10 OF THE BEST

NHMRC Research Projects 2016

showcasing significant projects that support the improvement of human health

WORKING TO BUILD A HEALTHY AUSTRALIA
CONTENTS

Saving lives—one vaccine at a time 2
Forty years of mental health research 4
Achieving in the classroom 7
Zinc on the brain for healthy ageing 8
New technology to spot skin cancer sooner 10
Linking the data to close the gap in heart health 12
Adding immune T cells to the mix 14
Protecting premature babies from kidney disease 16
Precision medicine for blood cancer 18
Starving bacteria—beating antibiotic resistance 20

Copyright
© Commonwealth of Australia 2018

All material presented in this publication is provided under a Creative Commons Attribution 4.0 International licence (www.creativecommons.org.au), with the exception of the Commonwealth Coat of Arms, NHMRC logo and any content identified as being owned by third parties. The details of the relevant licence conditions are available on the Creative Commons website (www.creativecommons.org.au), as is the full legal code for the CC BY 4.0 International licence.

Attribution
Creative Commons Attribution 4.0 International Licence is a standard form licence agreement that allows you to copy, distribute, transmit and adapt this publication provided that you attribute the work. The NHMRC's preference is that you attribute this publication (and any material sourced from it) using the following wording: Source: National Health and Medical Research Council.

Use of images
Unless otherwise stated, all images (including background images, icons and illustrations) are copyrighted by their original owners.

Contact us
To obtain information regarding NHMRC publications or submit a copyright request, contact:

E: nhmrc.publications@nhmrc.gov.au
P: (02) 6217 9000
Research is critical to understand, prevent, detect and treat disease. NHMRC, as the Australian Government’s lead agency for the support of health and medical research, plays a key role in funding research across the spectrum of national health needs. In the last financial year, NHMRC distributed more than 1,000 grants worth over $800 million—all with the ultimate goal of improving the length and quality of human lives.

Here we showcase ten research projects which illustrate the extraordinary quality and diversity of work being undertaken with NHMRC support—combating antibiotic resistance, improving memory function in ageing, increasing vaccination rates, reducing the risk of infection from cancer treatment, understanding the origins of mental illness, and more.

One of NHMRC’s strengths is its capacity to fund a broad range of research initiatives put forward by individual researchers and teams in universities, medical research institutes, hospitals and other public research institutions. Investigator-initiated research is the origin of many of Australia’s greatest contributions to human health, from lithium for the treatment of bipolar disorder to the human papilloma virus vaccine and a new drug for chronic lymphocytic leukaemia. Given the quality and passion of our health and medical research sector, we can be confident the research and researchers we support today will contribute to the major advances of the future.

On behalf of NHMRC, I hope you enjoy learning about these groundbreaking projects led by some of Australia’s most brilliant researchers.

Professor Anne Kelso AO
CEO, NHMRC

---

1 See page 9 of annual report 2016–2017
SAVING LIVES—ONE VACCINE AT A TIME

IMMUNISATION PRACTICE AND POLICY DEVELOPMENT IN AUSTRALIA: RESPONDING TO URGENT PRIORITIES IN PREVENTION OF ENDEMIC AND EPIDEMIC INFECTIOUS DISEASES IN CHILDREN, ADOLESCENTS AND PREGNANT WOMEN

Professor Helen Marshall

‘There has been a 73 per cent reduction in children hospitalised from severe chicken pox infection since the introduction of the (varicella) vaccine to the National Immunisation Program in Australia in 2005.’

Immunisation is second only to clean water in having the highest impact on improving public health—but deaths still occur from vaccine-preventable diseases. Professor Helen Marshall and her team are at the forefront of research into understanding and ensuring vaccine safety and effectiveness and identifying immunisation barriers to increase vaccine uptake.

Professor Marshall is an international leader in vaccinology and the public health impacts of infectious diseases. Her research is aimed at providing evidence to improve immunisation practice and influence immunisation policy nationally and internationally.

‘I was inspired by the idea that in public health you can improve the health of a whole population by making good policy decisions based on sound evidence,’ Professor Marshall said.

Professor Marshall’s research has been crucial for improving immunisation rates.

‘We improved uptake of vaccines in pregnancy by implementing a midwife delivered immunisation program, following our research findings showing the need for increased awareness, health care provider recommendation and incorporation of immunisation into standard pregnancy care.’

Her research investigates the safety and effectiveness of new vaccines, determining how health conditions can affect vaccine efficacy and how effective vaccines are, following introduction into a population program. Essential to Professor Marshall is working with the community to understand acceptance of new vaccines and any barriers to uptake. Professor Marshall’s research has led to a myriad of achievements, including:

- Providing evidence to inform optimal immunisation schedules for Australian children
- Recommendation of a gender-neutral Human Papillomavirus vaccine program through community engagement
- Identifying disadvantage as the primary reason infants remain incompletely immunised rather than anti-vaccination attitudes and findings that women of culturally and linguistically diverse backgrounds have lower uptake of maternal vaccines.

‘Vaccines currently in use in many countries including Australia have been licensed based on our clinical trial findings and our research has identified factors leading to improved immunisation uptake in the population,’ she said.

‘Being granted two NHMRC Career Development Fellowships has provided me with the opportunity to develop a multidisciplinary academic program of research in vaccinology and infectious diseases to improve health outcomes for children.’

‘My vision is to eliminate serious vaccine preventable diseases in children by improving the effectiveness of vaccine programs for children, adolescents and pregnant women.’
Professor Jackob Najman and his team have been following the lives of mothers and their children for almost 40 years to identify the genetic and environmental contributions to mental illness. With over 250 publications to date, this study uses a large amount of previously and recently collected data to understand the genetic markers of vulnerability to mental disorders and how they interact with environmental factors, such as childhood trauma.

Still ongoing today, this study received its first NHMRC grant in 1981—following a sample of 4,000–5,000 mothers and their children from birth to 30 years of age.

‘With over 5,000 variables for each person in the study, the logistics of gathering and storing this large body of linked data has been challenging,’ Professor Najman said.

This study specifically examined the effects of environmental exposures—such as marital breakdown, poverty and childhood traumas like neglect and abuse—on the mental health of both the child and the mother over 30 years.

One of the key questions was why some children who experience high levels of trauma show little evidence of negative outcomes, while others who experience more minor adverse events experience negative mental and physical health outcomes.

‘The most common mental disorders include anxiety, depression and substance use, which together constitute a major disease burden and cost on the health system. The challenge is to track these conditions across generations and identify the contribution of genetic and environmental factors to their generational continuity,’ he explains.

‘Little is known about their causes and patterns of occurrence over the life span.’

‘This study has contributed to knowledge in such diverse areas as the impact of maternal mental health and family poverty on child health outcomes, the link between mental health and such physical health outcomes as obesity, and the development of cardiovascular disease and diabetes,’ Professor Najman concluded.

‘One in every ten mothers experience repeated episodes of major depression over their life course—on average, experiencing depression one in every six days of their lives.’

‘This is a population based study that has gathered a large amount of data on a large cohort. It is one of the few studies of its type internationally to track both mothers and their children for such a long time period.’

Continuing to follow their lives, the researchers are now turning to the next generation—the ‘children of the children’—looking at the generational transmission of mental illness. A major challenge is to distinguish the impact of grandparents from parents as they predict child health and mental health outcomes. Professor Najman’s team is also interested in the broader health inequalities that can continue from one generation to the next and how lifestyle and environmental factors through poverty can contribute to these inequalities.
‘Working memory—the ability to briefly hold and manipulate information in a mental headspace.’
Learning difficulties can have lifelong effects. Typically they are picked up late—only after the child has already experienced school failure and poor self-esteem. Preventive programs are therefore very attractive to schools and to parents. Professor Melissa Wake and her team set out to understand more about working memory and how current intervention strategies might improve academic achievements in young students at risk of learning difficulties. Working memory—the ability to briefly hold and manipulate information in a mental headspace—is a core element of executive functioning. Likened to the air traffic control system at a busy airport, executive functioning refers to the cognitive processes that enable children to successfully navigate their environment by filtering distractions, setting goals, prioritising and self-regulating.

Working memory deficits are often associated with academic under-achievement. Brain training programs targeting working memory have shown promise in some clinical groups. In response, many schools worldwide are routinely implementing commercially available programs, despite a lack of evidence that translating these programs into schools is beneficial to students.

The team tested the potential benefits of one of the most popular brain training programs as a population level prevention strategy for children with low working memory. ‘As the largest and only rigorous population trial, we expect its results to have a major impact,’ Professor Wake explained. ‘The Memory Maestros trial offered a working memory screen to all Grade 1 students in 44 schools, testing over 1,700 children in the process. We offered children in the lowest 25 per cent either a one-on-one 25-session computerised adaptive working memory intervention program or usual classroom teaching. Unfortunately, six month gains in short-term and working memory largely disappeared by one year and did not translate into academic benefits at two years.’

Not implementing such programs could save money and allow other more effective interventions to be tested, preventing children from needlessly missing valuable classroom time.

‘More than 90 per cent of children six to seven years of age with reading difficulties have low working memory.’

Professor Wake and her team now plan to link birth, school entry and later learning outcomes with genetic testing to help understand how genetic differences interact with cognitive and environmental factors to determine long-term learning and mental health related outcomes.
Impaired memory is one of the most debilitating features of ageing—with little understanding and treatment available. Associate Professor Paul Adlard and his team wanted to understand how zinc is critical for normal cognitive function and how restoring zinc levels in the brain could lead to improved memory as we age.

Associate Professor Adlard’s interest in neuroscience are motivated by the plasticity of the brain and the fact that losing brain function does not need to be an inevitable consequence of ageing or neurodegeneration.

‘The aged brain remains capable of performing with appropriate intervention. Simple behavioural modifications through to targeted pharmacological interventions can positively impact brain structure and biochemistry, resulting in improved cognition across age and also in disease.’

One of these targeted pharmacological interventions could be through the regulation of zinc—found to play a critical role in regulating communication between brain cells. The highest concentrations of zinc have been found among the brain cells in the hippocampus, one of the key centres of learning and memory in the brain.

‘If there is a deficit in zinc in the hippocampus—resulting from genetic factors, age or disease for example—then it precipitates a decline in cognitive function,’ Associate Professor Adlard said.

‘We tested whether we could pharmacologically restore these metal levels in key regions of the brain required for learning and memory, and subsequently, whether this translated into improved memory.’

Associate Professor Adlard’s main scientific discovery has been that zinc at the synapses—the signalling connection between brain cells—is vital for normal learning and memory. Critically, his team are investigating the use of a targeted therapeutic drug that restores zinc levels.

‘As this work progresses, it is anticipated that a prototype cognitive therapeutic approach will be developed for clinical translation with our commercial partner,’ he concluded.

‘In Australia, 15 per cent of the population are aged 65+, estimated to grow to 21 per cent (8.4 million) by 2050.’

1Australian Institute of Health and Welfare (2015), Australia’s welfare
‘The brain is not a static organ. I strongly believe that with sufficient knowledge and insight we can harness the brain’s complexity and plasticity to improve its function and promote healthy, happy ageing.’

Associate Professor Adlard is now looking at how to better target this intervention—finding at the optimal therapeutic approach to achieve prolonged cognitive benefit throughout life. This involves investigating the metal transporters and associated metal-dependent proteins that alter with age. It also involves large scale population approaches to determine whether we can predict cognitive decline by identifying specific variations in metal transporter proteins.
NEW TECHNOLOGY TO SPOT SKIN CANCER SOONER

DERMATOLOGY RESEARCH
—TELEDERMATOLOGY, MELANOMA, AND KERATINOCYTE CANCER

‘Based on my lifelong dedication to this field I am confident of making a significant contribution to the ultimate goal—no one should die of melanoma.’
The number of skin cancers, including melanomas, continues to rise in Australia. Detecting melanoma early is critical for survival—rates worsen as the thickness of the melanoma increases. Professor H. Peter Soyer is a world leader in dermatology and preventative measures for skin cancers.

Professor Soyer and his group at The University of Queensland have been researching and implementing a number of programs using the latest technologies to help detect skin cancers sooner.

Professor Soyer’s lifelong vision is to reduce the burden of skin cancer through early detection of melanoma and other skin cancers. One of his unique projects is the Skin Emergency Telemedicine Service (SETS) program. This service uses asynchronous Store-and-Forward Technology to provide rapid and accurate dermatological diagnosis and is critical in Queensland’s emergency departments.

‘This eliminates the days or weeks of waiting to obtain a specialist consultation in rural Queensland,’ Professor Soyer said.

Professor Soyer is also involved in several areas of pigmented naevus (moles) and melanoma research. One development is the use of total body 3D photography and dermoscopy—allowing monitoring of moles at high risk of developing into melanoma.

‘A major goal of our research are to understand the genetic basis of the clinical presentation of mole phenotypes and human pigmentation traits (skin, hair and eye colour) to provide better melanoma risk stratification,’ Professor Soyer explained.

‘Expertise in naevus and melanoma research has led to NHMRC funded Centre of Research Excellence for the Study of Naevi,’ he concluded.

Professor Soyer is now coordinating findings from current genomics, diagnostics and consumer-based research projects to identify individuals at high and ultra-high risk. These individuals will then be screened using a combination of 3D total body photography, consumer-driven mobile teledermoscopy, and minimally invasive microbiopsies for suspicious lesions.

‘It is the first program of research to test these technologies in the context of the Australian health care system, and will be used to drive evidence-based changes to clinical practice,’ he said.

Professor Soyer is also collaborating with the Queensland University of Technology and the University of Arizona, Tuscon, USA in developing mobile melanoma screening—using mobile phones and dermatoscopes—to detect melanoma earlier.

Professor Soyer and his team will continue their research program on Early Detection of Melanoma with a particular focus on integration into clinical networks. He will also lead the Brisbane Diamantina Health Partners Skin and Skin Cancer Theme, with the aim of promoting and enabling collaborative and translational research to generate clinical outcomes in this field.

‘Melanoma is the most common cancer for 15–39 year old Australians—with the highest ‘years of life lost’ of any cancer.'

1 Burnet NG, et al, 2005, Years of life lost (YLL) from cancer is an important measure of population burden—and should be considered when allocating research funds. Br J Cancer. 2005 Jan 31;92(2):241–5
Cardiovascular diseases occur at much higher rates in Aboriginal than non-Aboriginal Australians—contributing 19 per cent of the total health gap. Doctor Judith Katzenellenbogen and her team at the University of Western Australia set out to compare health outcomes of Aboriginal and non-Aboriginal Australians. They used linked health data to study Aboriginal heart disease, examining system issues that influence service delivery in order to build capacity in Aboriginal health.

Dr Katzenellenbogen arrived in WA in 2002, soon realising she was at an epicentre of data linkage capability in Australia. ‘I used the opportunity of a PhD to hone my linked data analytic skills—applying these methods to the burden of stroke,’ she said.

After completing her PhD, Dr Katzenellenbogen was given the opportunity by Professor Sandra Thompson to research disparities in Aboriginal heart disease. The project had a strong translation focus resulting in enduring research partnerships and producing practical initiatives to improve Aboriginal heart disease. ‘The analytic methods developed will also assist in monitoring progress towards closing the gap in cardiovascular burden.’

Dr Katzenellenbogen published a large body of work describing wide-ranging aspects of the epidemiology of heart diseases in Aboriginal Western Australians for the first time. The high cardiovascular Disease rates at young ages, co-existing chronic conditions, and logistical and cultural barriers to service access underlie the poorer outcomes seen among Aboriginal patients.

Dr Katzenellenbogen produced a comprehensive stakeholder report drawing on the experiences of Aboriginal and non-Aboriginal stakeholders, documenting successful initiatives and providing practical suggestions for improving cardiac outcomes. Workshops with policy makers and rural health professionals were held to build workforce capacity and promote system change to improve Aboriginal heart health. ‘We aim to use data to direct improvements in the health of Aboriginal people.’

‘I also used linked data to estimate the burden of Acquired Communication Disorders (ACD). For example aphasia, in Aboriginal stroke and traumatic brain injured patients in collaboration with an innovative team of speech pathology researchers. A culturally safe screening tool for ACD was developed and will ensure better identification of ACD in the future,’ she concluded.

‘The research suggested that a well-supported Aboriginal health workforce and better integration between services were the two most important health system improvements required to address heart health inequities.’
‘Chronic diseases account for 70 per cent of the life expectancy gap between Indigenous and non-Indigenous Australians.’

1 Australian Institute of Health and Welfare (AIHW), 2016. Australian Burden of Disease Study: Impact and causes of illness and death in Aboriginal and Torres Strait Islander people

Dr Katzenellenbogen, now a Heart Foundation Future Leader Fellow, continues to analyse the impact of the Closing the Gap initiatives in Aboriginal cardiovascular outcomes. She leads a multi-jurisdictional project to monitor the burden of rheumatic heart disease and is also engaged in a trial of culturally safe rehabilitation services for Aboriginal Western Australians with acquired brain injury.

THE UNIVERSITY OF WESTERN AUSTRALIA

TEAM MEMBERS
Professor Sandra Thompson
Professor Michael Hobbs
Professor Matthew Knuiman
Professor Dawn Bessarab
Ms Lyn Dimer
Dr Frank Sanfilippo
Ms Emma Haynes
Dr Tiew Hwa Teng
Dr Derrick Lopez
Dr John Woods

EARLY CAREER FELLOWSHIP
$307,946 2012

THE NEXT STEPS

Chronic diseases account for 70 per cent of the life expectancy gap between Indigenous and non-Indigenous Australians.”

1 Australian Institute of Health and Welfare (AIHW), 2016. Australian Burden of Disease Study: Impact and causes of illness and death in Aboriginal and Torres Strait Islander people

Photo: iStock
ADDING IMMUNE T CELLS TO THE MIX

GIVING BONE MARROW TRANSPLANT PATIENTS A FIGHTING CHANCE

Patient tailored immunity transplant for the prevention of viral infections post haemopoietic stem cell transplantation

Professor David Gottlieb

UNIVERSITY OF SYDNEY

PROJECT GRANT
$567,968
2011

TEAM MEMBERS
Dr Emily Blyth
Dr Kenneth Micklethwaite
Dr Leighton Clancy

Photo: iStock
‘In the future, new products being developed will target not only infections but also the patient’s own blood cancer to further increase the likelihood of a cancer cure with lower impact on patients’ lives.’

Professor David Gottlieb was determined to reduce the high risk of infection for his patients after watching them suffer from the debilitating chemotherapy administered prior to bone marrow (stem cell) transplantation. His team at the University of Sydney have added specific immune T cells to treatment to help the body rapidly rebuild an effective immune response to reduce the risk of infection.

Most patients undergoing a stem cell transplant for malignant blood cancer receive powerful chemotherapy before their transplant is given. This chemotherapy causes severe damage to the immune system and this in turn results in patients being very prone to developing serious infections after the transplant. Standard treatment is to wait for the immune system to recover though this can take up to and sometimes beyond a year, during which patients may have serious, even fatal infections.

‘My research has identified and promoted the concept of immune reconstitution as a key plank in dealing with infection in stem cell transplant and other immunocompromised patients,’ Professor Gottlieb explained.

‘Using responsive T cells to speed up immune recovery after stem cell transplant offers an alternative and sometimes lifesaving option to patients in whom standard treatment has failed. Without this treatment many of these patients would have spent long periods in hospital, and some would have died from their infections.’

‘I have established a clinical adoptive immunotherapy program in the setting of one of Australia’s largest stem cell transplant units. The program has run a number of important clinical trials demonstrating the benefits of administering virus and fungus specific T cells to transplant recipients,’ he said.

‘Over 2,000 stem cell transplants are performed in Australia each year. For many patients, infections after transplant result in suffering and poor quality of life even if their original disease is cured.’

Professor Gottlieb and his team will test specific adoptive immunotherapy strategies that target individual opportunistic pathogens and cancers. From there they hope to identify how these can best be combined to minimise infections and cancer recurrence after stem cell transplant or chemotherapy.
With nine per cent of Australian infants and 14 per cent of Indigenous Australians born prematurely, Professor Mary Jane Black and her team at the Biomedicine Discovery Institute at Monash University are examining the effect of preterm birth on the kidneys and what that means for long-term kidney health. Normally the kidneys are formed prior to birth, with no new nephrons (functional units of the kidney) made after birth. However, in premature babies this formation continues to occur after birth, making the kidneys vulnerable to impaired development, injury and potential kidney disease in later life.

Professor Black decided to examine the causes, risk factors and the environment of premature babies to gain a better understanding of the processes of development after birth and how to mitigate any damage to the kidneys during this period.

‘In particular we looked at the effect of common causes of preterm birth—intrauterine growth restriction (IUGR) and infection of the amniotic sac—and how they affect the development of the kidneys in the first month of life,’ Professor Black said.

‘Our studies have shown that both IUGR and amniotic sac infection can adversely impact nephron development—leading to a significant reduction in the number of glomeruli (filtering components of the nephron), affecting kidney function.’

The outcomes of this research will lead to a better understanding by clinicians of the adverse effects of preterm birth and its causes on renal structure and function. ‘It is envisaged this will lead to both IUGR and premature birth being considered as risk factors for long-term kidney disease, and will facilitate more rigorous assessment of kidney function in premature babies,’ she said.

The very high incidence of kidney disease in adult Indigenous Australians may be a legacy of the improved survival of these infants over recent decades. ‘Our findings indicate that many Indigenous infants will be discharged from hospital whilst still suffering kidney impairment,’ she explained.

‘It is envisaged that when clinicians are alerted to our findings that these infants will be more closely monitored following discharge to help prevent further kidney impairment and also help to improve overall the health in Indigenous children who were born preterm.’

1Australian Institute of Health and Welfare (AIHW), 2016, cardiovascular disease, diabetes and chronic kidney disease—Australian facts: Aboriginal and Torres Strait Islander people, in Cardiovascular, diabetes and chronic kidney disease series.
‘Overall it will lead to better follow-up of kidney function by paediatricians in infants born prematurely, which will help to prevent the progression to chronic kidney disease.’

Professor Black and her team are now preparing to conduct new research in this study, with the specific aim of determining the underlying causes of kidney vulnerability in Indigenous premature infants. They consider that the early life injury to the kidneys of Indigenous infants following premature birth is a major contributor to their exceptionally high incidence of chronic kidney disease in adulthood.
PRECISION MEDICINE FOR BLOOD CANCER

EPIGENETIC THERAPY IN MYELODYSPLASIA (MDS) ANAONIC MYELOMONOCYTIC LEUKAEMIA (CMML)
About half of patients who receive drug treatment for Myelodysplasia (MDS) and Chronic Myelomonocytic Leukaemia (CMML) (types of blood cancer) do not respond and about half of those who do respond, relapse when on treatment.

Professor John Pimanda and his team at the Lowy Cancer Research Centre have developed a method of predicting whether a patient will respond to drug treatment or not.

‘There is an urgent need to identify predictors of response and therapeutic alternatives for patients with primary or secondary 5-Azacytidine (AZA) resistance,’ Professor Pimanda said.

‘We have developed a test that can now be applied in the clinical setting to predict which patients are likely or unlikely to respond to AZA treatment without having to receive months of potentially futile treatment.’

Professor Pimanda’s team has shown that the haematopoietic progenitor cells (immature blood cells) of patients who do not respond to AZA treatment proliferate less in comparison to patients who do respond.

‘Drug responsiveness can be predicted using flow cytometry—a biophysical laser cell-counting and protein detection method—using pre-treatment bone marrow samples,’ Professor Pimanda explained.

‘We have also developed a parallel test that could use peripheral blood to monitor drug response.’

‘Our explorations were born out of curiosity to explore processes that control cell proliferation and identity during blood development in the embryo and in maintenance of healthy adult blood stem cells, and how these systems fail in leukaemic cells,’ he said.

Professor Pimanda’s team is adapting the flow cytometry test to suit the machines in the clinical laboratory and has initiated a clinical trial to develop a drug response score that will utilise this and other markers to determine early response.

‘We now have a better understanding of the relationship between diseased blood stem cells and their function and are pursuing these leads to understand how mutated cells gain an advantage in our bone marrow.’

‘Drug resistance has many causes and each broad type of resistance requires a different treatment strategy. Professor Pimanda and his team has gained significant insights into the molecular pathways that need to be activated for drug response and is pursuing these in the search for better alternatives.'
STARVING BACTERIA—BEATING ANTIBIOTIC RESISTANCE

INHIBITORS OF BIOTIN PROTEIN LIGASE: A NEW CLASS OF ANTIBIOTIC TARGETING STAPHYLOCOCCUS AUREUS

‘Nineteen per cent of serious blood infections in Australia are resistant to antibiotics—a rate higher than in France, Germany and the United Kingdom.’


The World Health Organisation (WHO) has described antimicrobial resistance as one of the key global health issues facing our generation. The lack of new antibiotics coupled with their over-prescription has led to bacteria becoming increasingly resistant—rendering existing antibiotics less effective and placing patients at greater risk of dying from common infections. Without antibiotics, complex surgical procedures such as organ transplants would also not be possible.

With only two new antibiotic classes discovered and developed in the last 50 years, Professor Andrew Abell and his team at the University of Adelaide are going back to the fundamentals of chemical science in an attempt to develop a new class of antibiotics.

Motivated by a desire to understand the molecular basis of key biological processes, Professor Abell saw an opportunity to use small molecules that selectively bind to bacterial proteins, as a potential mechanism for limiting bacterial survival.

‘This project successfully employed chemistry and biochemistry to understand the complex nature of biotin—vitamin B7—both in the test tube and inside the bacteria,’ Professor Abell said.

‘We are using this knowledge to discover a new antibacterial by inhibiting a key protein—known as Biotin Protein Ligase (BPL)—to disrupt how bacteria use this important micronutrient, rendering the bacteria unable to survive.’

‘We are particularly excited about one compound—BPL199—showing potent activity against multiple strains of Golden Staph, including drug resistant strains like MRSA (Methicillin-resistant Staphylococcus aureus),’ Professor Abell explained.

Professor Abell and his team’s approach to antibacterial discovery involves ‘smart medicinal chemistry’ to design, make and then test new compounds that have the potential to be developed into antibiotics. It brings together a large group of scientists, working in a highly collaborative fashion.

‘This strategy requires the contribution of medicinal chemists, biochemists, structural biologists, microbiologists and pharmacologists,’ Professor Abell said.

‘Medicinal chemistry can then draw upon this fundamental knowledge to best exploit our approach. This requires a truly multidisciplinary approach to science with a strong awareness of commercial opportunities and demands.’

‘Drug discovery projects often fail as researchers do not understand enough about the fundamentals of the drug targets they work on,’ he said.


Photo supplied by University of Adelaide

Professor Andrew Abell

THE NEXT STEPS

Professor Abell and his team are now working towards improving the pharmacological properties of BPL199. This involves designing new chemical products that will improve the activity of the compound in animal models of disease. The team will also begin to expand their research and findings to new areas of human health and disease to improve the health of all Australians.
'There is a desperate need to replenish the antibiotic pipeline with new products to combat drug resistance. We are developing novel classes of antibiotics with potential to treat infections caused by pathogenic bacteria, including Golden Staph.'