural and remote Australia aren't so lucky. And Indigenous Australian mothers living in rural and remote communities are at a particular disadvantage.

Professor Lesley Barclay is an Australian researcher dedicated to improving this situation. She is a Professor and Head of the University Centre for Rural Health, University of Sydney, and began her career as a midwife. As a midwife, she saw that few women received evidence-based care and most care was delivered in ways that weren't respectful to women or were not family-centred.

"While recently much progress has been made in mainstream services, Aboriginal women and their infants still receive less than optimal services," Professor Barclay says.

"My career over the last two decades has used research to change systems and train others to continue this work into the future."

Professor Barclay and her team's research was carried out in the 'Top End' of the Northern Territory in two large remote communities and their regional centre. Their goal was to address problems identified by the local Aboriginal women, health practitioners and policymakers, and through earlier work they conducted.

Professor Barclay's team collected data through lengthy observations, dozens of interviews and the study of hundreds of mother-infant records. Analysis of the data led to researchers, health system leaders and communities working in partnership to implement evidence-based changes.

The NT health system has already implemented a number of improvements, most importantly the Midwifery Group

Practice (MGP) model. This model ensures continuity of care through a single midwife who provides pregnancy, birth and post-birth services.

Before the MGP model was implemented, local women were seen by numerous carers across pregnancy and birth, received inconsistent advice and didn't develop rapport with any individual caregiver. This was not the case following implementation of the MGP. Further, attempts were made to provide a well-educated child health nurse for the first year of the baby's life.

When the research team evaluated these changes, they found the MGP helped improve clinical effectiveness and quality of care for women – though attempts to provide skilled nurses for infants were unsuccessful. A cost analysis nearly two years later showed a saving of around \$700 per mother-infant (cohort).

While the care provided to infants living in those communities is still not satisfactory, the partnership between researchers and health systems leaders has made a huge difference.

Professor Barclay says, "Our evaluation data has confirmed that maternity care in the regional centre is now of a better quality. It is also more culturally informed and acceptable."

NEXT STEPS:

With further NHMRC funding support, Professor Barclay and her team are now working to develop The Australian Regional Birthing Index; an Australian version of a tool designed by Canadian researchers. This tool estimates the level of maternity service required for a given regional population based on its characteristics and isolation.

N|H|M|R|C