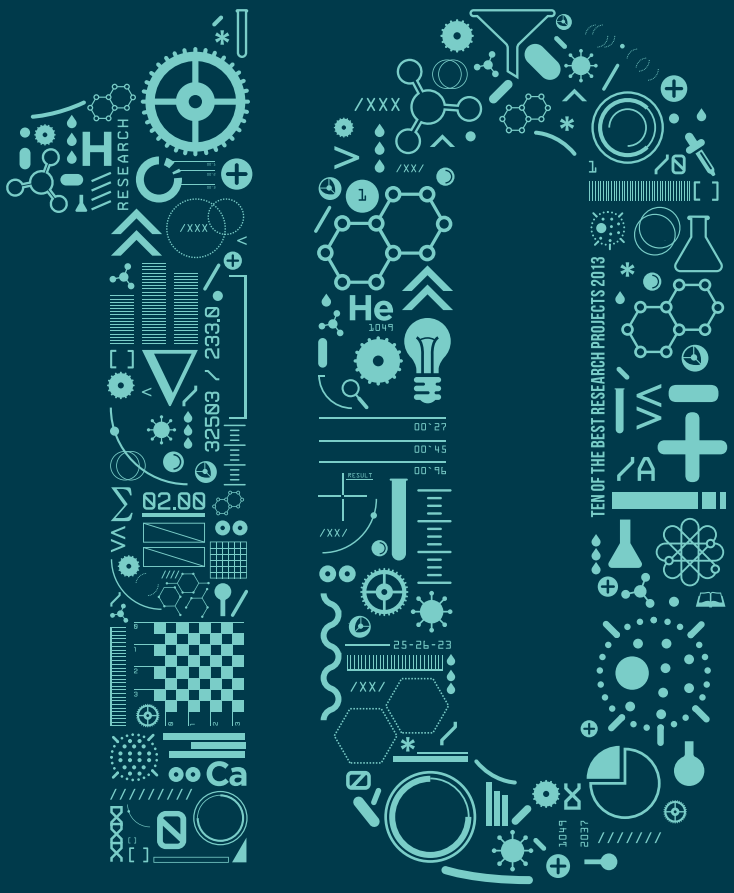
Australian Government

National Health and
Medical Research Council



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THE BEST RESEARCH PROJECTS 2013

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CONTENTS

THE HON PETER DUTTON MP

MINISTER FOR HEALTH

COMBINING INNOVATION AND EXCELLENCE FOR A HEALTHY NATION

In the words of Sir Winston Churchill, "Healthy citizens are the greatest asset any country can have."

This is a statement not lost on the outstanding health and medical researchers in Australia who have dedicated their lives to the relentless pursuit of better health, and better ways of treating illness.

In *Ten of the Best Research Projects 2013* the Australian Government and the National Health and Medical Research Council (NHMRC) recognise the outstanding achievements of just a few of Australia's finest scientists and researchers.

The breadth of challenging issues that these researchers have chosen to tackle is truly inspirational, and is set to have profound consequences for health, not just in Australia, but also around the world.

The featured research spans the development of new vaccines and treatments that could help save hundreds of millions of people from being infected with a range of tropical diseases, including malaria, to new approaches that will reduce side effects caused by chemotherapy.

This publication also shines a spotlight on improving immunisation strategies against rotavirus, which will help to narrow the health divide between Aboriginal and Torres Strait Islander people and non-Indigenous Australians.

Sometimes, solutions to health problems come from the most unlikely places. Parasitic worms, for instance, which cause disease and misery for many, are now offering hope for treating inflammation.

These are just a few examples of the innovative research projects from our leading scientists that will one day open the door to new and exciting approaches towards improving health here, and around the world.

Australian research continues to be a powerhouse of innovation. I am constantly reminded of the untiring commitment of so many people in health and medical research, all dedicated to improving our health and quality of life.

I am proud of our health and medical research innovators, and am pleased to be able to bring you this small glimpse into their exciting work.

PROFESSOR WARWICK ANDERSON AM

CHIEF EXECUTIVE OFFICER, NHMRC

PUSHING THE BOUNDARIES OF INNOVATION AND DISCOVERY

NHMRC proudly serves Australia by supporting our talented researchers in their endeavours to uncover new discoveries that help prevent, treat and cure ill health that continues to wreak such a personal toll on so many lives.

Each year, the work of our researchers adds new evidence to our growing knowledge and understanding of health, improving our ability to treat disease and to tackle conditions once considered untreatable.

History reflects well on the contribution of Australians to the great leap in health due to medical science in the last century. From the discovery of penicillin to the invention of spray-on skin, there seems to be no stopping Australian innovation.

Does the world's next big discovery lie within the pages of this book?

This year's Ten of the Best highlights outstanding dedication in the pursuit of an idea, innovation in seeking to expand the boundaries of knowledge and discovery, and novel ways for tackling ill health.

The research outcomes highlighted here represent just a small sample of the many outstanding lines of inquiry Australia's world class researchers are now focusing on.

This truly is an exciting time for health and medical research.

On behalf of the NHMRC, I thank all those researchers who have contributed to improving health both here in Australia, and around the world. NHMRC is proud to be able to continue to support our researchers as they make pivotal contributions to the huge advances now being made by the scientific community around the world.

Together, we will work to improve the health of our future generations.

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NEW INSIGHTS TO FIGHT A GLOBAL PROBLEM

L to R: (back row) Professor Geoff McFadden, Professor Graham Brown, Professor Louis Schofield
L to R: (front row) Dr Malcolm McConville, Dr Emanuela Handman, ***Professor Alan Cowman,*** *Professor Brendan Crabb*

Key Facts

- → WHO ESTIMATED THAT IN 2010, THERE WERE APPROXIMATELY 219 MILLION CASES OF MALARIA AND ABOUT 660,000 DEATHS.
- → WHO ESTIMATES THE WORLDWIDE PREVALENCE OF LEISHMANIASIS TO BE APPROXIMATELY 12 MILLION CASES, WITH 60,000 DEATHS ANNUALLY.

CHIEF INVESTIGATOR
Professor Alan Cowman

AFFILIATION
The Walter and Eliza Hall Institute

TEAM MEMBERS
See NHMRC Ten of the Best Honour Roll Page 28

GRANT TYPE
Program Grant

FUNDING AMOUNT
$13,738,897 (2006–2011)

Professor Alan Cowman, long fascinated by infectious diseases, has drawn together a team of some of Australia's leading scientists to tackle two globally significant infectious diseases: malaria and leishmaniasis.

While not major health problems in Australia, these diseases are devastating internationally, including for some of our near neighbours.

"We believe that Australia has a moral imperative to assist where we can to alleviate major health problems in developing countries in our region, and around the world," says Professor Cowman.

Malaria, which is caused by a microorganism (protists) transmitted by the mosquito, can produce symptoms such as headache, fever, shivering, joint pain, vomiting, jaundice, and convulsions.

Leishmaniasis, caused by protozoan parasites transmitted by the bite of some species of sand fly, can lead to skin sores, fever, and spleen and liver damage.

The goal of Professor Cowman and his team's research was to better understand the ways these parasites survive and prosper in humans, how the parasites cause the diseases, and the way our immune system fights the diseases.

From this knowledge, the team sought to develop new drugs and vaccines to improve prevention and treatment of the diseases.

By exploring the chemical makeup of the parasites that helps their survival, the team identified how the parasites infect cells, and how our cells could fight off infection and also remove the parasites after infection.

With these new insights, the team were able to understand the important chemical structures of the surface of the parasites. These findings are now providing promising new approaches: "We have unravelled the mystery of the metabolic pathways of the parasite to find proteins that might be susceptible targets for new drugs or vaccines."

To date, Professor Cowman and his team's most significant discovery is that the family of parasites that malaria belongs to evolved from photosynthetic algae which long ago lived inside animals such as corals, jellyfish, anemones and molluscs. About 450 million years ago, this group of algae transitioned to parasitism.

"Using this new insight into the origins of the malaria parasite, we hope to find new ways to kill the parasites based on their ancient plant-like ancestry."

→ *Next steps*

Following the successful development of new vaccines, particularly for malaria, human trials are now underway. Further to this, Professor Cowman and his team have identified numerous new proteins that may be susceptible to new therapies. Their search has also shown that several proteins currently favoured for drug development are not ideal. This will allow ongoing work to be better focused on more promising targets.

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MAKING CHEMOTHERAPY SAFER

L to R: Associate Professor Jean-Pierre Levesque, ***Associate Professor Ingrid Winkler***

Key Facts

- → IN 2013 ABOUT 125,000 AUSTRALIANS WILL BE DIAGNOSED WITH CANCER.
- → ABOUT ONE THIRD OF ALL CANCER PATIENTS SUFFER FROM AN INFECTION DURING OR SOON AFTER THEIR CHEMOTHERAPY BECAUSE OF IMMUNOSUPPRESSION ASSOCIATED WITH TREATMENT.
- → BY 2020, THIS NUMBER IS SET TO RISE TO ABOUT 150,000 PEOPLE.
- → IN AUSTRALIA ALONE, OVER 5000 CANCER PATIENTS ARE HOSPITALISED EACH YEAR DUE TO THE SIDE EFFECTS OF THEIR CHEMOTHERAPY TREATMENT, NOT THE UNDERLYING DISEASE.

CHIEF INVESTIGATOR
Associate Professor Ingrid Winkler

AFFILIATION
Mater Medical Research Institute, Brisbane

TEAM MEMBERS
See NHMRC Ten of the Best Honour Roll Page 28

GRANT TYPE
Project Grant

FUNDING AMOUNT
$434,883 (2009–2011)

Early in her career, Associate Professor Ingrid Winkler worked in hospitals helping cancer patients. It was during this time, as she treated the side effects of chemotherapy, that she became determined to find new ways to protect the body during cancer treatment.

"While cancer treatment fights the disease, it can also lead to side effects which range from inconvenient to life threatening," Associate Professor Winkler says.

In an effort to reduce some of the more damaging impacts of chemotherapy, Associate Professor Winkler and her team at the Mater Medical Research Institute in Brisbane looked for ways to protect the bone marrow, an essential part of our body's immune system and our ongoing fight against infection.

Haematopoietic stem cells (HSC) in adult bone marrow make all our blood and immune cells. But HSCs can be damaged by chemotherapy leading to blood and bone marrow failure.

This happens because chemotherapy kills rapidly growing cells, like cancer cells. But chemotherapy also kills normal, rapidly growing healthy cells in the bone marrow. As a result, the cancer patient's immune system is weakened, giving rise to potentially life-threatening infections.

Associate Professor Winkler and her team identified an adhesion molecule, E-selectin, in the bone marrow which regulates HSC behaviour, and in turn can protect these vital cells during chemotherapy.

Associate Professor Winkler explains, "We discovered the molecular switch that the body uses to put bone marrow cells to sleep and protected during chemotherapy, or awake and regenerating the blood and immune system following chemotherapy."

It is anticipated that inhibiting this molecule will help to minimise HSC damage during chemotherapy, and also enhance the success of bone marrow transplantation.

"This breakthrough is particularly important for patients undergoing repeated rounds of high-dose chemotherapy, as these patients are most at risk of treatment-induced immune suppression leading to infections and treatment-associated death."

→ *Next steps*

The exciting outcomes from this research may make chemotherapy treatment far less dangerous, reduce secondary infections, and help patients recover far more quickly – getting back to normal life at work, with their families and in their communities.

Next steps include exploring how treatment strategies can be optimised to accelerate recovery from chemotherapy.

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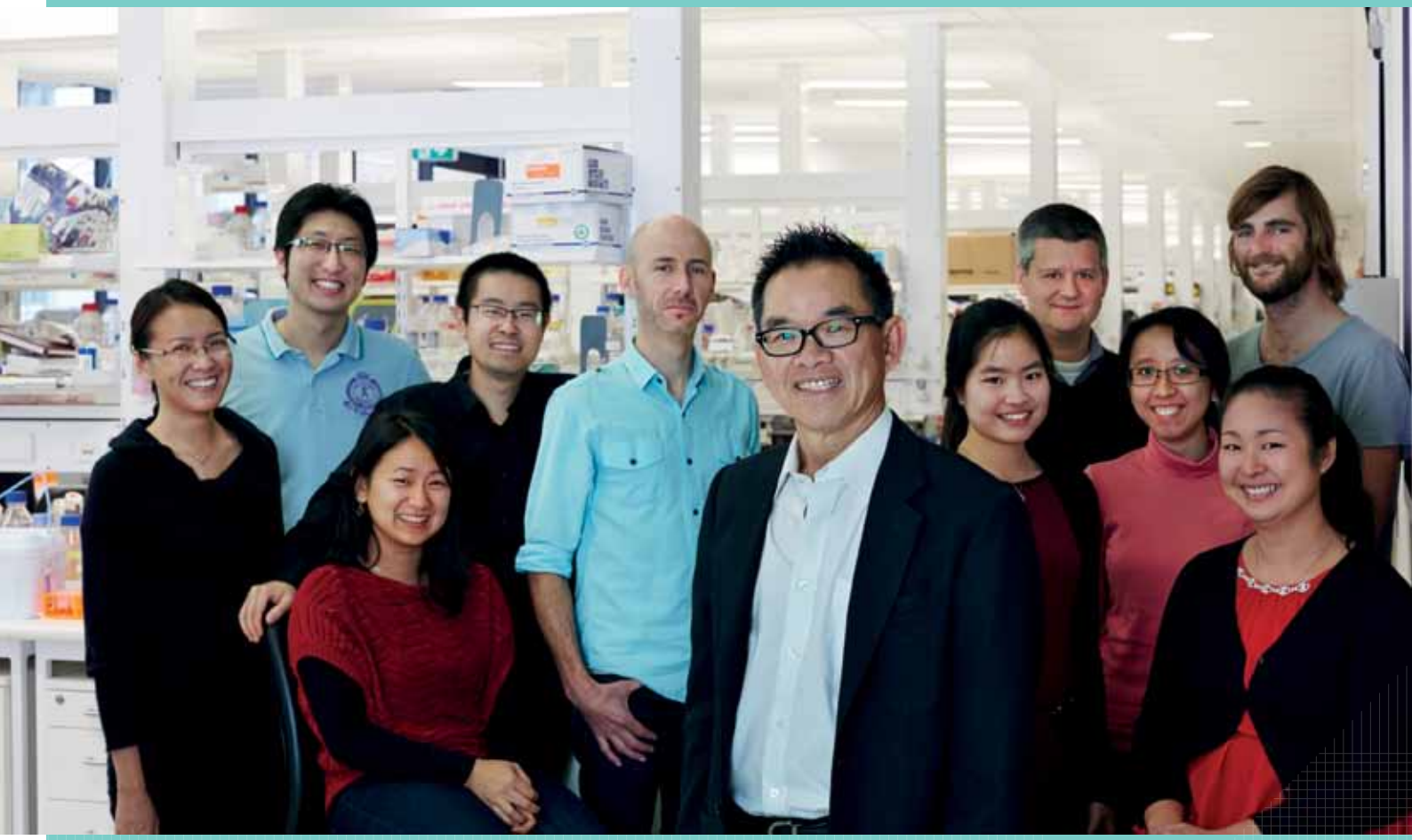
THE DEFENSIVE BRAIN



L to R: Dr Choo-Peng Goh, Dr Ley Hian Low, Ms Anh Doan, DrYijia Li, Dr Jason Howitt, ***Professor Seong-Seng Tan****, Ms Sophia Mah, Dr Ulrich Putz, Ms Yuh Lit Chow, Ms Michelle Tang, Mr Ulrich Sterzenbach*

Key Facts

- → THE BIGGEST RISK OF DYING FOR YOUNG MALES UNDER 35 YEARS OF AGE IS A TRAFFIC ACCIDENT OR VIOLENCE.
- → IN STROKE, INJURED AND HEALTHY NERVE CELLS DIE AT A RATE OF 2 MILLION CELLS PER MINUTE OVER SEVERAL DAYS.
- → OVER 22,000 AUSTRALIANS WERE ADMITTED TO HOSPITAL WITH A TRAUMATIC BRAIN INJURY IN 2004-05.

CHIEF INVESTIGATOR
Professor Seong-Seng Tan

AFFILIATION
The University of Melbourne

TEAM MEMBERS
See NHMRC Ten of the Best Honour Roll Page 28

GRANT TYPE
Project Grant

FUNDING AMOUNT
$836,225 (2009–2011)

While there is currently no effective treatment for brain injury, the brain is armed with some very impressive defence strategies.

The brain can defend itself against dying. Finding out how it does this and exploiting this for treatment is a serious unmet need. Since 1957, over 1000 drugs have been trialled but none have been effective.

When the brain is injured, such as in an accident or in stroke, the site of the injury is not recoverable due to damage from bleeding and swelling. However, what is not commonly known is that a large number of healthy cells surrounding the injury also die because of signals coming from damaged cells.

This wave of death occurs over a few days, providing a small window of opportunity for treatment.

When Professor Seong-Seng Tan and his team at the Florey Institute of Neuroscience and Mental Health looked into healthy brain cells for evidence of protective signals, they discovered a survival protein called Ndfip1.

Ndfip1 behaves like a bar-coding tool. By putting a mark on harmful proteins that are produced during injury, these proteins can be recognised by the waste disposal system in the brain cell and removed. It can also regulate other survival proteins.

"When we removed Ndfip1 from healthy brain cells, the cells suffered greater injuries compared to brain cells where the protein was not removed. This showed that Ndfip1 played an important role in cell survival," Professor Tan says.

Professor Tan looked at brain cells damaged following road trauma. Ndfip1 levels were massively increased in the cells showing the traumatised cells had initiated a response to try to protect against the injury.

Professor Tan and his team's discovery of a natural protein in the brain that can improve brain cell survival after injury and stroke is a world first.

"We have discovered how the brain protects itself by identifying the actual mechanisms involved. Understanding these mechanisms will help us design exciting new drug therapies that will hopefully help people in the first critical hours after stroke or brain injury."

"Even by halving the number of brain cells that normally die after injury, and preserving what is left behind after injury or stroke, we will provide the patient with a stronger foundation for recovery and less functional loss."

→ *Next steps*

Professor Tan and his team are now working on practical therapies to prevent brain cell death following injury, including a compound that will increase Ndfip1.

If methods can make bystander brain cells stronger following injury, there is a strong potential for reducing the number of brain cells that die following trauma or stroke.

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PREDICTING SIDE EFFECTS: MAKING CANCER THERAPY MORE TOLERABLE

L to R: Associate Professor Bruce Charles, Associate Professor Ross Norris, Dr Catherine Shannon, ***Dr John Duley****, Dr Gareth Price*

Key Facts

- → ABOUT 10% OF CANCER PATIENTS SUFFER ADVERSE SIDE EFFECTS FROM TAKING THE CHEMOTHERAPY DRUG FLUOROURACIL.
- → ABOUT 190,000 HOSPITAL ADMISSIONS IN AUSTRALIA EACH YEAR ARE MEDICATION-RELATED.
- → MEDICATION-RELATED HOSPITAL ADMISSIONS IN AUSTRALIA COST OUR ECONOMY $660 MILLION PER YEAR.

CHIEF INVESTIGATOR
Dr John Duley

AFFILIATION
University of Queensland

TEAM MEMBERS
See NHMRC Ten of the Best Honour Roll Page 28

GRANT TYPE
Project Grant

FUNDING AMOUNT
$225,526 (2009–2011)

For over 50 years, the chemotherapy drug fluorouracil has been commonly used to treat solid tumours of the abdomen, neck and breast. While this drug has been effective in treating cancer, adverse side effects from fluorouracil impact one in ten cancer patients.

Side effects vary from inflammation of the hands and feet, slowed growth of white blood cells that serve as our primary defence against infection, to life-threatening stomatitis, where the cells lining the mouth and gut are depleted and the patient begins bleeding internally. Tragically, about one in a hundred patients die from such side effects.

The result of cancer patients suffering adverse side effects from fluorouracil is that they may become hospitalised, often for long periods. In addition, their therapy is stopped, which risks a relapse of the cancer.

To control these unwanted side effects, what was needed was a way of predicting which patients might develop severe side effects, then adjusting the dose to balance the side effects against an adequate therapeutic dose. But this required an understanding of the mechanism behind the problem.

This was a challenge that Dr John Duley could not ignore.

Research had already shown that the side effects caused by fluorouracil in some patients were linked to two specific genes: "Analysing these genes seemed to hold the answer to predicting adverse events for fluorouracil," Dr Duley says. "But it was found that this predicted less than half of the cases of toxicity – which meant it was not possible to tell the difference between normal patients and false negatives."

After further testing, Dr Duley soon discovered a safe, simple and effective method for predicting side effects from fluorouracil. It involved the patient swallowing a small amount of a natural chemical, then observing the reaction that resulted.

"We feel we have finally opened up the possibility of predicting severe toxicity for fluorouracil. This will alleviate a lot of patient suffering, allowing for therapy to be tailored to each patient's needs."

→ *Next steps*

Dr Duley's method for testing currently takes several hours per patient. He says that the challenge now is to convert his chemical test into a genetic test that can be automated.

"Our next step is to find the gene that controls the predictive chemical response. A rapid genetic test would be far cheaper and would also mean that patients do not have to wait around to begin a personalised course of therapy."

*

PUTTING OUR IMMUNE SYSTEM BACK ON TRACK

L to R: Ms Melanie Le Page, Dr William Figgett, ***Professor Fabienne Mackay****, Mr Damien Saulep-Easton, Ms Pin Shie Quah, Dr Fabien Vincent, Ms Indzi Katik*

Key Facts

- → AUTOIMMUNE DISEASES AFFECT 5% OF AUSTRALIANS AND THEIR INCIDENCE IS ON THE RISE.
- → LUPUS AFFECTS ABOUT 17,000 AUSTRALIANS, MOSTLY WOMEN AGED BETWEEN 15 AND 45.
- → INDIGENOUS AUSTRALIANS ARE TWO TIMES MORE LIKELY TO SUFFER FROM SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) COMPARED TO THE GENERAL POPULATION.

CHIEF INVESTIGATOR
Professor Fabienne Mackay

AFFILIATION
Monash University

TEAM MEMBERS
See NHMRC Ten of the Best Honour Roll Page 28

GRANT TYPE
Research Fellowship

FUNDING AMOUNT
$618,722 (2007–2011)

The nagging question of why our immune system sometimes suddenly derails and attacks a person's tissues drove Professor Fabienne Mackay and her team to try to understand the complexities of the autoimmune disease Systemic Lupus Erythematosus (SLE).

The main role of our immune system is to fight foreign invaders such as bacteria, moulds and viruses. In autoimmune diseases, the immune system produces antibodies that instead of protecting the body against infection, can actually turn against our body's own healthy cells.

For some people with SLE, these rogue antibodies attack their kidneys, lungs, heart, blood vessels, and even the brain.

Our immune system has a built-in quality control process, allowing good immune cells to be retained while discarding defective immune cells. This constant regulation helps prevent autoimmune disease. However, it is not a perfect system and some potentially defective or harmful immune cells can populate our immune system.

Understanding the quality control process of B lymphocyte cells, including how outside influences affect that process, has been important in guiding the development of exciting new treatments.

"For many years we have been studying the immune system from within, assuming it is a 'closed-box' regulated from the inside by immune cells," says Professor Mackay. "We've been forgetting that immune functions are influenced by outside factors, such as microbes, diets, hormones, cancers, brain functions and the ageing process."

The research by Professor Mackay and her team has led to the discovery that BAFF, a naturally occurring protein in our body that plays an important role in B cell proliferation and function, is essential for B cell survival and maturation.

BAFF is necessary for maintaining the body's normal immunity. While inadequate levels of BAFF will fail to make B cells produce a sufficient quantity of antibodies, in excessive levels it causes the production of antibodies to go into overdrive, which can lead to SLE and other autoimmune diseases.

Professor Mackay's discovery that excessive BAFF levels drives SLE was a significant breakthrough. It led to the development of Belimumab, a BAFF inhibitor, which is the first new treatment for SLE in over 50 years.

Approved by the United States Food and Drug Administration in 2011, this therapy will soon be available in Australia. It's showing significant advantages over existing steroidal treatments, which are often poorly tolerated by patients and commonly the source of severe side effects.

→ *Next steps*

Following Professor Mackay and her team's success with Belimumab, they have turned their attention to unexplored areas of the immune system and other vital biological functions. They have recently initiated a project that examines the role of blood cancers in disabling vital immune processes. Further down the track, they hope to conduct research that addresses health problems in more innovative ways, such as by manipulating immunity.

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FROM FOE TO FRIEND: HOW WORMS WILL ONE DAY TREAT INFLAMMATION

L to R: Dr Cinzia Cantacessi, Mr Leon Tribolet, Ms Ivana Ferreira, Dr Annette Dougall, Dr Severine Navarro, ***Professor Alex Loukas****, Ms Cathy Sepherd, Dr Javier Sotillo, Dr Atik Susianto*

Key Facts

- → HOOKWORM DISEASE AFFECTS AROUND 700 MILLION PEOPLE IN DEVELOPING COUNTRIES AROUND THE WORLD.
- → INFLAMMATORY DISEASE AFFECTS 20% OF ALL AUSTRALIANS AND COSTS OUR ECONOMY ALMOST $8 BILLION ANNUALLY.
- → SCHISTOSOMIASIS AFFECTS MORE THAN 200 MILLION PEOPLE IN DEVELOPING COUNTRIES AND IS RESPONSIBLE FOR MORE THAN 200,000 DEATHS EVERY YEAR.

CHIEF INVESTIGATOR
Professor Alex Loukas

AFFILIATION
James Cook University

TEAM MEMBERS
See NHMRC Ten of the Best Honour Roll Page 29

GRANT TYPE
Research Fellowship

FUNDING AMOUNT
$559,560 (2007-2011)

The World Health Organization recognises 17 neglected tropical diseases. These diseases, which impact upon almost 2 billion people, particularly those living in the poorest communities throughout the developing world, have typically failed to attract attention and funding for vaccine research and development.

Parasitic blood-feeding worms, hookworms and schistosomes (trematode worms) cause two of these diseases, leading to serious infection and deaths in children and adults alike.

For over 20 years, Professor Alex Loukas has had a scientific interest in parasitic worms, particularly their ability to survive in their host.

"Parasitic worms secrete proteins that suppress their host's inflammatory response – one of the ways our body fights infection. This highlights the ability of these worms to manipulate our immune system for their own survival," he says.

This defence mechanism makes these worms a formidable foe in developing countries, but potential allies in developed countries such as Australia.

"Our research has highlighted the Jekyll and Hyde nature of hookworms – many people need to be rid of them, while others could benefit by acquiring them."

Understanding how evolution has armed these worms with their unique survival skills has allowed Professor Loukas and his team at James Cook University to explore two very different avenues for improving human health.

Professor Loukas' research has identified critical enzymes used by hookworms to help it digest its food, and a protein used by schistosomes that helps to form the outer coat of the parasite.

"These discoveries have allowed us to develop exciting new vaccines which will combat these parasites by blocking these two vital biological functions."

Not resting there, Professor Loukas and his team have also used these discoveries to look at inflammatory and autoimmune diseases such as asthma and inflammatory bowel disease.

"We could only have dreamed that our research might lead to vaccines with the potential to help hundreds of millions of the world's most needy," Professor Loukas says.

"The thought that this research might also lead to therapies that help millions in Australia and around the world who suffer from allergies and inflammatory disease has made the tireless efforts of our team truly worthwhile."

→ *Next steps*

Parasitic worms are promising to provide an enormous range of new treatments for inflammatory diseases, but more work needs to be done to unlock their full potential.

Professor Loukas and his team's vaccines against hookworms and schistosomes are currently undergoing early clinical trials in developing countries. Their new therapies for allergic and autoimmune conditions are in a pre-clinical phase.

*

TACKLING PREVENTABLE DISEASES: IMPROVING ROTAVIRUS VACCINES

Associate Professor Ross Andrews

Key Facts

- → SINCE INFANT AND CHILDHOOD VACCINATION WERE INTRODUCED IN AUSTRALIA FROM THE EARLY 1930S, CASES OF VACCINE-PREVENTABLE DISEASES HAVE DECLINED DRAMATICALLY.
- → CHILDREN UNDER FIVE YEARS OF AGE ARE AT GREATEST RISK OF ROTAVIRUS.
- → THE AUSTRALIAN GOVERNMENT NOW PROVIDES FREE VACCINATION FOR 16 VACCINE-PREVENTABLE DISEASES, INCLUDING ROTAVIRUS.
- → ROTAVIRUS IS THE MOST COMMON CAUSE OF SEVERE DIARRHOEAL DISEASE IN INFANTS AND YOUNG CHILDREN GLOBALLY.

CHIEF INVESTIGATOR
Associate Professor Ross Andrews

AFFILIATION
Menzies School of Health Research, Charles Darwin University

TEAM MEMBERS
See NHMRC Ten of the Best Honour Roll Page 30

GRANT TYPE
Project Grant

FUNDING AMOUNT
$465,860 (2009–2011)

It is important that vaccines, especially those provided to all children as part of Australia's National Immunisation Program, work as well in real-life as they do in clinical trials.

Some vaccines actually work better because of what is known as the "herd effect" where, because of fewer cases of disease in the community, even unvaccinated children or people not targeted for routine immunisation, are less likely to be exposed to the disease.

But for some vaccines, protection against disease can be lower than that seen in trials. Understanding why is important to improving vaccines, and the delivery of vaccines in the community.

Associate Professor Ross Andrews, and his group at the Menzies School of Medical Research in Darwin set out to assess the real-world effectiveness of rotavirus vaccination in the Northern Territory, a setting with historically very high rates of hospitalisation for rotavirus gastroenteritis especially among Aboriginal and Torres Strait Islander children.

Over a two-year period, nurses at Alice Springs Hospital and Royal Darwin Hospital identified children who were admitted to hospital with acute gastroenteritis, and children who were admitted with respiratory illnesses.

The immunisation status of all the children in the study was established using the Northern Territory Immunisation Register.

"We expected that the children admitted with gastroenteritis, especially those confirmed to have rotavirus infection, would be less likely to be vaccinated than the children admitted for respiratory illness. Our study confirmed this to be the case," Associate Professor Andrews says.

This work showed that vaccination for rotavirus reduced the risk of gastroenteritis by 50 to 60%.

"While we found rotavirus vaccination to be protective, levels of protection were lower than estimates from clinical trials and from other developed countries. Further work allowed us to explore possible reasons for this."

Protection from rotavirus vaccination was highest among young infants who are at the greatest risk of severe disease, but the protective effect started to decline among older children.

The decline in protection was most pronounced against rotavirus strains that were least like the vaccine strain, suggesting that rotavirus vaccines are more strongly protective against strains of rotavirus they're most similar to.

"We also found evidence that many Aboriginal children with rotavirus gastroenteritis are infected with other gut pathogens. Rotavirus vaccination appeared less protective among children who were also infected with other pathogens."

They demonstrated that rotavirus vaccination has a protective effect amongst Aboriginal children, but that the residual burden of rotavirus gastroenteritis specifically, and diarrhoeal disease in general, remains high.

"Understanding which factors influence immune responses to rotavirus vaccines is likely to bring us closer to improved immunisation strategies against this disease."

→ *Next steps*

Associate Professor Andrews and his team are particularly interested in identifying how existing rotavirus vaccines can be delivered more effectively for Aboriginal children. This work will involve measuring the immune responses of rotavirus vaccinated children.

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BEST RESULTS FOR KIDS WITH COCHLEAR IMPLANTS

L to R: Ms Colleen Holt, Professor Richard Dowell, ***Dr Karyn Galvin****, Ms Jennifer Holland*

Key Facts

- → IN 1978 THE FIRST COCHLEAR IMPLANT, PIONEERED BY GRAEME CLARK, WAS IMPLANTED.
- → COMPLETE OR PARTIAL DEAFNESS AFFECTS 10% OF THE AUSTRALIAN POPULATION.
- → EACH YEAR IN AUSTRALIA ABOUT 480 CHILDREN ARE BORN WITH MODERATE TO PROFOUND PERMANENT CHILDHOOD HEARING IMPAIRMENT IN ONE OR BOTH EARS.

CHIEF INVESTIGATOR
Dr Karyn Galvin

AFFILIATION
University of Melbourne

TEAM MEMBERS
See NHMRC Ten of the Best Honour Roll Page 30

GRANT TYPE
Project Grant

FUNDING AMOUNT
$452,844 (2007-2011)

For over three decades, cochlear implants have helped many deaf people hear for the first time. While it is well known that for people with normal hearing, binaural hearing is generally superior to monaural, Dr Karyn Galvin and her team at the University of Melbourne sought to discover the extent of the benefits of binaural hearing for deaf people.

In particular, they wanted to determine the benefits for children, who for many years typically received a single cochlear implant.

"We wanted to help children with implants participate as fully as possible in the classroom and socially, to give them the same opportunities as children with normal hearing," Dr Galvin says.

What she and her team discovered was that children with single implants struggle to communicate in difficult listening situations, such as high levels of background noise, or fast moving group conversations.

Dr Galvin explains "A single implant will enable a child to hear, but bilateral implants can give the gift of music and significantly improve their ability to interact socially."

"For the majority of children, their ability to correctly identify the source of a sound arriving from left versus the right was not much better than 50-50 using only one implant. This improves to greater than 90% correct when using two implants."

Given the extent of surgery required to fit bilateral cochlear implants in a young child, Dr Galvin and her team knew it was important to understand the clinical implications of such surgery.

One of their early findings was that children who received a bilateral implant from the outset adapted much faster to having two implants than children who experienced a delay between receiving their implants.

Further, they found that children who experienced a lag between receiving their two implants took longer to achieve the same level of hearing as a child who had received bilateral implants in the one surgery.

"It was also clear how important it is for families and children to receive adequate support during the adaptation process when a second implant is received some time after the first – rejection of the second device is a possibility even amongst young children," Dr Galvin says.

→ *Next steps*

Dr Galvin and her team's research findings have already had a significant impact on clinical practice at the Royal Victorian Eye and Ear Hospital Cochlear Implant Clinic, where bilateral cochlear implants are now routinely offered to young children.

They are now continuing to investigate the wider benefits of bilateral implantation for children and young adults with childhood deafness. She is also considering the factors which influence outcomes, in order to ensure that parents can make informed choices and that clinical management can be tailored for individual children.

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IT'S NOT CHILD'S PLAY: TAKING INFLUENZA SERIOUSLY

L to R: Professor Robert Booy, ***Professor Elizabeth Elliott****, Dr Gulam Khandaker, Dr Nicholas Wood*

Key Facts

- → THERE ARE AROUND 90 MILLION NEW CASES OF INFLUENZA ANNUALLY AMONGST CHILDREN UNDER THE AGE OF 5, WITH BETWEEN 28,000 TO 111,500 DEATHS IN THIS AGE GROUP.
- → EACH YEAR, INFLUENZA COSTS THE AUSTRALIAN HEALTHCARE SYSTEM ABOUT $115 MILLION.
- → 18,400 HOSPITALISATIONS ARE ATTRIBUTABLE TO INFLUENZA IN AUSTRALIA EACH YEAR.

CHIEF INVESTIGATOR
Professor Elizabeth Elliott

AFFILIATION
University of Sydney

TEAM MEMBERS
See NHMRC Ten of the Best Honour Roll Page 30

GRANT TYPE
Urgent Call for Research on H1N1 Influenza 09 to inform public policy

FUNDING AMOUNT
$120,883 (2009-2011)

During the outbreak of the 2009 swine flu (or H1N1 Influenza) pandemic, health officials around the world were scrambling to get a clear picture of the scale of the problem and how quickly it was escalating.

At the time H1N1 hit Australia's shores, Professor Elizabeth Elliott and her team of researchers at the University of Sydney had been studying influenza for several years. Through the turmoil, they saw an opportunity and called on surveillance technology to learn more.

They turned to Paediatric Active Enhanced Disease Surveillance or PAEDS; a surveillance system they established in 2007, currently based in five hospitals across the country. It allows for the collection and analysis of data on children hospitalised with influenza and other vaccine-preventable diseases.

Using PAEDS, Professor Elliott and her team collected clinical data and biological specimens from children hospitalised with laboratory-confirmed influenza from four Australian states during the H1N1 pandemic. In analysing this data, they discovered how the disease impacted on the community and hospitals, how it was managed, and what the outcomes were for children.

"Infection with various strains of influenza is one of the most common causes of hospital admission for young children," Professor Elliott says. "Children are an important reservoir of the flu virus, which they can spread throughout the community."

Professor Elliott and her team looked at 601 patients under the age of 15 with influenza, mostly with H1N1.

The team's findings were two-fold: even in the midst of the H1N1 pandemic, influenza vaccination rates amongst children were low; and that rates of complications from influenza, including neurological complications and pneumonia, were high; even in otherwise healthy children.

The team was able to show the extent and severity of neurological complications, underuse of flu vaccination and antiviral drugs, delay in diagnosis, inappropriate use of laboratory tests and overuse of antibiotics. They also found significant rates of acquisition of flu in hospital and that clinicians often failed to recognise and investigate the diverse clinical signs of flu, particularly in infants.

"Higher vaccination rates could do much to decrease the infection, admission and severe complication rates from influenza," says Professor Elliott says. "Our findings also indicated that antiviral agents should be used more readily in young children with proven influenza."

"Our study changed the perception that influenza is a mild illness in children. Influenza in children is serious, and needs to be treated seriously."

→ *Next steps*

Since completing this project and demonstrating the value of PAEDS as a tool for helping researchers and clinicians understand the pattern and nature of infectious diseases in our community, Professor Elliott has received additional support to expand the PAEDS network to include another hospital, additional clinicians and new studies. She is currently seeking to expand PAEDS to all states and territories aiming for national coverage.

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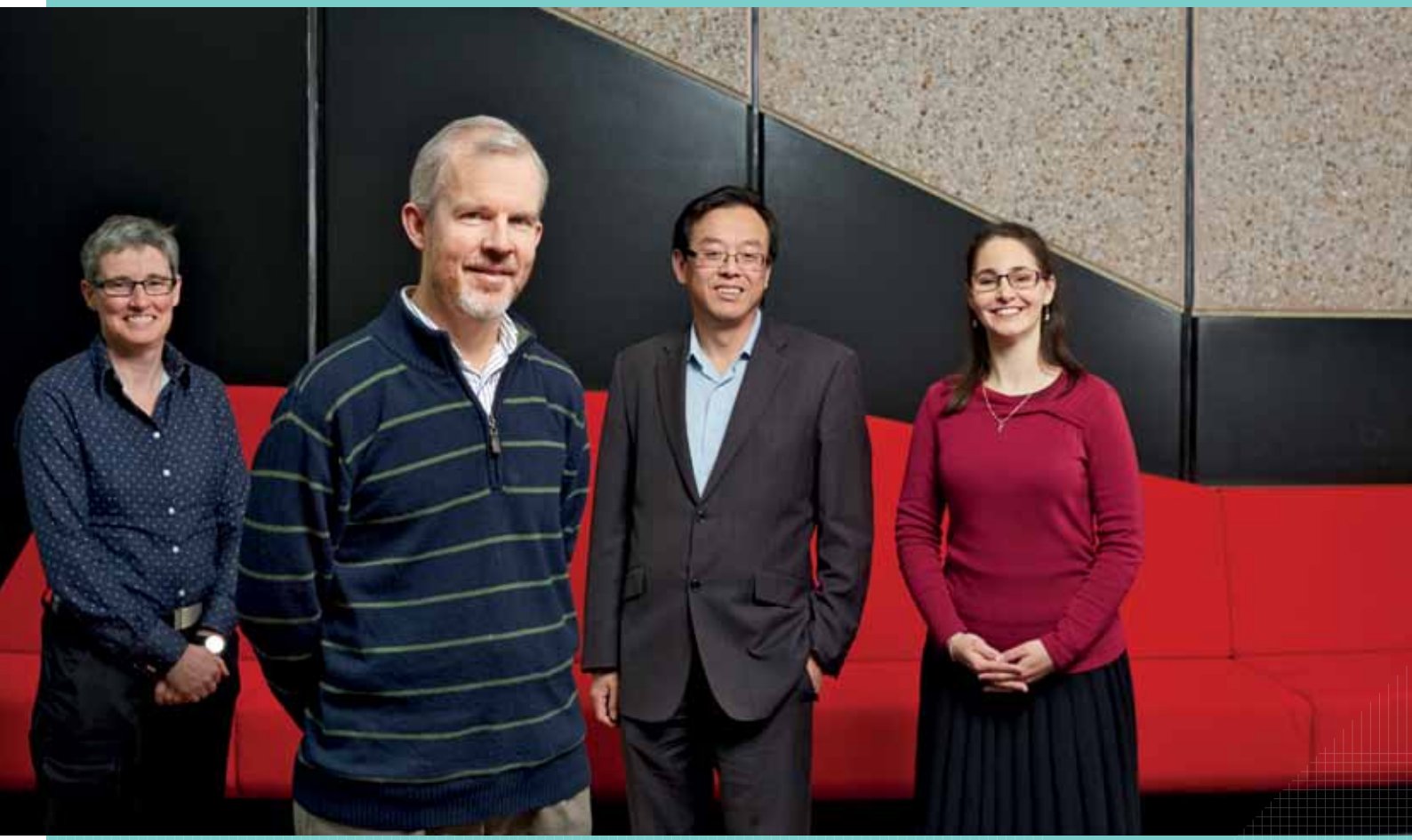
NEW OPTIONS TO DELAY JOINT REPLACEMENT



L to R: Associate Professor Tania Winzenberg, ***Professor Graeme Jones****, Associate Professor Changhai Ding, Dr Laura Laslett*

Key Facts

- → ARTHRITIS AND OTHER MUSCULOSKELETAL CONDITIONS AFFECT ABOUT 6.3 MILLION AUSTRALIANS.
- → OSTEOARTHRITIS CAN SEVERELY DAMAGE JOINTS, PARTICULARLY THE KNEES AND HIP.
- → OSTEOARTHRITIS IS THE MOST COMMON FORM OF ARTHRITIS, AND ESTIMATED TO AFFECT OVER A MILLION AUSTRALIANS OVER THE AGE OF 55.

CHIEF INVESTIGATOR
Professor Graeme Jones

AFFILIATION
University of Tasmania

TEAM MEMBERS
See NHMRC Ten of the Best Honour Roll Page 30

GRANT TYPE
Practitioner Fellowship

FUNDING AMOUNT
$360,313 (2007–2011)

When Professor Graeme Jones was starting out in Rheumatology training in the early 1990s, very little was known about what caused osteoarthritis and how best to treat it.

At that time, few treatments were available, and those that were being used had significant potential for adverse side effects.

Osteoarthritis, the most common form of arthritis, causes pain, reduced mobility and loss of independence for more than a million Australians, mostly over the age of 55, and it often leads to expensive hip and knee replacement surgery.

Professor Jones and his team at the University of Tasmania wanted to make a real difference to the quality of life for these patients, and to delay the onset of this disease in our ageing population.

"The last ten years have seen tremendous improvements in rheumatoid arthritis therapy and my desire was to match this progress for patients suffering osteoarthritis," Professor Jones says.

The first step was to understand the disease by seeing how it developed, and exciting new advances in medical imaging made this possible.

"Through dual-energy X-ray absorptiometry we were able to examine bone density, and through magnetic resonance imaging we could see what was actually happening to the internal structures of the joint in osteoarthritis sufferers, long before these arthritic changes could possibly be detected using existing X-ray technology."

This was a real advantage for Professor Jones in developing a better understanding of the early factors that lead to the disease, and made it possible for the team to start designing trials of innovative new therapies that would target these early changes.

"Until relatively recently, we simply didn't have sophisticated enough tools to accurately measure this disease. Our almost total reliance on X-rays set the field back rather than encouraged progress. New medical imaging changed all this."

By watching and precisely describing the early changes occurring in knee joint osteoarthritis and then specifically targeting these changes, Professor Jones has been able to design new early preventative interventions that will improve symptoms and slow progress of this disease.

Some treatments showing great potential include new bone agents to reduce bone swelling, vitamin D therapy for cartilage repair, gastric banding surgery to preserve joint structures in patients who are overweight or obese, statin agents to reduce inflammation and improve cartilage regeneration, and fish oil supplements to improve patients' symptoms and reduce cartilage damage.

Professor Jones says, "We hope these new options will delay the need for joint replacement surgery, lessen the burden on our health system and allow much more functional and healthy joint ageing."

→ *Next steps*

Professor Jones and his team will continue to research the effectiveness of these treatments to assess whether therapy both alleviates the symptoms and improves bone and joint structures in osteoarthritis patients, with a view to expanding the list of effective therapies.

*

TEN OF THE BEST RESEARCH PROJECTS 2013: HONOUR ROLL

NEW INSIGHTS TO FIGHT A GLOBAL PROBLEM

Professor Alan Cowman

Dr Emanuela Handman

Professor Terry Speed

Dr Malcolm McConville

Professor Brendan Crabb

Professor Graham Brown

Professor Geoff McFadden

MAKING CHEMOTHERAPY SAFER

Associate Professor Ingrid Winkler

Ms Valerie Barbier

Associate Professor Jean-Pierre Levesque

Mrs Bianca Nowlan

THE DEFENSIVE BRAIN

Professor Seong-Seng Tan

Dr Jason Howitt

Dr Ulrich Putz

Dr Ley-Hian Low

Dr Choo-Peng Goh

Dr Yijia Li

Dr John Silke

Ms Ahn Doan

Ms Yuh Lit Chow

Mr Ulrich Sterzenbach

Ms Sophia Mah

Ms Michelle Tang

PREDICTING SIDE EFFECTS: MAKING CANCER THERAPY MORE TOLERABLE

Dr John Duley

Dr Catherine Shannon

Associate Professor Ross Norris

Associate Professor Bruce Charles

Associate Professor Les Sheffield

Professor Peter George

Dr Marion Harris

Dr Ming Ni

Ms Rani George

Dr Gareth Price

Prof Deon Venter

Dr Scott Mead

Dr Andre van Kuilenburg

Scientists and clinicians in Brisbane, Melbourne, Christchurch, and Amsterdam.

In Brisbane, the research support by both Mater Health and The University of Queensland has been invaluable.

PUTTING OUR IMMUNE SYSTEM BACK ON TRACK

Professor Fabienne Mackay

Dr William Figgett

Professor Paul Hertzog

Dr Kirsten Fairfax

Mr Damien Easton-Saulep

Ms Indzi Katik

Ms Pin Shie Quah

Dr Fabien Vincent

Ms Melanie Le Page

Mr Michael Taylor

FROM FOE TO FRIEND: HOW WORMS WILL ONE DAY TREAT INFLAMMATION

Professor Alex Loukas

Dr Mark Pearson

Dr Paul Giacomin

Dr Cinzia Cantacess

Dr Severine Navarro

Dr Michael Smout

Dr Annette Dougall

Dr Javier Sotillo

Dr Atik Susianto

Dr Beata Urban Klein

Mr Darren Pickering

Ms Ivana Ferreira

Ms Cathy Sepherd

Mr Leon Tribolet

Ms Leisa McCann

Dr Mai Tran

Dr Najju Ranjit

Dr Soraya Gaze

Dr Henry McSorley

Dr Jason Mulvenna

The following principal investigators have played an instrumental role in the research program:

- Dr John Croese (Prince Charles Hospital, Brisbane, QLD)
- Professor Peter Hotez (Baylor College of Medicine, Houston, TX, USA)
- Associate Professor Jeff Bethony (George Washington University, Washington DC, USA)
- Professor Paul Brindley (George Washington University, Washington DC, USA)
- Professor Phil Felgner (University of California, Irvine, CA, USA)
- Professor Robin Gasser (University of Melbourne)
- Professor Banchob Sripa (Khon Kaen University, Thailand)
- Associate Professor Thewarach Laha (Khon Kaen University, Thailand)

The following chief investigators have played key roles in the research outcomes through past and current NHMRC program grants:

- Professor Michael Good
- Dr Christian Engwerda
- Professor James McCarthy
- Professor Istvan Toth
- Professor Don McManus
- Professor Denise Doolan

TEN OF THE BEST RESEARCH PROJECTS 2013: HONOUR ROLL

TACKLING PREVENTABLE DISEASES: IMPROVING ROTAVIRUS VACCINES

Associate Professor Ross Andrews

Dr Tom Snelling

Professor Jonathan Carapetis

Dr Carl Kirkwood

Professor Roy Robins-Browne

Ms Paula Binks

This success of this study was built upon a collaborative effort between researchers at:

- The Menzies School of Health Research
- The Murdoch Childrens Research Institute
- The University of Melbourne
- Staff of the Royal Darwin and Alice Springs Hospitals, and the Centre for Disease Control at the Northern Territory Department of Health and Families.

BEST RESULTS FOR KIDS WITH COCHLEAR IMPLANTS

Dr Karyn Galvin

Professor Richard Dowell

Associate Professor Robert Briggs

Dr Richard van Hoesel

Dr Mansze Mok

Ms Kathryn Hughes

Ms Jennifer Holland

Ms Colleen Holt

Ms Meredith Prain

Ms Leonie Fewster

Ms Katie Hill

Ms Alexandra Tomov

IT'S NOT CHILD'S PLAY: TAKING INFLUENZA SERIOUSLY

Professor Elizabeth Elliott

Professor Robert Booy

Professor Peter McIntyre

Associate Professor Yvonne Zurynski

Dr Gulam Khandaker

Dr Jim Buttery

Dr Peter Richmond

Professor Michael Gold

Dr Helen Marshall

Dr Jennifer Royle

Dr Nicholas Wood

Clinicians and research staff contributing to the Paediatric Active Enhanced Disease Surveillance system, the Australian Paediatric Surveillance Unit and the National Centre for Immunisation Research and Surveillance.

NEW OPTIONS TO DELAY JOINT REPLACEMENT

Professor Graeme Jones

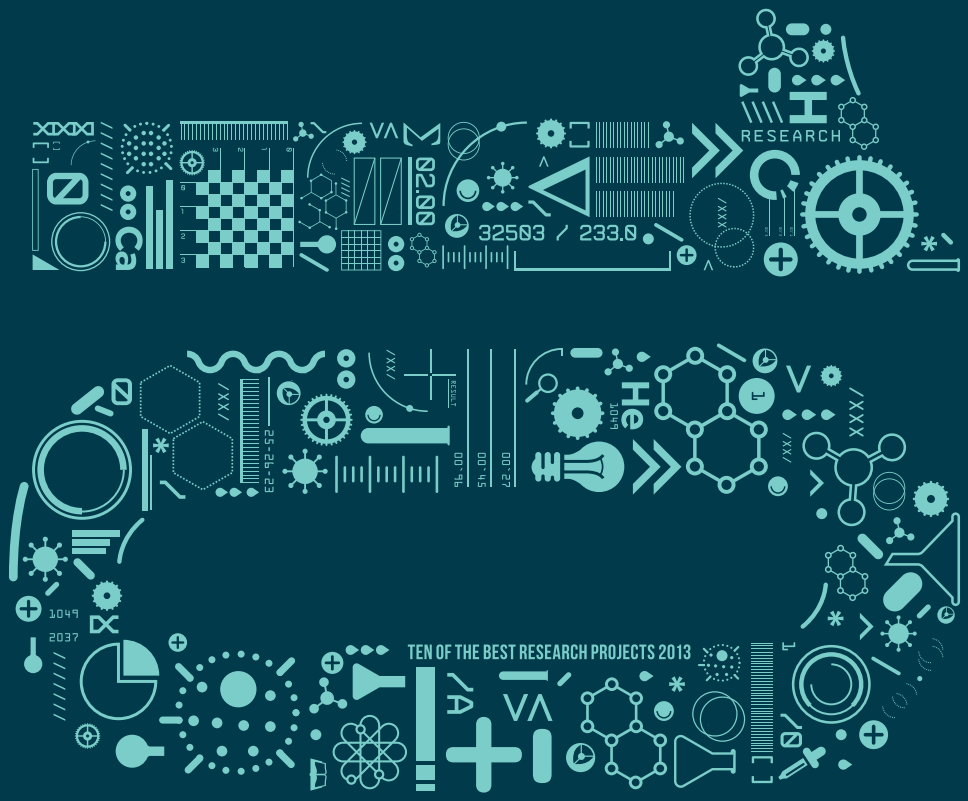
Professor Flavia Cicuttini

Associate Professor Changhai Ding

Associate Professor Tania Winzenberg

Dr Dawn Aitken

Dr Laura Laslett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