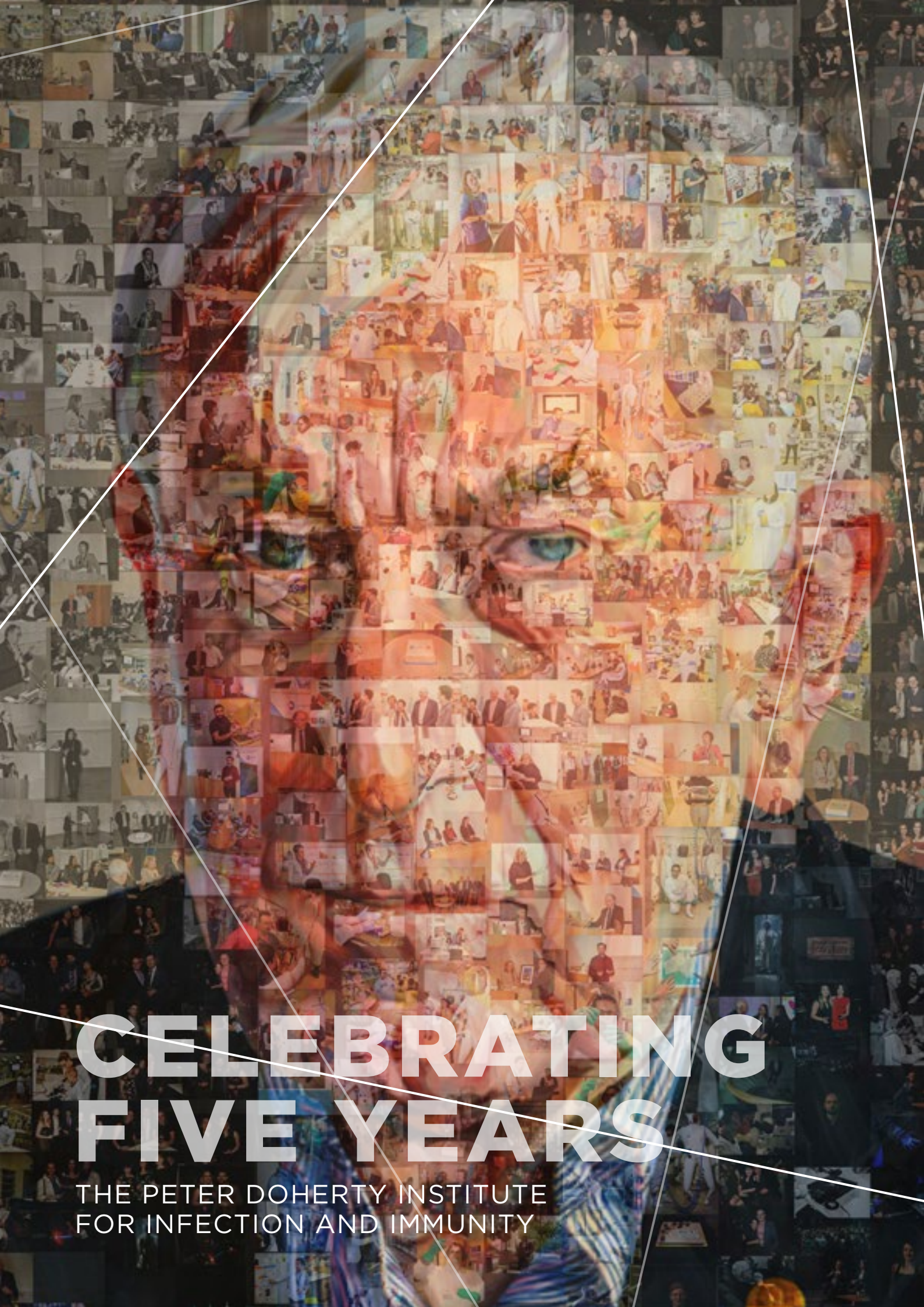

CELEBRATING FIVE YEARS

THE PETER DOHERTY INSTITUTE
FOR INFECTION AND IMMUNITY

A NOTE ABOUT COVID-19

The Peter Doherty Institute for Infection and Immunity (Doherty Institute) - a joint venture between the University of Melbourne and The Royal Melbourne Hospital - celebrated its fifth anniversary in September 2019.

This report, *Celebrating Five Years,* was due to be published in February, but in early January news reports began to surface about a mysterious virus emerging out of Wuhan in the Hubei Province of China.

That virus needs no introduction. SARS-COV-2, the virus that causes the disease COVID-19, is something that we're all too familiar with, changing life as we know it not only here at the Doherty Institute, but the world over.

On Tuesday, 28 January, only a few days after diagnosing Victoria's first positive COVID-19 case, Director of the Victorian Infectious Diseases Reference Laboratory and Deputy Director of the Doherty Institute, Dr Mike Catton, along with Head of the Virus Identification Laboratory, Dr Julian Druce, confirmed they had successfully grown the virus in cell culture in the laboratory. The Doherty Institute was the first to grow the virus outside of China and the first to share it with the World Health Organization and public health laboratories across the globe.

The following day, news of this crucial first step in the response to COVID-19 went global. With access to the virus, researchers could not only validate test results, but also commence work on better diagnostic tests, treatments and a vaccine.

As you will read over the following pages, our team of infection and immunity experts at the Doherty Institute have been training for this moment for years. The Doherty Institute was conceived and purpose-built to respond to a pandemic.

Over the last six months, Dr Catton and his team, along with other diagnostic teams within the Institute, have been continuing to perform tests on suspected cases. Our clinicians have been preparing hospitals and treating patients with COVID-19. Our epidemiologists have been working closely with the State and Federal Governments, executing mathematical models to devise policy to help flatten the curve.

As a new virus, there is no treatment or cure for COVID-19. Our researchers have established clinical trials to identify treatments for the virus, are screening existing drugs for efficacy in the laboratory, are seeking to understand the immune response to the virus, and working on multiple vaccine strategies. In what we call "peace time", much of this work would take years. But these are extraordinary times and we were prepared.

A full report on our work on COVID-19 to date is underway and we look forward to sharing this with you. Until then, we hope you enjoy reading about our work over the last five years, which has led us to be the powerhouse in infection and immunity we are today.

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FIND OUT MORE ONLINE

Scan the QR code to read more on our dedicated *Celebrating Five Years* webpage.

MESSAGE FROM THE PATRON

Laureate Professor Peter Doherty AC, FAA, PhD, FRS

You usually don't get an institute named after you until you're dead, so naming it the Peter Doherty Institute for Infection and Immunity was a little ahead of the game, but a big honour nonetheless.

The motto of the family name, Doherty, which is in Gaelic, roughly translates to 'born of a destructive person'. But I would like to think it means 'born of a deconstructive person', because that's what we do as scientists – we deconstruct, take things apart, try and put things together and understand how we can make improvements.

Modern science is tremendously interactive and involves people from multiple disciplines with various expertise. To bring together expertise in research, education and public health in the one institute is a real positive. It is a unique structure for our country, and indeed, the world.

Being located right in the heart of Melbourne's Biomedical Precinct — with the Victorian Comprehensive Cancer Centre directly across the street and the Walter and Eliza Hall Institute, the Florey Institute of Neuroscience and Mental Health and Murdoch Children's Research Institute close by — is an enormous plus.

I think Melbourne is the leading biomedical research city in the country, and we're certainly up there with many other international cities. The Doherty Institute will keep Australia on the map scientifically, and in the world of infection and immunity, which is very important as it enables collaborations with comparable or complementary expertise. Our collaborations span the globe; from right here in this Precinct, across the Asia-Pacific region, to the US and Europe, and everywhere in between.

It's enormously gratifying to work in the Institute. Our work covers the major health threats globally including antimicrobial resistance, influenza, HIV, viral hepatitis and emerging infectious diseases. More recently, our work has extended to infectious diseases of major concern in Indigenous communities, including HTLV-1, hepatitis B and skin infections. We have the capacity to work on any infectious disease; from diagnosis, epidemiology, clinical care and eventually vaccine and drug development. This is pretty impressive!

Underpinning all we do is a deep understanding of immunology. We have always known the immune system is key to controlling an infection but we now know that immunology is also key to the control of cancer. New therapies for cancer that are leading to outstanding clinical benefit all harness the immune system – retraining our killer T-cells to eliminate cancer cells.

I've always thought that senior scientists should stay out of the way when it comes to the future, and one of our key roles is to bring on that next generation, the young scientists, to make new discoveries. They can ask us for our advice and guidance, but that is it.

My hope for the Doherty Institute is to see it maintain its very high intellectual standards, excellence in teaching and continue its impact on the community and public health globally. Within infectious diseases, we solved a lot of the easy problems fairly early on. But there are some very difficult problems out there that need to be tackled. To be successful we need resources. No scientific institute works without significant funding, so we need continued support from governments and philanthropy.

MESSAGE FROM THE DIRECTOR

Professor Sharon Lewin AO, FRACP, PhD, FAHMS

Rarely, if ever, in a career are you given the opportunity to shape and lead an organisation that has the potential to make a truly meaningful, decades-long (and maybe even centuries – long) impact on human health. By taking on the position of Director of the Doherty Institute in September 2014, I was given that very opportunity.

The Doherty Institute itself was a bit of an experiment. With the generous support of the State and Commonwealth governments, as well as the University of Melbourne, a state-of-the-art building went up in record time. As an unincorporated joint venture between the University of Melbourne and The Royal Melbourne Hospital, the experiment could only work with the enthusiasm and passion of our staff, and sufficient financial resources to realise an ambitious vision and strategy.

I can confidently say, after five years, that we have received all of that – and more. Looking back over the first five years, I am greatly encouraged that we are well on track to achieving our grand vision: to improve human health globally through discovery research and the prevention, treatment and cure of infectious diseases.

Our achievements over the last five years are many, but I would like to highlight a few that stand out for me as Director. Our leadership of genomics in public health has transformed clinical practice. This work allows far more rapid diagnosis and understanding of how organisms move through hospitals or populations. Our staff have led the way in using these tools to understand outbreaks of gastrointestinal, skin and sexually transmitted infections.

Our public health laboratories have supported the response to major outbreaks in the Asia-Pacific region, including measles in Samoa and polio in Papua New Guinea.

Our work in influenza informs and evaluates the efficacy of the annual vaccine across the Southern Hemisphere. Scientists in our discovery research laboratories are aiming to develop a one-shot influenza vaccine with far higher efficacy than our current vaccines.

Our work on finding a cure for HIV and hepatitis B is critical for people living with either virus. Despite the great success of antiviral therapy for chronic blood-borne virus infections such as HIV and hepatitis B, both infections require lifelong treatment. Although the two viruses are very different, the approaches to their cure have many scientific similarities and need global collaboration and multi-disciplinary engagement. I am enormously proud that the Doherty Institute was one of the founding partners of ICE-HBV (International Coalition for the Elimination of Hepatitis B Virus).

Finally, and consistent with our institutional title, our work extends well beyond the world of infection and also focuses on immunity. Stemming from Peter Doherty's own discovery of killer T cells back in the early 70s, we now know that the immune system is critical for controlling and potentially curing cancer. Our staff are experts in the different types of immune cells needed to fight infection and are now applying this knowledge to develop new treatments for cancer of the skin, breast and brain.

The success of an organisation is dependent entirely on its people. It's their passion, hard work and commitment to excellence that makes the Doherty Institute a wonderful place in which to work. I have been greatly supported in leading the Institute by members of the Doherty Council; the Directorate team led by our Executive officer, Andrea Fischer; our Deputy Directors, Professor Andrew Brooks and Dr Mike Catton; the heads of each department; the Doherty Executive; our Theme and Discipline leaders; and many others across the organisation.

We have much to be proud of from our first five years. I think the experiment might have worked!

A SHORT HISTORY

Professor James McCluskey AO, FAA, FAHMS

The history of the Doherty Institute dates back to 2006 when I was the Head of the University of Melbourne's Department of Microbiology and Immunology. The idea was sparked following the University's unsuccessful tender to manage the World Health Organization (WHO) Collaborating Centre for Reference and Research on Influenza. And it just so happened that the Department of Microbiology and Immunology needed a new building.

That tender was won by The Royal Melbourne Hospital's Victorian Infectious Diseases Reference Laboratory (VIDRL), directed by Dr Mike Catton, who remains as VIDRL's Director today, and the Doherty Institute's Co-Deputy Director. University of Melbourne Professor Roy Robins-Browne, the then Deputy Head of the Department of Microbiology and Immunology, and I went to see Mike to discuss how we could work better together; we wanted to try and create something bigger than the sum of its parts.

From this conversation, the concept emerged of bringing together the University's Department of Microbiology and Immunology, including the Microbiological Diagnostic Unit Public Health Laboratory, and parts of the Department of Medicine (Royal Melbourne Hospital), with the Royal Melbourne Hospital's VIDRL, WHO Collaborating Centre for Reference and Research on Influenza, VICNISS Coordinating Centre and the Victorian Infectious Diseases Service.

This initiative drew on existing entities. We were not creating a new entity that would require a massive recruitment exercise, rather an ecosystem that would work closely with the State and Commonwealth Governments and could be a one-stop-shop for infectious disease threats and the immune response to them. We wanted to integrate our research, education and public health activities. It was a compelling logic for co-location focused on infrastructure and idea exchange; those tearoom and corridor conversations are the genesis of so much collaboration.

We had two strokes of luck. The first was that the then Prime Minister of Australia, John Howard, had created the Higher Education Endowment Fund for capital developments at '*universities of national importance or local significance.*' This meant we had something we could apply for. The second was the converging force of the Global Financial Crisis. The Prime Minister that followed Howard was Kevin Rudd, and his response was to hunt around for shovel-ready infrastructure projects, and we had one.

The Commonwealth gave us $90 million, the Victorian State Government, led by Premier John Brumby, provided $55 million and the University contributed the remaining $65 million.

I will confess, there were lots of bumps in the road, including a heritage claim on the *'magnificent'* building that used to operate on the site – The Elizabeth Tower Hotel – with its beautiful single helix staircase that people in the tram liked when it was lit up in the evenings. We had to go to the Victorian Civil and Administrative Tribunal to make the case that a major new initiative in combatting infectious diseases was more important than the staircase.

We have been blessed with Nobel Laureate Peter Doherty as our namesake. In an early meeting between Mike, Roy and myself, Roy said, *'Why don't we call it The Peter Doherty Institute for infection and Immunity?'*. That was an immediately compelling suggestion because it set the bar high. It was a wonderful gesture that Peter agreed to the use of his name.

The inaugural Director of the Doherty Institute, University of Melbourne Professor Sharon Lewin, is a great leader. It's a very challenging job because of the breadth of activity and the many stakeholders. She has to foster collaboration between the groups by persuasion, argument and influence. I think she has been an outstanding Director and the Institute is very well known internationally in just five years of operation because of her efforts.

We have outstanding people, and it is all about the people. I think the Doherty Institute has performed magnificently, not just in research grants, but actually more importantly, in the impact of the work we do. We are signed up to some big projects — a cure for HIV, a one-shot flu vaccine — to name a few. If we could throw out a Nobel Prize winner or a vaccine for a major pathogen that would be fantastic.

Congratulations Sharon, and congratulations to all of you at the Doherty Institute.

TIMELINE

This timeline captures major events associated with the Departments within the Doherty Institute, along with some of the most signifcant infectious disease events in the last 250 years.

1804	Smallpox vaccine becomes available
1897	Microbiological Diagnostic Unit Public Health Laboratory (MDU PHL) established at the University of Melbourne
1904	Fairfield Infectious Diseases Hospital opens its doors, eventually housing the Victorian Infectious Diseases Reference Laboratory (VIDRL)
1918	Spanish Influenza epidemic kills 50 -100 million globally
1929	Department of Bacteriology established at the University of Melbourne
1938	Last known case of smallpox in Australia
1951	WHO Regional Influenza Centre established at the Commonwealth Serum Laboratories (CSL) in Melbourne
1965	Department of Bacteriology becomes the School of Microbiology, moves to the new medical complex near the corner of Royal Parade and Grattan Street
1979	WHO announces smallpox has been eradicated worldwide
1982	First case of AIDS diagnosed in Australia
1992	VIDRL formally designated as a Victorian public health reference laboratory
	CSL receives designation as the WHO Collaborating Centre for Research and Reference on Influenza
1996	Professor Peter Doherty wins the Nobel Prize for Physiology or Medicine with Rolf Zinkernagel
	Fairfield Infectious Diseases Hospital closes down
	VIDRL becomes part of Melbourne Health and relocates to North Melbourne
1997	Department of Microbiology and Immunology established in place of the School of Microbiology, houses MDU PHL
	Victorian Infectious Diseases Service established at The Royal Melbourne Hospital
1999	Laureate Professor Peter Doherty moves to the University of Melbourne
2002	VICNISS established
2008	WHO Collaborating Centre for Reference and Research on Influenza relocates to purpose-built facilities at VIDRL in North Melbourne
	VIDRL designated as WHO Collaborating Centre for Mycobacterium Ulcerans
2014	Doherty Institute opens and all departments relocate
2015	VIDRL designated as WHO Collaborating Centre for Viral Hepatitis
2019	Austin Health's Infectious Diseases Department becomes the first department of the Doherty Institute to be located offsite

FAIRFIELD INFECTIOUS DISEASES HOSPITAL

Originally named Queens Memorial Hospital, the Fairfield Infectious Diseases Hospital was located at Yarra Bend. The Spanish Influenza epidemic saw patient numbers rise to 6000 a year, which remained the average until the late '80s.

NOBEL PRIZE

Laureate Professor Peter Doherty has been involved in research on infection and immunity for over 50 years. He won the Nobel Prize for the discovery of how the immune system recognises virus-infected cells.

AUSTIN HEALTH ID

This partnership was forged to strengthen existing collaborations between Austin Health ID and departments within the Doherty Institute in areas such as the translation of genomics into clinical practice and clinical infection control interventions.

OPENING – SEPTEMBER, 2014

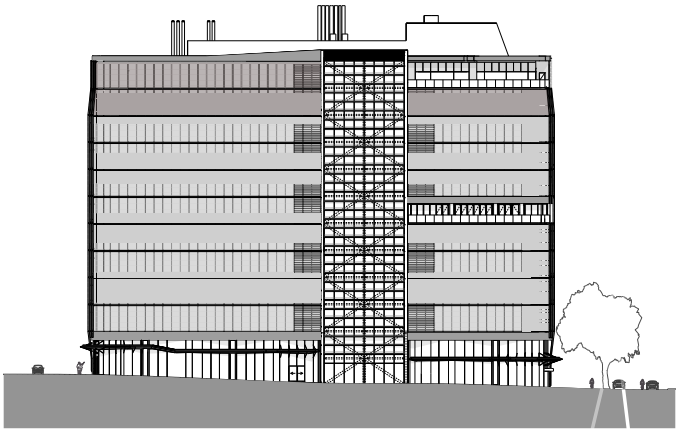
The Doherty Institute was built on the site of the former Elizabeth Tower Hotel, renowned for its imposing spiral staircase. The $210 million purpose-built facility was designed by architecture firm, Grimshaw.

The Doherty Institute was officially opened on Thursday, 12 September, 2014 by the then Prime Minister of Australia, Tony Abbott.

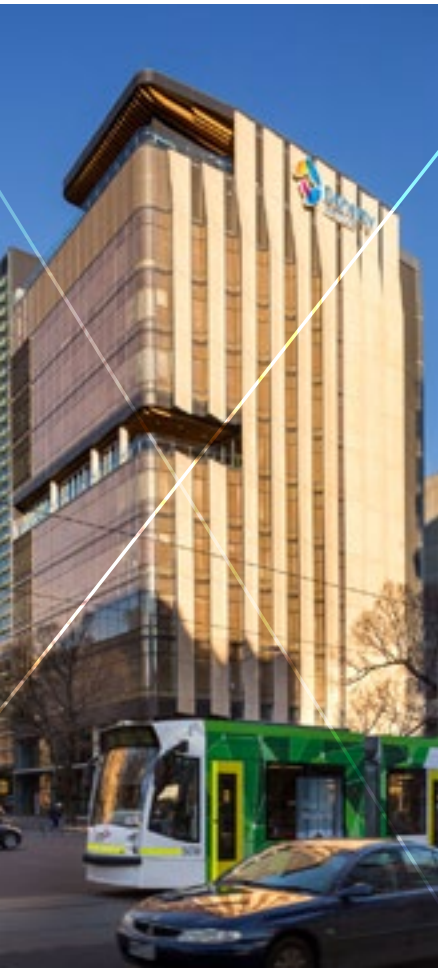
Before...The Elizabeth Tower Hotel

Director of the Doherty Institute, University of Melbourne Professor Sharon Lewin's maiden speech

Former Prime Minister Tony Abbott on a tour of the building



Grimshaw's elevation drawing of the exterior of the building

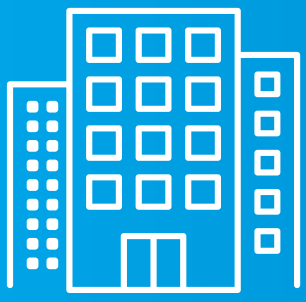


After...The Doherty Institute

A brick from the Elizabeth Tower Hotel that was kept by University of Melbourne Professor James McCluskey

The opening of the Doherty Institute garnered significant media interest

IN NUMBERS



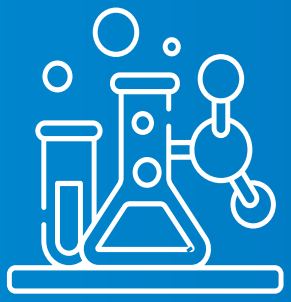
$210m
Purpose-built facility

4 NHMRC
Centres of Research Excellence

700+
Staff

3
World Health Organization Collaborating Centres

120+
PhD Students



2
Public health laboratories

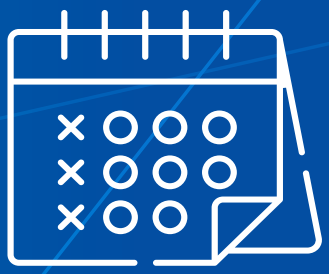
40+
Research groups

20+
Physicians

ACHIEVEMENTS

$159m+
Competitive grant funding

1980+
Journal publications



566+
Events

25k+
People trained

2.5m+
Tests processed

18k+
Media mentions

40+
Awards

2338+
Outbreaks investigated

38
Countries we have collaborations in

THEMES AND CROSS CUTTING DISCIPLINES

Work at the Doherty Institute is centred around the following themes and cross-cutting disciplines. The articles that follow are a selection of highlights over the last five years.

IMMUNOLOGY

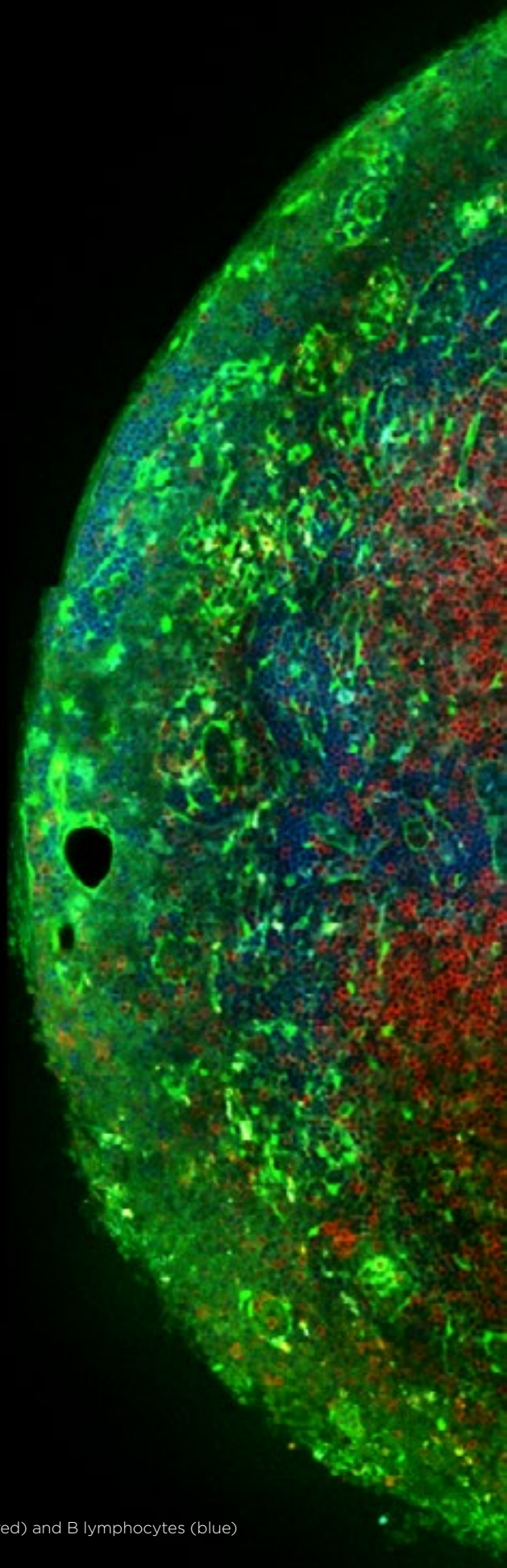
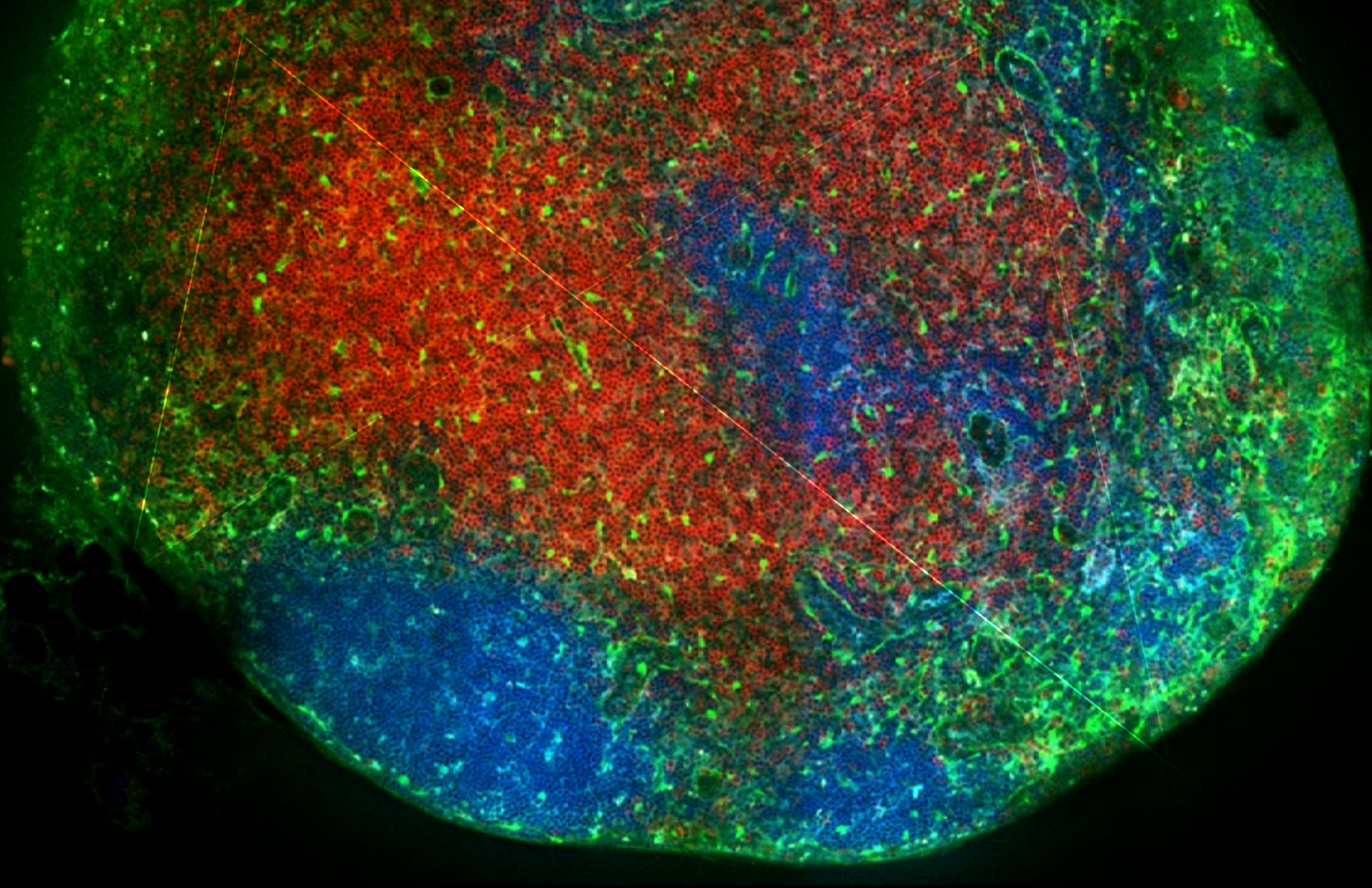


Image credit: Lymph node showing fibroblasts (green), T lymphocytes (red) and B lymphocytes (blue) by University of Melbourne Dr Sapna Devi



UNRAVELLING A NEW ARM OF IMMUNITY

An important immune cell offering a second arm of protection against infectious diseases could also be involved in regulating tumour cells.

While 1999 marked the first scientific description of this unique immune cell type, mucosal associated invariant T cells, researchers had to wait 13 years for the next big breakthrough. An interdisciplinary team found MAIT cells, as they're more commonly known, responded to a different class of molecule compared with most immune T cells.

In order to elicit a response to an infection, most T cells usually first recognise and respond to peptides and lipids on foreign invaders. But MAIT cells respond to a third class of molecule – vitamin-based metabolites that are generated when bacteria grow. The research effort was led by Professor James McCluskey, the Deputy Vice-Chancellor of the University of Melbourne and laboratory head at the Doherty Institute, with collaborators from Monash University and the University of Queensland.

"Once you know which molecule a cell is responding to you can unlock the biology of that cell," says Professor McCluskey.

"This allows you to define the classes of organisms involved and to create the agents and tools to track these cells."

MAIT cells make up to 10 percent of the T cells in human blood and are even more abundant in organs such as the liver, yet little is known about their role in the immune response.

"Undoubtedly, one of the roles of MAIT cells is to add a layer of protection in diseases such as Legionnaires' disease and other lung infections," says Professor McCluskey.

"Our experiments show that they're kind of a secondary arm of immunity that becomes very important if the primary arm is not working well. That difference could mean life or death."

Studying MAIT cells was previously not possible. But following their discovery, the research team created analytical research tools called *MR1 tetramers*, which can identify and study MAIT cells in the blood and tissues of humans and mice.

These tools have led to an explosion of MAIT cell research in over 40 laboratories in 14 countries and are licensed to the US National Institutes of Health for distribution worldwide.

While Professor McCluskey's group is focussed on assessing the function of MAIT cells in models of infection, other laboratories at the Doherty Institute are exploring their role in different aspects of infection. This work includes research to uncover how MAIT cells respond to foreign molecules produced by infectious agents (University of Melbourne Professor Jose Villadangos' group); their role in influenza infection (University of Melbourne Professor Katherine Kedzierska's group); and function in models of HIV (University of Melbourne Professor Stephen Kent's group).

Meanwhile, University of Melbourne Professor Dale Godfrey's group is right at the cutting edge of understanding the fundamental biology of MAIT cells, having made important discoveries about their development. He has recently commenced a project with the Peter MacCallum Cancer Centre to understand how MAIT cells regulate tumour immunity.

"We're getting interesting results that suggest MAIT cells can regulate tumours in mice and they might make a difference in humans," he says.

Image credit: Small capillary blood vessels of the liver with T lymphocytes (yellow) that patrol the liver against pathogens by University of Melbourne Dr Sapna Devi

ON THE FRONTLINE OF IMMUNE PROTECTION

A type of immune cell lurks in tissues ready to jump into action to offer protection from infection.

Most immune cells migrate throughout the body via the blood. But a subset of T cells, coined tissue-resident memory T cells (Trm cells) by University of Melbourne Professors Francis Carbone and Thomas Gebhardt in 2009, were found to do what their name suggests.

These cells reside in tissues such as the skin, liver, lungs or gut, ready to fight infection at the site. Most importantly, their long-term persistence in tissues was shown to be key for swift and efficient protection.

"Essentially, our bodies deposit the 'police' to the areas where there's always going to be trouble," explains Professor Gebhardt.

"If you relied on circulating cells in the blood to control disease at sites where they're needed, they would arrive too late, or potentially would never find the problem area."

Over ten years, the last five at the Doherty Institute, researchers have been studying the role of Trm cells, with the ultimate goal of harnessing them to create better vaccines and immunotherapies for cancer.

University of Melbourne Professor Laura Mackay and her collaborators have made a series of discoveries to help unravel the function of Trm cells.

Professor Mackay uncovered the genes responsible for keeping the Trm cells in the tissues at the site of infection. This work was published in seminal studies in 2013 and in 2016, together with Professor Gebhardt and University of Melbourne Professor Axel Kallies.

Professor Mackay then demonstrated that Trm cells in the skin can proliferate and remain there to fight infection by adding new populations of cells as required. This work was in collaboration with University of Melbourne Professor Scott Mueller.

Most recently, University of Melbourne PhD student, Simone Park, discovered how Trm cells control melanoma on the skin in a mouse model.

The research was performed in the laboratories of Professors Gebhardt and Mackay and showed the Trm cells were able to control tumours in the mice for the lifetime of the animal, which would equate to decades of protection in humans.

"Trm cells are hugely important, but we're still at the stage of translating what we know from the basic biology," says Professor Gebhardt.

VACCINE RESEARCH PIPELINE FLOURISHES

Six vaccine strategies in development at the Doherty Institute are driving the search for solutions to some of the world's nastiest infectious diseases.

Vaccination is arguably one of history's greatest inventions. Vaccines eradicated smallpox globally and have significantly reduced many other infectious diseases. Yet, vaccines remain elusive for many high-impact diseases such as malaria and HIV.

Researchers across the Doherty Institute are at varying stages of creating vaccine strategies for a number of infectious diseases.

TWO VACCINE STRATEGIES AGAINST MALARIA

University of Melbourne Professor Bill Heath is investigating two paths for the development of a vaccine for malaria.

Professor Heath's team discovered that memory immune cells residing in the liver were more efficient against liver-stage malaria parasites than memory cells circulating in the blood.

Based on this finding, they developed a 'prime and trap' vaccine method involving two injections.

The 'priming' injection sets the immune response in motion, boosting the army of immune cells against malaria and helping to attract those cells to the liver. The 'trapping' injection captures an abundance of these immune cells in the liver and then converts them into liver-resident immune cells that permanently guard the liver from malaria infection.

"Since this work was published in 2016, we've tested this method on real molecules associated with malaria (known as antigens) and we've identified a novel malaria antigen that is highly protective," says Professor Heath.

"However, 'prime and trap' is a complex vaccine that has three components and requires two separate injections, making real world use difficult. We've worked hard to simplify the vaccine; now all components can be injected at the same time."

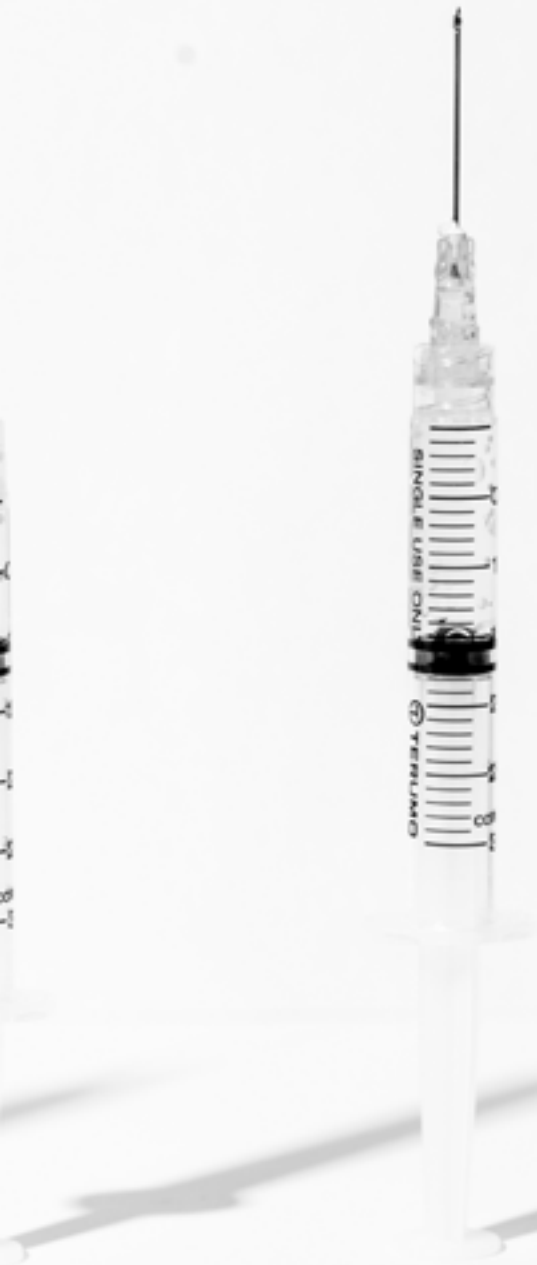
The second strategy is a simpler vaccine that also generates the required immune cell response but comprises a single molecule containing all the critical components. This approach is patented and is a collaboration with University of Melbourne Professor Dale Godfrey and researchers from Victoria University in New Zealand and Avalia Immunotherapies.

A VACCINE PLATFORM AGAINST ZIKA VIRUS

University of Melbourne Professor Jason Mackenzie and his team investigate viruses such as dengue and the newly emerging Zika virus. The mosquito-borne illness can cause microcephaly and other congenital malformations in children of mothers who contracted the virus during pregnancy.

"Our research on dengue and Zika virus has shown us that these viruses use human proteins to replicate efficiently and they can change the fats of the host cell, which can induce inflammation," explains Professor Mackenzie.

To advance treatment options against these diseases, they have constructed a vaccine platform against Zika virus. It is extremely effective in producing specific antibodies that recognise the virus and neutralise its ability to infect cells. The team is working with other colleagues at the Doherty Institute to advance these developments further and to move the vaccine into clinical trials.



ANTIBODIES FROM COWS COULD BE THE KEY TO AN HIV VACCINE

University of Melbourne Professor Damian Purcell and his team are working on a vaccine for HIV – using cows.

"We think that cows have a genetic advantage and make special antibodies against tricky viruses," explains Professor Purcell.

"The HIV virus has a spike on its envelope, which it uses to enter cells. It is shrouded in protective sugars.

"The cow antibodies can more easily reach through these sugars and bind tightly to important underlying protein structures, which enables the antibody to be effective against a wide range of HIV strains."

Professor Purcell says that some of the antibodies they have made from the cow have been remarkably potent.

"If we could achieve the same results in humans then we would be closer to an effective HIV vaccine."

RESEARCH NEEDS TO TARGET VIRUS-INFECTED CELLS AS WELL AS FREE VIRUS PARTICLES

University of Melbourne Professor Stephen Kent and his team made an important discovery when studying how broadly neutralising antibodies prevent transmission of simian immunodeficiency virus (SIV) – an HIV-like virus that infects monkeys.

"During sexual transmission of HIV, virus is present in the form of the seminal plasma that can either be free virus or virus-infected cells," explains Professor Kent.

Professor Kent and his team administered macaque models with virus-infected cells followed by broadly neutralising antibodies and found that in many cases they couldn't protect against the cell-associated virus.

"Virus-infected cells are not visible to any immune intervention you might use. You could have the most potent microbicide that stops sexual transmission of the free virus, but if the cells get across, you're still going to get infected."

NANOPARTICLES TO BOOST THE IMMUNE RESPONSE

Professor Kent is also a Chief Investigator for the Australian Research Council Centre of Excellence in Convergent Bio-Nano Science and Technology. In collaboration with University of Melbourne Professor Frank Caruso, Professor Kent and his team are investigating the use of nanoparticles as vaccine-delivery tools.

"Particles with a wide range of properties – size, charge and material – can be fabricated, and each will interact with cells of the immune system in a different way," explains Professor Kent.

"We're trying to determine which nanoparticle properties will elicit the desired immune responses, and we're using imaging to see how these particles affect vaccine responses in vivo."

MY JOURNEY OF DISCOVERIES

By University of Melbourne Dr Amy Chung, Laboratory Head

I recall being a young student, alone in the lab and pausing in wonder as the results of a painfully long and intricate experiment solidified. Then, coming to the sudden realisation that I, a mere PhD student, had helped to discover something.

In that one moment, I held a tiny piece of knowledge about how the human immune system worked that no one else in the world knew.

It's a heady, adrenaline-filled sensation to be the sole knowledge holder of an intricate piece of the puzzle.

In my case, that was to better understand how immune proteins called antibodies are able to activate innate immune cells to help control HIV, the virus that causes AIDS.

These rare but precious moments overshadow everything else. Suddenly, the hours of reading, planning, training, fumbling around like a lost chick (don't get me started on the number of experimental errors made and wrong experimental pathways followed!) and intense labour were worth it.

Now, fast forward ten years, it's rare to find me personally running complicated experiments in the lab.

Instead, I'm in the very privileged position to be leading an amazing, enthusiastic and talented team of young researchers. Our group is fascinated by how antibodies might be harnessed to eliminate infectious diseases.

It's my goal to have each member of my group personally experience these precious *Eureka!* moments, so that collectively we can all share in a journey of discoveries that ultimately may contribute to the development of better vaccines and treatments against infectious diseases.

Image credit: Small capillary blood vessels of the liver by University of Melbourne Dr Sapna Devi

VIRAL INFECTIOUS DISEASES

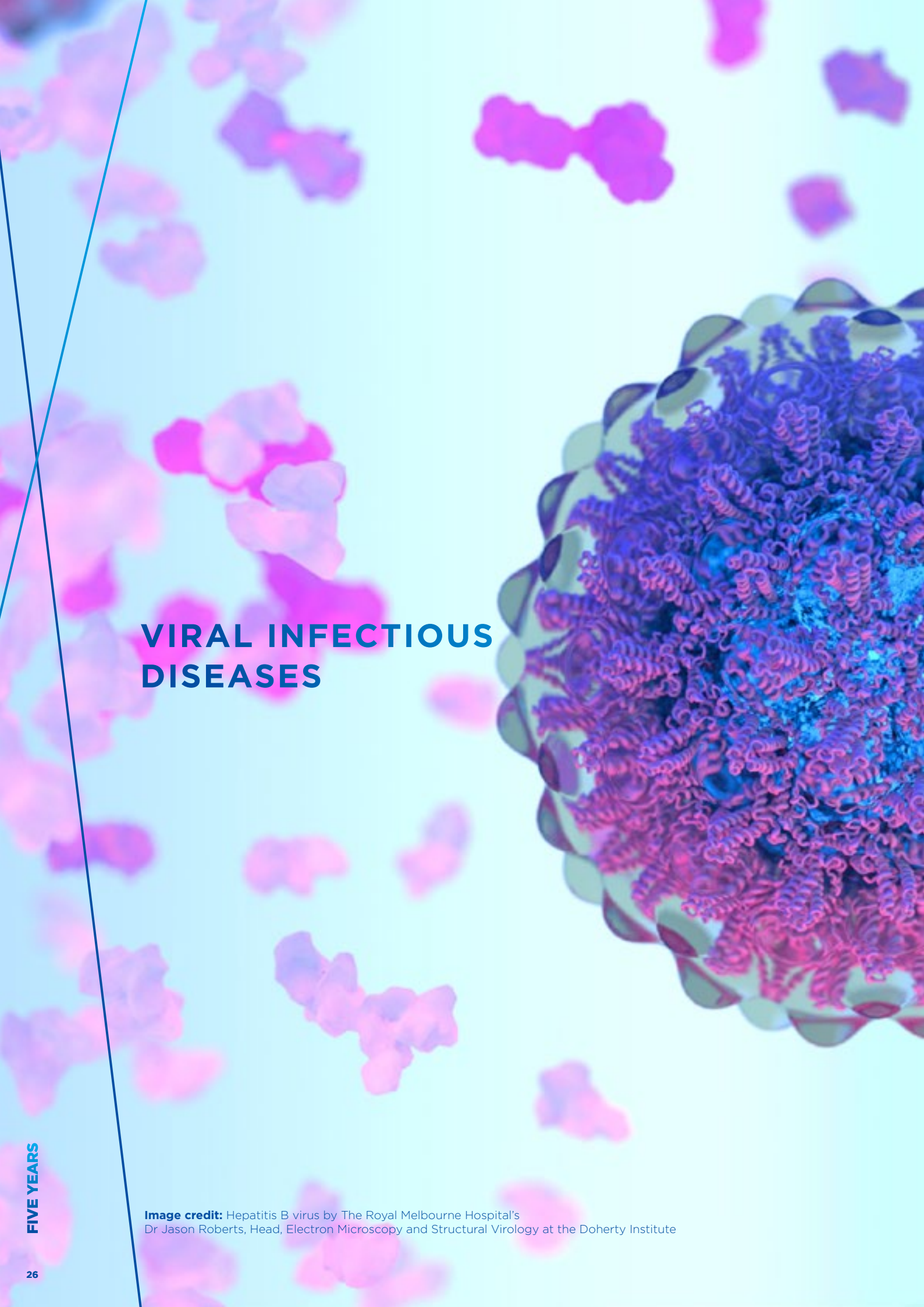
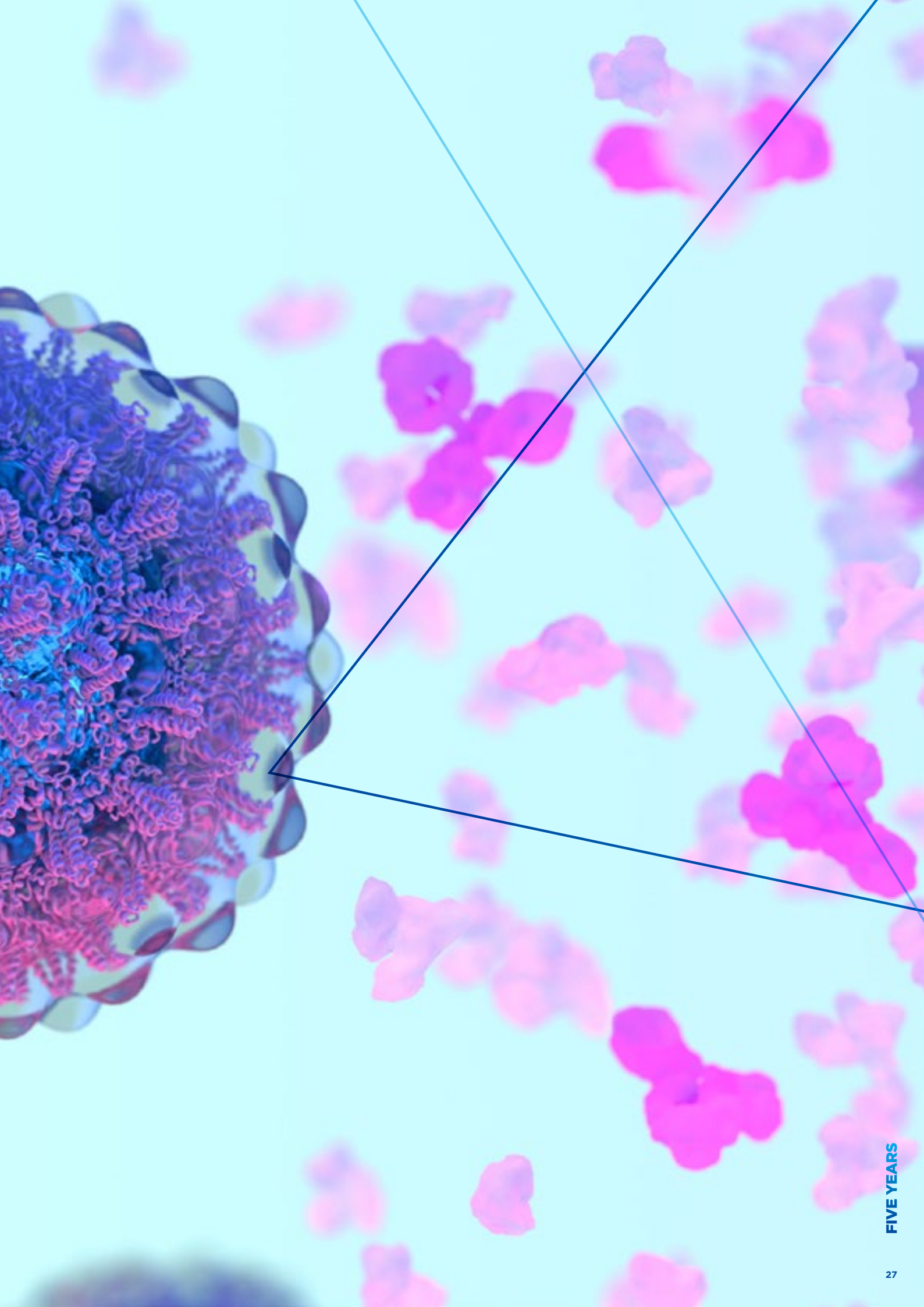


Image credit: Hepatitis B virus by The Royal Melbourne Hospital's Dr Jason Roberts, Head, Electron Microscopy and Structural Virology at the Doherty Institute



THE SEARCH FOR AN HIV CURE CONTINUES

People can now live healthy lives with HIV treatment, so why is it important to find a cure?

The last 25 years have been revolutionary in the field of HIV. What was a death sentence can now be managed thanks to antiviral therapy. Not to mention the fact people living with HIV can have a normal life expectancy. A cure remains elusive – but why do we need a cure if treatment is so effective?

"Only 40 per cent of people globally are on antiviral treatment," says University of Melbourne Professor Sharon Lewin, Director of the Doherty Institute and an infectious diseases physician and basic scientist. "The contribution needed from the global community to maintain current levels of treatment is about $20 billion a year.

The 27,000 people living with HIV in Australia have access to fully subsidised medicines funded by the Commonwealth Government. Low and middle income countries have access to generic antiviral drugs which only cost $100 per year but even to fund this, these countries are dependent on contributions from the international community.

"If we were to reach the UNAIDS goals of 95-95-95 – by 2030, 95 per cent of people living with HIV knowing their status, 95 per cent of those diagnosed on treatment and 95 per cent on treatment achieving viral suppression – that figure would be $30 billion. That's $30 billion each year forever, which is virtually unattainable."

Professor Lewin has dedicated her career to finding a cure for HIV. She was one of the first investigators in the world to accurately measure very low levels of HIV that can 'hide' inside cells in people living with HIV, even while they are on treatment, known as HIV latency – the major barrier to a cure.

Understanding HIV latency and why it persists on treatment is a major objective of her laboratory. In collaboration with investigators in Perth and San Francisco, Professor Lewin and her team have been able to identify the exact gene where HIV is sitting and why it likes going into some genes more than others.

"This work has led to a very successful collaboration with our close colleagues in San Francisco funded by the US National Institutes of Health where we can look at whether the virus goes into different parts of the DNA when it's in different cells," explains Professor Lewin.

Professor Lewin is also known for her pioneering role in investigating the use of immunotherapy, which has revolutionised cancer treatments, as a possible cure for HIV.

"We know the immune system is dysfunctional in cancer, but you can re-educate it to work against the cancer by reversing exhaustion of the immune system," explains Professor Lewin.

"When cells of the immune system, killer T cells, get worn out they express certain flags or proteins on their surface. One commonly expressed marker is a protein called PD1.

"The real breakthrough in cancer treatments was developing an antibody that blocked the exhaustion markers – immune checkpoint blockers – and allowed the killer T cell to recover function and kill the cancer."

Professor Lewin and her team are currently trialling these immune checkpoint blockers in both HIV persistence and cancer to see if this approach could be used as a strategy for cure.

"We have shown that these exhaustion markers are important, not just for the immune response. They also allow the virus to go into hiding. If you block these exhaustion markers the virus is lured out of hiding."

Professor Lewin concedes that while they think it is an important area of research, it's not straightforward to bring this approach to the clinic in people living with HIV without cancer.

"The side effects of immunotherapy currently are significant, for example, five to 10 per cent of people will get an autoimmune disease.

"In a cancer setting this isn't a major concern as you have a life-threatening illness, but in HIV, the situation is very different. People can now live normal and healthy lives with HIV, so any intervention for a cure must have very low toxicity."

Clinical trials to date have only been in people living with HIV who also have cancer, however, they're currently preparing for the first study in people without cancer thanks to funding through the Melbourne HIV Cure Consortium.

In a seperate clinical trial conducted over the last five years, Professor Lewin and her team proved that people living with HIV have very little or no viral replication on treatment.

"HIV becomes undetectable, but we know the virus is hiding in certain spots."

The team was also the first to evaluate drugs that can wake up the virus from its hiding spot. These drugs are called latency reversing agents. Most recently, in partnership with the Alfred Hospital and University of California San Francisco, they demonstrated that a drug called Disulfiram, which is commonly used to treat alcoholism, can also wake up latent HIV virus.

In collaboration with University of Melbourne Professor Damian Purcell's laboratory and the Walter and Eliza Hall Institute, Professor Lewin's team have contributed to finding new latency-reversing drugs.

"Excitingly, these compounds seem to be quite active on cells we collected from people living with HIV and in particular, are able to synergise with other interesting compounds," explains Professor Purcell.

"We're also trying to understand how these compounds work. We think that these latency-reversing drug compounds are interreacting with a molecular switch that can turn the virus on and off."

MAPPING VIRAL HEPATITIS TO IMPROVE THE LIVES OF PEOPLE LIVING WITH INFECTION

When it comes to the uptake of treatment for the 380,000 people living with viral hepatis nationally, there's good news and bad news.

The good news is that by the end of 2017, it was estimated that one quarter of all Australians living with chronic hepatitis C had received treatment. This was a marked increase following the inclusion of effective direct-acting antivirals (a cure for the hepatitis C virus) on Australia's Pharmaceutical Benefits Scheme in March 2016.

The bad news? Only 8.3 per cent of Australians were receiving treatment for hepatitis B, and in some parts of the country, uptake was less than three per cent. Each year, a national project is run to improve understanding of chronic hepatitis B and C in Australia and to assess geographic variation in the proportion of people with an infection and the management and treatment of the diseases. The National Viral Hepatitis Mapping Project is run by the Doherty Institute through the World Health Organization (WHO) Collaborating Centre for Viral Hepatis in partnership with ASHM.

Data and analysis from the Mapping Project are then used by a range of stakeholders to inform targeted awareness and intervention campaigns localised to suit the needs of people living with viral hepatitis and those providing services to them.

While the Mapping Project has been reporting on hepatitis B for seven years, it was only in 2016, following the revolution of highly effective cures for hepatitis C, that the Project included both viruses.

"We saw more people treated in the first two years of the introduction of these direct-acting antiviral drugs than have been treated in the history of hepatitis C treatment in Australia up to that point in time," remarks Professor Benjamin Cowie, Director of the WHO Collaborating Centre for Viral Hepatitis at the Doherty Institute. "We are tracking towards the elimination of hepatitis C as a major public health threat, which is an amazing achievement, but we see inequity in access to these treatments in different parts of the country.

"The Mapping Project report includes local area level data to highlight the areas of greatest need to support the health workforce and engage with communities living with viral hepatitis."

Hepatitis B and C are the major drivers of liver cancer. The 2017 report also included data on liver cancer incidence developed from the Australian Cancer Atlas. An online portal went live in 2019 to enable healthcare workers to interact with the data and drill down into local areas.

"We're also working on getting more timely data in the year it's happening, meaning we can take action more quickly," says Professor Cowie.

In addition to the Mapping Project, Professor Cowie and his epidemiology team are working on a Commonwealth Government-funded project using mathematical modelling to explore the proportion of people with hepatitis B nationally. They are also looking at the burden of associated liver disease and liver cancer to try and identify what the trends are going to be over the next 10 to 20 years. The model examines the impact of the hepatitis B vaccine on case numbers, the proportion of people living with hepatitis B who should be on treatment, and the number of people losing their lives to liver cancer and cirrhosis.

They're also working on a liver cancer prevention linkage project, funded by The Royal Melbourne Hospital Home Lottery Grants.

"This large study examines the de-identified records of all people diagnosed with hepatitis B and C from 1991 onwards in Victoria – over 100,000 people – and links these records to hospitalisation data, liver cancer cases reported to the Victorian Cancer Registry, the Medicare Benefits Scheme and the Pharmaceutical Benefits Scheme, together with other datasets," explains Professor Cowie.

"This will mean that for the first time, we'll be able to see the impact treatment of viral hepatitis is having on mortality, cancer prevention and hospitalisation on the whole population in Victoria."

Thanks to a grant from the Victoria Cancer Agency, Professor Cowie and his team have also embarked on a project titled HEP-LOGIC. Partnering with three Primary Health Networks – Eastern Melbourne, South Eastern Melbourne, and Gippsland – the team are able to access de-identified data from hundreds of general practices covering over one million active patients. It allows them to examine, down to individual practice levels, what proportion of people who would be recommended for testing for hepatitis B are actually being tested, and the levels of uptake of treatment and care for hepatitis B and C among those who have been diagnosed.

"If you're a busy GP working in a practice, viral hepatitis might affect one or two per cent of your patients. So this project is about supporting doctors to provide care for their patients in a way that's respectful when viral hepatitis is only a small proportion of their total workload," says Professor Cowie.

"The idea is to implement the findings into practice management software so notifications are triggered for certain patients to deliver best quality care."

COLD AND FLU AND THE SEARCH FOR SIMILARITIES TO TARGET FOR BETTER TREATMENT

Researchers want to know if cold and flu viruses have anything in common to target with vaccines or treatments.

There are more than 10 different respiratory viruses that can cause what we know as the common cold. And that cold can land people with emphysema, chronic obstructive lung disease, or any kind of pre-existing lung condition, in hospital.

University of Melbourne Professor Patrick Reading and his team are currently investigating whether this group of viruses share similarities with the influenza virus.

"We understand influenza virus pretty well, how it infects cells and spreads, but we don't know so much about other respiratory viruses," explains Professor Reading.

"We want to understand if cold viruses share some common mechanisms with influenza in how they grow and spread, which we could potentially target for a vaccine or treatment. For example, can we turn on specific genes in a host cell that will protect against a whole range of respiratory viruses, including the flu?"

Most respiratory viruses target the cells lining the nose and lungs (epithelial cells). Inside the respiratory tract there are also a type of immune cell (macrophages) roaming around, chewing up debris, including viruses.

"If you put epithelial cells and macrophages side by side, influenza virus will infect them both, and then replicate and make hundreds to thousands of new viruses," explains Professor Reading.

"But the difference is the macrophage won't let the new viruses escape, whereas in an epithelial cell, one virus goes in and hundreds come out. The same is true for some of the other respiratory viruses that also infect humans.

"We want to know what it is about macrophages that stops viruses from escaping. If we can find particular genes that are important in blocking replication of influenza virus in macrophages, we'll be looking to see if we can somehow turn these genes on in epithelial cells.

"We can then hopefully develop a strategy to stop respiratory viruses from growing in epithelial cells."

COLLABORATION IS KEY

By University of Melbourne Dr Brad Gilbertson, Senior Research Officer

We recently discovered evidence of a major interaction between gene segments that the influenza virus uses to package its genome. However, we had no evidence for a physical interaction.

Unbeknown to us, a research group from the University of Oxford had produced structural evidence for exactly the same interaction, but no evidence for its functional relevance.

After being contacted by this group, we realised that we had both independently identified the same interaction. We had complementary pieces of the same puzzle, which led to the start of an amazing scientific collaboration and the eventual publication of this work in *Nature Microbiology.*

This was one of the best moments of my scientific career. To know, at that moment, that we had solved the mechanism by which the influenza virus co-packages particular genes during viral assembly is a feeling that is hard to describe. Not merely satisfaction, but also relief that we were correct; that our work could be independently verified in the hands of others.

Collaboration is such a wonderful and integral part of science. Truly great things can be discovered by collective minds working together using an interdisciplinary approach – even 16,960 kilometres is not a barrier!

This work provides a major advance in the understanding of the structure of the influenza genome and how this can affect the viruses that are produced in nature when different influenza viruses exchange gene segments.

This process, known as reassortment, is so important as it can lead to the creation of pandemic strains. Hopefully our findings will allow better prediction of which influenza viruses can be created by reassortment and therefore allow us to prepare for the risk of their emergence.

FIND OUT MORE ONLINE

Scan the QR code to read more about our **Viral Infectious Diseases work.**

ANTIMICROBIAL RESISTANCE AND HEALTHCARE ASSOCIATED INFECTIONS

TACKLING ANTIMICROBIAL RESISTANCE IN OUR REGION

Like infectious diseases, antimicrobial resistance (AMR) doesn't respect borders.

Confronting this significant issue requires a global response, and thanks to the UK Government's Fleming Fund Fellowship Scheme, a Doherty Institute-led consortium is helping low and middle-income countries do just that.

Designated a Host Institution under the Scheme in 2018, the Doherty Institute, in collaboration with the University of Melbourne's Faculty of Veterinary and Agricultural Sciences and CSIRO's Australian Animal Health Laboratory, is providing mentorship and career enhancement opportunities for professionals across Asia and Sub-Saharan Africa working in fields relevant to their national AMR response.

"The Fellowships bring together key in-country clinicians, vets, pharmacists and scientists already working in AMR," explains University of Melbourne Professor Ben Howden, Director of the Microbiological Diagnostic Unit Public Health Laboratory at the Doherty Institute.

"It allows them to build workforce capacity to implement appropriate, achievable and sustainable programs to detect and monitor antimicrobial resistance and use across human and animal health."

The Fellowships consist of on-the-job training and mentoring, visits by the Fleming Fellows to Melbourne, with reciprocal visits by the mentors.

Fellowships are offered across human and veterinary settings, in clinical microbiology and laboratory quality management related to AMR of priority pathogens; and surveillance, epidemiology and data analysis related to AMR and antimicrobial usage.

The Doherty Institute is currently training twenty Fellows across Bhutan, Timor-Leste and Nepal. Mentors have visited institutions in each country and worked with the Fellows to develop activities to improve their capacity to detect and monitor AMR.

"The visits have also allowed the team to understand the current AMR work in these countries, important for the development of achievable and meaningful fellowship work plans," says Professor Howden.

"It will also give us the opportunity to develop a long term, collaborative relationship with in-country institutions."

Doherty Institute mentors with Fleming Fund Fellows in Bhutan

MONITORING INFECTIONS IN HOSPITALS TO IMPROVE PATIENT OUTCOMES

A centre at the Doherty Institute is providing vital information about infections in hospitals and other health facilities.

The VICNISS Coordinating Centre at the Doherty Institute provides an integrated system in Victoria for the monitoring, analysis and reporting of infections in public and private hospitals on behalf of the Department of Health and Human Services (DHHS).

"We've seen diminishing rates of infections in public hospitals just by virtue of capturing and monitoring data," says Associate Professor Leon Worth, the Acting Director of VICNISS.

"For example, some surgical site infections have reduced by approximately 10 per cent per year since the program commenced.

"Coordinated surveillance is necessary to support prevention activities and to reduce the burden of illness to improve patient outcomes."

In 2018, the Health Act passed that private hospitals were now required to participate in surveillance provided by the VICNISS program.

"The driver was to ensure private hospitals were documenting monitoring activities in a comparable manner to hospitals in the public sector," says Associate Professor Worth.

The system is expanding further with more than 180 of Victoria's public residential aged care facilities also joining the pilot program in 2018 to monitor and report infection rates.

"It's been recognised for a very long time that infections may arise in aged care facilities, which could have implications for hospitals when residents are transferred back and forth."

One of the components of the aged care program is monitoring seasonal influenza vaccination rates of aged care staff.

"We're seeing very high uptake. In excess of 80 or 90 per cent in some of the larger facilities for both staff and residents.

This is an important way that risks for influenza infection can be reduced in this highly vulnerable population."

There's also an emphasis on collecting data on antimicrobial resistant organisms such as methicillin-resistant Staphylococcus aureus (MRSA), carbapenemase-producing Enterobacteriacaea (CPE) and vancomycin-resistant Enterococci (VRE).

VICNISS is now advocating for specific surveillance programs to be implemented into sub acute and rehabilitation facilities.

"We require an integrated approach to understand infection burden in all sectors, as patients may be transferred from acute to sub acute care, and from hospitals to aged care settings," says Associate Professor Worth.

"These transfers may increase the risk of acquiring infections, and therefore become a focus when infection containment and prevention strategies are necessary."

AHEAD OF THE CURVE – IDENTIFYING AND CONTROLLING SUPERBUGS BEFORE THEY SPREAD

Researchers are using DNA analysis to identify potential superbug outbreaks before they become a threat.

Assessing whether genomics could track the transmission of antibiotic-resistant bacteria in real time across multiple hospitals was the focus of a comprehensive study conducted by the Doherty Institute through funding from the Melbourne Genomics Health Alliance.

"The aim of the project was to see if we could identify potential superbug outbreaks before they became a threat, and therefore prevent further infections," explains Austin Health infectious diseases physician and University of Melbourne researcher, Dr Norelle Sherry, the lead clinician on the project.

"The hypothesis was that rapid genomic sequencing of superbugs would enable us to detect transmission in a matter of days, enabling real time action on reducing infection risk.

"Genomics has been used in research for a long time, so we knew we could use it to detect transmission.

"What hasn't been done before is applying this across multiple hospitals and multiple superbugs, and looking ahead; getting all the isolates as they come in, rather than going back after an outbreak has already occurred."

Between April 2017 and November 2018, the team sequenced over 2200 isolates from 1900 patients across four hospital networks in Melbourne.

"By combining genomic information with patient movement data from the hospitals, for the first time we were able to define the number of patients who seemed to have acquired a superbug in hospital," explains Dr Sherry.

"Overall, we found that 648 patients who had a superbug detected while they were in hospital probably acquired it there, rather than in the community. Importantly, most of these transmissions would not have been detected through usual methods.

"We were also able to show that there was more transmission of two common superbugs – Methicillin-resistant Staphylococcus aureus (MRSA) and Extended Spectrum Beta-Lactamases Escherichia coli (E.coli) – than currently thought, really challenging the existing dogma in hospital infection control."

The second phase of the project fed information back to the hospitals to see if they could intervene to stop further transmission.

"There were challenges in communicating really complicated genomic information back to clinicians, and in trying to help them work out how to integrate this genomic data into their infection control programs," says Dr Sherry.

"Through focus groups, we found that infection control teams wanted quite simplified information because they've got so much data coming from different places. This helped us formulate a communications strategy."

The Controlling Superbugs study was led by University of Melbourne Professor Benjamin Howden, Director of the Microbiological Diagnostic Unit Public Health Laboratory, and Professor Lindsay Grayson, Director, Department of Infectious Diseases & Microbiology, Austin Health.

melbournegenomics.org.au

Austin Health infectious diseases physician and University of Melbourne researcher, Dr Norelle Sherry

HERE'S A QUICK SIDE PROJECT BEFORE YOU START YOUR PHD

University of Melbourne Dr Jean Lee, Infectious Diseases Physician and PhD candidate

Staphylococcus epidermidis is the most common bacteria on human skin, found on everyone. Accordingly, it frequently contaminates diagnostic specimens and many doctors dismiss it. However, serious infections can occur.

In 2012, I was an Infectious Diseases Registrar, and University of Melbourne Professor Ben Howden my Consultant at the Austin Hospital. We cared for a patient who was the first recognised case in a series of difficult-to-treat *S. epidermidis* infections. These cases occurred in unrelated patients and were all serious manifestations (such as a brain abscess) that failed therapy with the first line antibiotic treatment, vancomycin.

When I started my PhD in 2014, determining if there was an outbreak was supposed to be a "quick" side project before starting my PhD on a different organism. However, one finding led to another and this became my entire PhD.

Rather than an outbreak, we discovered three lineages of multidrug-resistant *S. epidermidis* were endemic in the Austin Hospital. Surprisingly, the Austin wasn't unique.

These same clones had been globally disseminated for decades, but no one noticed. Some European isolates were even resistant to the last resort antibiotics, making them potentially untreatable.

We found that the mutations causing resistance to the antibiotic rifampicin, that were common to all the clones, also caused vancomycin cross-resistance, explaining why patients failed therapy.

Current guidelines recommend the co-prescription of rifampicin and vancomycin for serious staphylococcal infections, assuming they cross-protect one another. However, our results suggest these guidelines warrant review. These findings were published last year in *Nature Microbiology*.

Our study demonstrates the unintended consequences of antibiotic use, where an ignored colonising organism has evolved to become resistant to all standard treatment options, driven by rifampicin used as general prophylaxis and antibiotics prescribed to treat other organisms. Good antimicrobial stewardship remains key against losing remaining treatment options.

The research done by our group under University of Melbourne Professors Tim Stinear and Ben Howden attempts to bring infectious diseases from the bedside to the bench, using the laboratory and bioinformatics to answer pertinent clinical questions. If we are lucky, our findings come full circle to inform clinical practice.

FIND OUT MORE ONLINE

Scan the QR code to read more about our **Antimicrobial Resistance and Healthcare Associated Infections work.**

HOST-PATHOGEN INTERACTIONS

ERADICATING MALARIA IN THE ASIA-PACIFIC

Researchers are attacking the problem of malaria in the Asia-Pacific region using a multi-pronged research approach.

Ridding the Asia-Pacific region of malaria by 2030 is an ambitious target, but is, nonetheless, the Holy Grail for the $2.5 million National Health and Medical Research Council (NHMRC)-funded Australian Centre of Research Excellence in Malaria Elimination (ACREME), awarded in October 2017.

Each year, more than 200 million people become ill with malaria, and nearly half a million people, mostly children under five, die from the disease.

Based at the Doherty Institute and led by University of Melbourne Professor Stephen Rogerson, a world-leader in the pathogenesis of malaria in pregnant women and young children, ACREME brings together existing research groups across Australia and in Myanmar, Papua New Guinea, Malaysia and Indonesia, amongst other countries. It aims to accelerate the development of better tools to monitor, detect, prevent, and treat malaria to improve health and economic outcomes for regional neighbours.

ACREME is also focussed on promoting collaborative research across the network and, to date, has issued 12 seed grants to postdoctoral and PhD investigators.

"It's important to bring together different groups that might otherwise work in isolation from each other to allow for the cross-fertilisation of ideas," says Professor Rogerson.

As an example of how multidisciplinary research can speed up early drug evaluation and get drugs into clinical trials more quickly, researchers in Brisbane are giving volunteers malaria infection in hospital to test new malaria drugs or vaccines. Blood samples from the volunteers are then used to examine malaria immunity, while statisticians develop models of how the volunteers metabolise the drug.

And that's just the tip of the iceberg.

The clinical aspect of this work in Brisbane is led by Professor James McCarthy who will be moving to the Doherty Institute in April 2020 to become the inaugural Professor/Director of The Royal Melbourne Hospital's Victorian Infectious Diseases Service.

Professor Rogerson says some of ACREME's research will have positive impacts on communities at risk of malaria.

"The thing I'm most excited about personally is the idea of developing new antibody-based surveillance tools, which will allow us to identify the communities where malaria transmission is ongoing, even if we're not seeing the cases," enthuses Professor Rogerson.

"The other area we can make a big difference is in the treatment of vivax malaria, especially getting more people access to drugs that can eliminate the infection from the liver."

Image credit: Pearl Gan Photographer in residence, Oxford University Clinical Research Unit, Vietnam

BEATING BURULI IN VICTORIA

How has a flesh-eating bacterium found in West Africa become endemic on the Bellarine and Mornington Peninsulas in Victoria?

That's the question that's puzzling a team of researchers and public healthcare workers led by University of Melbourne Professor Tim Stinear.

Buruli ulcer (also known as Bairnsdale ulcer) is an infection of the skin and soft tissue caused by the bacterium, *Mycobacterium ulcerans*. The toxin made by the bacteria attacks fat cells under the skin, which leads to localised redness and swelling or the formation of a nodule (lump) and then an ulcer. Although Buruli ulcer is not fatal, the infection can often leave people with significant cosmetic, and sometimes functional, damage to limbs.

In the last 10 years, annual cases in Victoria have increased by 1000 per cent.

"We've been studying the Buruli ulcer for more than 20 years now and we have strong evidence to suggest that mosquitos are vectors of the disease and possums are a wildlife reservoir," explains Professor Stinear.

Professor Stinear is leading a world-first transmission intervention study to stop the spread of the bacteria. The project is funded by the National Health and Medical Research Council (NHMRC). He is working in partnership with other investigators at the Doherty Institute, Barwon Health, Austin Health, CSIRO, Agribio, the University of Melbourne, Mornington Peninsula Shire, and Victoria's Department of Health and Human Services.

Based on a series of epidemiological, field and laboratory-based studies, the *Beating Buruli in Victoria* project aims to actively disrupt disease transmission for the first time and to develop policies and guidelines based on evidence that can help stop the spread around Victoria and even globally.

"While we have made major advances in detecting and treating Buruli ulcer, there remain major questions to resolve around disease transmission.

"Our hypothesis is that targeted mosquito control in Buruli ulcer-infected areas will substantially reduce the incidence of disease in humans."

Since the inception of the study in late 2018, Professor Stinear and his team have been systematically collecting possum faecal material from across the Mornington Peninsula. They have collected possum 'poo' from over 2000 sites between Portsea and Rosebud and are testing these samples for *Mycobacterium ulcerans.*

"We are showing the clear, positive correlation between areas where possums are carrying the bacteria and humans are getting Buruli ulcer."

In addition, the team are also continuing mosquito surveillance activities to test for the bacteria, while they plan for the mosquito control component of the study.

"When we have a disease outbreak, we have an obligation to the human population to control that disease. What we are trying to do is balance the need to control a devastating disease while minimising environmental impacts."

University of Melbourne Professor Tim Stiner and colleagues collecting possum faecal material on the Mornington Peninsula

UNDERSTANDING THE DRAMATIC RISE OF TYPHOID FEVER IN FIJI

A Typhoid Taskforce hunts for research clues about why Fiji has become a hot spot for typhoid and whether a vaccine could eradicate the problem.

Typhoid fever has been endemic in Fiji for many decades, but the incidence increased in the mid 2000s. This bacterial infection is caused by *Salmonella enterica serovar Typhi,* which can be transmitted either directly among humans or from infected humans to the environment and then back into humans.

"In the middle of the 2000s there was a big uptick in case numbers," says University of Melbourne Professor Dick Strugnell.

"It wasn't clear whether the incidence went up because the surveillance was better or because it was more infectious."

Professor Strugnell is part of a research taskforce working with the Murdoch Children's Research Institute and the Fiji Ministry of Health and Medical Services that's trying to work out why case numbers have risen so dramatically.

"The disease has a very strange epidemiology. If you test Fijians blind to their ethnicity, the serological footprint of disease is the same," explains Professor Strugnell.

"However, when you look at the clinical records, it's only the iTaukei Fijians who are presenting with the disease. There's an anomaly we don't understand."

Through the collection of isolates, University of Melbourne researcher, Dr Mark Davies, has conducted genomic analysis of the bacteria collected by the Typhoid Taskforce and found two major strains.

"We've now got quite a complex picture of how the disease is being transmitted and we're not seeing much antibiotic resistance, which is the good thing," says Professor Strugnell.

"There's a global strain circulating that's becoming increasingly resistant to commonly used antibiotics."

Most recently, the focus of the Taskforce has been on understanding local transmission, the role of the environment in transmission and hot spots of disease.

This work is being conducted by University of Melbourne PhD candidate, Dr Aneley Getahun, in collaboration with staff of the Fiji Ministry of Health and Medical Services.

Dr Getahun is a public health physician. One of her roles is to visit the households of typhoid patients identified in hospitals to understand the risk factors associated with the disease.

"We see a lot of people who live with very limited resources where there is overcrowding and poor sanitation," says Dr Getahun.

Professor Strugnell says the biggest opportunity to reduce numbers of typhoid cases in Fiji is to implement a new vaccine.

"The Typhoid Taskforce is working with the International Vaccine Institute in Seoul to implement a new vaccine approved by the World Health Organization, called the typhoid conjugate vaccine. Ideally, we'll endeavour to vaccinate everyone on Vanua Levu and then study the impact on the disease as a means of trying to eradicate it."

Typhoid Taskforce in Fiji

IT TAKES A GLOBAL RESEARCH EFFORT TO FIGHT AGAINST INFECTIOUS DISEASE IN RESOURCE-LIMITED COUNTRIES

By University of Melbourne Dr Sarah Dunstan

Enthralled by infectious diseases, I left the University of Melbourne after my PhD, studying typhoid fever in model systems, to begin a post-doc to study the human genetics of typhoid in "actual" people.

My change in country, and in research direction, coincided with the modern-day metamorphosis of human genetics, that is, the release of the first human genome sequence. A steep learning curve ensued as I grappled with the enormity and possibilities that the genomic era brought, but still, my focus on infectious disease was ever present.

The disease burden of typhoid fever falls squarely in resource-limited countries, so to get closer to the source, I moved myself, and my research, to Asia. Once working in Ho Chi Minh City, on the site of the largest infectious diseases hospital in southern Vietnam, my eyes were opened (wide!).

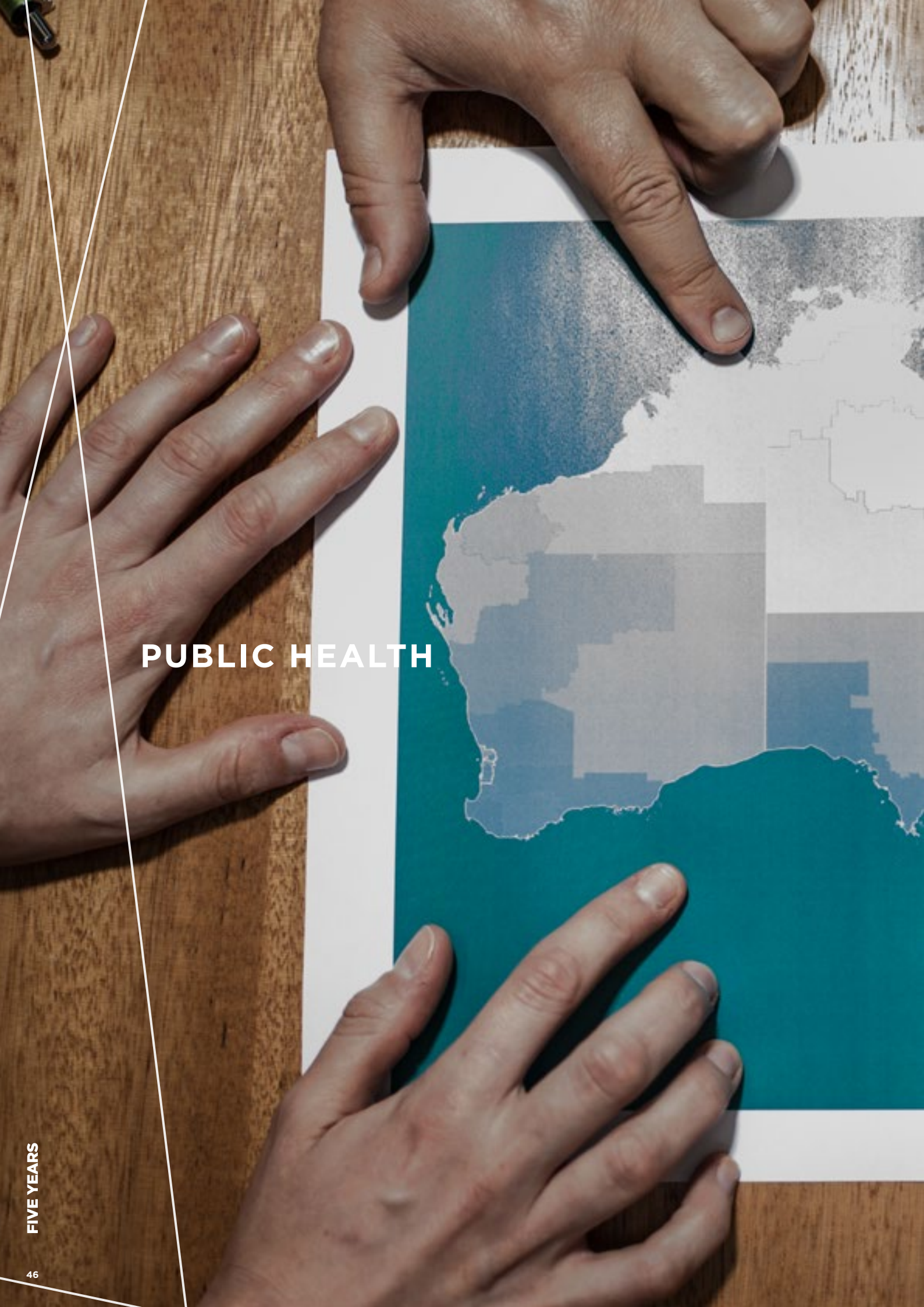
A basic laboratory scientist, working in a clinical environment, brought about steep learning curve number two, and a plethora of possibilities. We formed teams of multidisciplinary researchers working on the one patient cohort, and realisation set in that the only way to make a dent on enormous global disease problems, such as tuberculosis (TB), is with a collective of diverse minds tackling the problem from all directions.

Now at the Doherty Institute, the centre of gravity of my research on typhoid and TB remains in Asia. My research utilises genomic technology to interrogate the pathogen and host to acquire critical new knowledge that can be exploited to develop essential new tools for disease control. I recently led a team to show how drug resistant strains of TB can spread in different cities.

I am part of this diverse global research effort, working closely with multidisciplinary partners, to advance the fight against infectious disease in high burden, resource-limited settings.

FIND OUT MORE ONLINE

Scan the QR code to read more about our **Host Pathogen Interactions work.**



PUBLIC HEALTH

PREPARING FOR THE NEXT PANDEMIC

Pandemics are inevitable. So a group of researchers across Australia is taking a multidisciplinary approach to ensure we have vital systems in place to improve our response.

While we can't predict what the next pandemic will be, we can prepare for it. That's the focus of the $5 million National Health and Medical Research Council (NHMRC)-funded Centre of Research Excellence titled the Australian Partnership for Preparedness Research on Infectious Diseases Emergencies (APPRISE).

Awarded in 2016, APPRISE brings together Australia's leading experts in clinical, laboratory and public health research to address the key components required for a rapid and effective emergency response to infectious diseases.

"You have to prepare in advance. You can't do this sort of research on the run when an emergency happens," explains University of Melbourne Professor Jodie McVernon, a member of the executive leadership group of APPRISE and Director of Doherty Epidemiology.

"You need to establish relationships, begin to ask the questions and test the research in what we call "peace time", which is the time between emergencies. That way, you're ready to activate the response in the case of an emergency.

"Despite large numbers of travellers coming to Australia, Australia had no cases of Ebola or Zika virus disease during the global outbreaks, for example, but the threat of deadly infectious disease outbreaks happening closer to home is very real."

Comprising 20 investigators across the country, APPRISE research is categorised in four broad areas – clinical research and infection prevention; public health research; laboratory research; and key populations.

"One of the key projects our team have been working on is a pre-approved set of protocols to conduct research in an emergency outbreak setting. These protocols are approved for severe respiratory illness. Importantly, the protocols can be amended if the outbreak is of a completely different nature, such as gastroenteritis," says Professor McVernon.

Members of the APPRISE team are also developing relationships with various Aboriginal and Torres Strait Islander groups to understand community connections that allow for research to be conducted.

"During the 2009 H1N1 pandemic, Indigenous people were at higher risk of severe influenza. So it's important we have approved ethics and protocols created in partnership with Aboriginal and Torres Strait Islander populations and ready for when a pandemic strikes again," says Professor McVernon.

"I have been working with other members of APPRISE to form citizens' juries where tricky ethical issues are discussed with people in the community, such as the allocation of a limited supply of influenza vaccine – who will get it first in the early stages of an emergency? It's really important research to understand preconceived ideas around this issue of allocation.

"We have many projects, initiatives and partnerships in progress, but they are all designed to make sure Australia has the best people and systems ready to go so our research can produce rapid and meaningful improvements in our ability to save lives during future infectious diseases emergencies."

REVOLUTIONISING PUBLIC HEALTH THROUGH GENOMICS

Sequencing the entire genetic content of organisms has transformed public health microbiology and given researchers powerful tools to improve health globally.

"Techniques that have been in labs for nearly one hundred years have now been superseded by genomics," explains University of Melbourne Professor Deborah Williamson and Director of Clinical Microbiology, The Royal Melbourne Hospital at the Doherty Institute.

"It's also a massive shift for the people we generate the information for, such as epidemiologists, as it means they now have unprecedented insights into how outbreaks emerge and spread, which can help enormously in outbreak investigations."

A genome is the complete genetic content of an organism. Using cutting edge sequencing technologies and analyses of all the biological data, it has become easier, quicker and cheaper to sequence organisms.

University of Melbourne Professors Tim Stinear, Ben Howden, Deborah Williamson and Associate Professor Torsten Seemann at the Doherty Institute have led translational research to bring genomics into the clinical and public health microbiology interface.

This approach was employed when the Victorian Department of Health and Human Services asked the Microbiological Diagnostic Unit Public Health Laboratory (MDU) at the Doherty Institute to search for any contamination of a specific type of hospital equipment with a bacterium called *Mycobacterium chimaera.*

As part of a global investigation of heater/cooler machines used in cardiac surgery, MDU staff investigated whether machines in Victoria were contaminated with *Mycobacterium chimaera* and if so, whether the strains (also known as isolates) were the same as those found nationally and internationally.

"We were sent isolates from all over Australia, and thanks to our high throughput sequencing and working with Professor Stinear, an expert in mycobacterial genomics, we were able to rapidly determine that they were all the same," says Professor Williamson.

"The Centers for Diseases Control in the US had also detected the bacteria in Pittsburgh and we soon determined that the Australian isolates were also genetically identical. This wasn't just a national outbreak we were dealing with, it was a global outbreak.

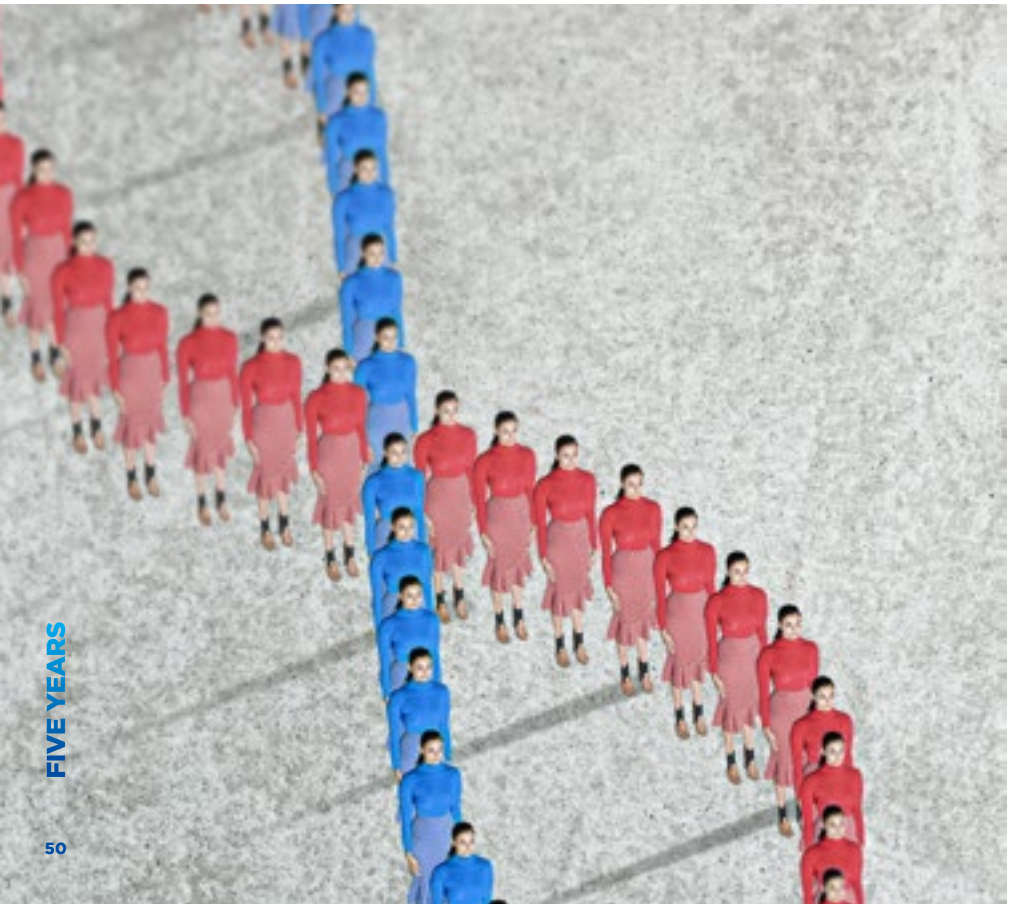
"It changed the way we thought about that outbreak, as we knew definitively it was a point source outbreak."

Another significant impact genomic technology has had on public health in Victoria in the last two years is in tracking tuberculosis. This work brings together several departments across the Doherty Institute.

"We meet with staff from these departments once a month to talk about the results. It is a great model for how laboratories, those involved in public health policy and practice, and clinicians can work together to prevent and control infectious diseases," says Professor Williamson.

In 2015, MDU established the Communicable Diseases Genomics Network in Australia, which aims to ensure equity in the sharing of expertise and capabilities across different jurisdictions, recognising that some are better resourced that others.

"We want to make sure genomics technology benefits all patients in Australia."



IMPROVING THE HEALTH OF PEOPLE WITH TUBERCULOSIS IN VICTORIA

Tuberculosis (TB) causes more deaths globally than any other infectious disease. But here in Australia, we tend to think TB is not really a problem. But is that true?

It might perhaps come as a surprise to many that each year there are approximately 450 new diagnoses of TB in Victoria.

"Most of the people I talk to in Australia think that TB isn't a thing anymore," says Associate Professor Justin Denholm, Medical Director of the Victorian TB Program at the Doherty Institute.

"That invisibility is testament to the 60 plus years of dedicated and consistent public health work in Australia to bring TB under control.

"But the reality is, 11 million people contracted TB globally last year, and nearly 1.8 million died.

"In a global society there is a lot of movement, so part of our role is in making sure people are aware of some of the risks of TB and identify opportunities to prevent them getting sick."

The Victorian TB Program is the state wide provider of public health services relating to TB, such as patient management and care, disease surveillance, and working with hospitals and general practitioners to help them support their patients.

"Being a part of the research and collaborative environment at the Doherty Institute over the last five years has placed the Program in a unique position in Australia. Researchers have the ability to apply a range of research approaches to significantly improve health outcomes for people," says Associate Professor Denholm.

In 2018, the Program was working with a patient who had a form of drug resistant TB and was experiencing a range of side effects to their complicated treatment.

"We were able to sequence the mutation here at the Doherty Institute. Then in collaboration with a PhD student working with us and at the Bio21 Institute, we built a computer model of that mutation and demonstrated that it was resistant to a certain drug – never shown before," explains Associate Professor Denholm.

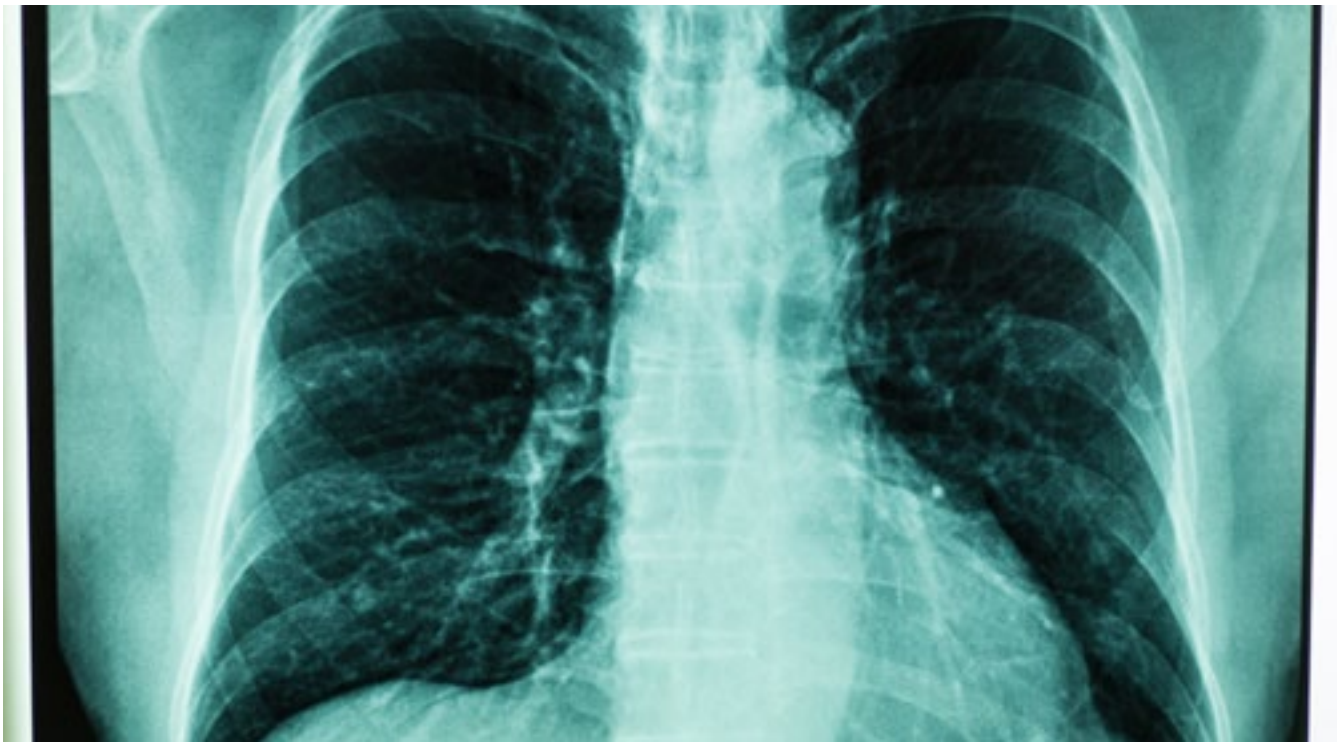
"This all happened in real time and the patient was safely cured of her TB."

The implementation of routine whole genome sequencing has been a game changer.

"We had a husband and wife who had just arrived from a country where TB is a high burden and both received a positive diagnosis," says Associate Professor Denholm.

"The natural assumption was that one person had contracted it from the other but through sequencing, we found they had two completely different strains that required different management."

The Program is considered a centre of regional expertise and is involved in building capacity internationally. Locally, they're also involved in new education development programs to up skill nurses and other healthcare workers with training and operational research.



IDENTIFYING A POLIO OUTBREAK IN PAPUA NEW GUINEA

A World Health Organization (WHO) laboratory based at the Doherty Institute was central to the global public health response during the polio outbreak in Papua New Guinea (PNG).

Thanks to the oral polio vaccine, the eradication of poliovirus transmission in all but three countries is one of modern medicine's greatest success stories.

So when a six-year-old from PNG tested positive to poliovirus in May 2018, there was cause for concern.

The Doherty Institute is home to the WHO Polio Regional Reference Laboratory and also acts as the National Polio Reference Laboratory for PNG. As part of its role, the Laboratory routinely receives stool specimens from cases of polio-like illness (acute flaccid paralysis) in children to monitor the country's polio-free status.

The lab, run by Associate Professor Bruce Thorley, conducted tests of specimens from community contacts of the positive case in PNG and confirmed it as circulating vaccine-derived poliovirus (cVDPV), which is caused by the virus in the oral polio vaccine.

"The polio vaccine is a weakened form of the virus which induces immunity and should not cause disease," explains Associate Professor Thorley.

"However, if the vaccine strain replicates in settings with low rates of polio immunisation, it can slowly mutate and then it starts to cause disease.

"Vaccine coverage in PNG has been as low as 40 per cent, while you need more than 90 per cent of the community vaccinated to protect against this happening."

Following the confirmation, an international public health response ensued to raise the polio vaccine coverage in PNG and to increase surveillance for cases of acute flaccid paralysis.

Over a 15-month period, Associate Professor Thorley and his team tested more than 1300 stool specimens and identified 26 cases of polio due to the outbreak.

At the time of writing, the polio outbreak was expected to be declared over soon.


22.8
SPEC

WORKING IN THE HIGH CONTAINMENT LABORATORY

By Dr Leon Caly, Safety Officer in The Royal Melbourne Hospital's Victorian Infectious Diseases Reference Laboratory

The phone rings and the person on the end of the line is a clinician, saying they have a returned traveller in the clinic from Sierra Leone with suspected viral haemorrhagic fever and the samples are on the way over to us. It's not as dramatic as you see in the movies but suddenly, we have to stir into action.

It takes us about 60 minutes to get ready. The first thing we have to do is pre-entry checks; it's similar to an airline pilot before they do the pre-boarding – we have to ensure that everything that supports us is functional so we're safe. For example, we check that the laboratory is under negative pressure, ensuring air only flows inwards. We check the breathing air compressors are running, that there's air in the tanks, and back-ups. We do a visual check of the lab to make sure everything we need is there as once we are in it is a lengthy process to get out again. We check the chemical shower to make sure there's enough disinfectant for when we shower out in our suits. Finally, we check that the liquid waste system is ready to accept waste.

Next, it's time to suit up. They're really heavy, so they're hard to handle until you're connected to the breathing air. Once connected, the suits inflate and they essentially self-support, and then you're weightless. It's surreal, euphoric, like when you are under water; it's like a different world.

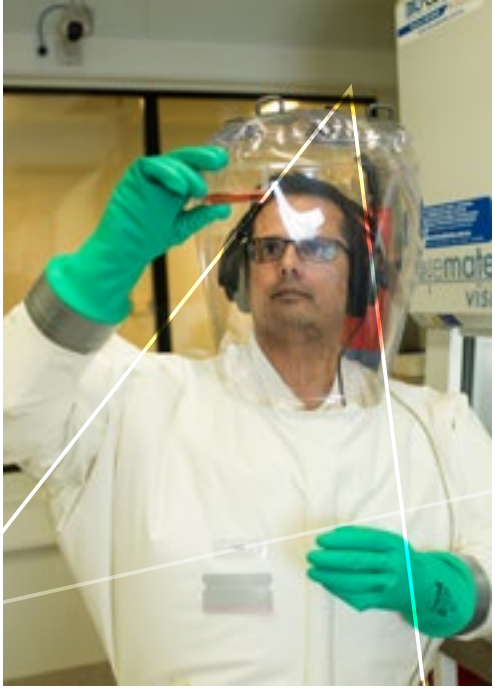
When you're inside the lab working, the passage of time seems to speed up. You might be in there for four hours, but it only feels like an hour and a half. It's because you're so focussed on what you're doing and your mind is constantly engaged. You don't even think about the high threat pathogens you're working with. We do so much training that it becomes second nature.

But what we do get nervous about are bathroom breaks, so we try not to drink too much coffee.

As the only high containment laboratory for human diagnostics in Australia, working in this environment is a highly rewarding experience.

FIND OUT MORE ONLINE

Scan the QR code to read more about our **Public Health work.**



INDIGENOUS HEALTH

CREATING MEANINGFUL PARTNERSHIPS WITH ABORIGINAL COMMUNITIES

Before even starting research projects, Doherty Institute researchers embrace fundamental principles to guide their work with Indigenous communities.

Respected Wurundjeri elder, Aunty Joy Murphy Wandin AO, posed a challenge at the opening of the Doherty Institute in 2014: *"What will this Institute do to improve the health of Aboriginal Australians?"*.

This challenge set the scene so that future projects would be guided by principles that would give the research the best chance of contributing to the body of knowledge and translating into clear benefits for Aboriginal Australians.

One of the most important principles is for researchers and healthcare workers across the Doherty Institute to collaborate with Aboriginal communities.

Research fellow, University of Melbourne Dr Simon Graham, says its essential to collaborate with Aboriginal communities to ensure the design and application of research findings have the best chance of success.

"A mistake many research projects make is to have a group of non-Aboriginal academics as investigators and then a sub-committee of Aboriginal people to provide advice," says Dr Graham.

"For success, it is best to follow the approach of *'nothing about us, without us'* and have Aboriginal people as senior investigators.

"Supporting the mentorship of Aboriginal trainees on research projects is also extremely important to further develop and enhance their research skills."

Doherty Institute staff are also guided by the principle to respect the values, history, culture, language, diversity, and context of the communities with which they work.

Continuous, clear communication and regular visits to communities is also essential.

"Projects must conduct regular community visits to ensure meaningful and respectful time is dedicated towards hearing the needs of communities related to the projects," says Dr Graham.

The Doherty Institute has committed to be transparent and accountable for the impact of its work and maintains the highest ethical standards, adhering to the guidelines of the Lowitja Institute and the National Health and Medical Research Council.

Each year, the Doherty Institute hosts an Indigenous Health forum titled *From Bush to Bench*, featuring speakers with strong links to various communities. Previous speakers have included community-based researchers from Galiwin'ku and Jonathan Lindsay-Tjapaltjarri Hermawan, Strategic Advisor and Strong Men and Boys Program Manager for Red Dust Role Models.

From *Bush to Bench* Indigenous Health Forum 2019

PREVENTING SKIN INFECTIONS WOULD SOLVE OTHER MAJOR HEALTH PROBLEMS IN REMOTE COMMUNITIES

Skin infections have major long-term impacts on health in remote Indigenous communities across Australia. Doherty Institute researchers are working with communities and using a range of research approaches to reduce the risk of skin infections and decrease the use of antibiotics.

Between 40 and 50 per cent of school-aged children in some remote communities have a skin sore at any one time, and three-quarters of adults visit a clinic with a skin infection at least once each year.

"Skin sores can lead to complications of rheumatic heart disease, a long-term chronic condition linked to premature mortality and the need for open heart surgery," says Royal Melbourne Hospital Clinician Researcher at the Doherty Institute, Associate Professor Steven Tong.

Skin infections also increase the use of antibiotics and this creates antimicrobial resistance that feeds back to exacerbate problems related to treatment of infections.

"Kids are going to clinic every two weeks in the first year of life and having up to six courses of antibiotics in that first year," says Associate Professor Tong.

"So there was a high rate of antibiotic use and a lot of it seemed to be driven by skin infections. Preventing these infections so that antibiotics aren't needed is a real priority,"

Associate Professor Tong and University of Melbourne Professor Jodie McVernon, in collaboration with the Menzies School of Health Research in Darwin, are currently combing through historical data with the aim of forming a more complete picture of the issue.

"When we combine all that with new data we're collecting about social relationships between families and households in remote communities, we can generate a much richer story about the way infections are transmitted," explains Professor McVernon.

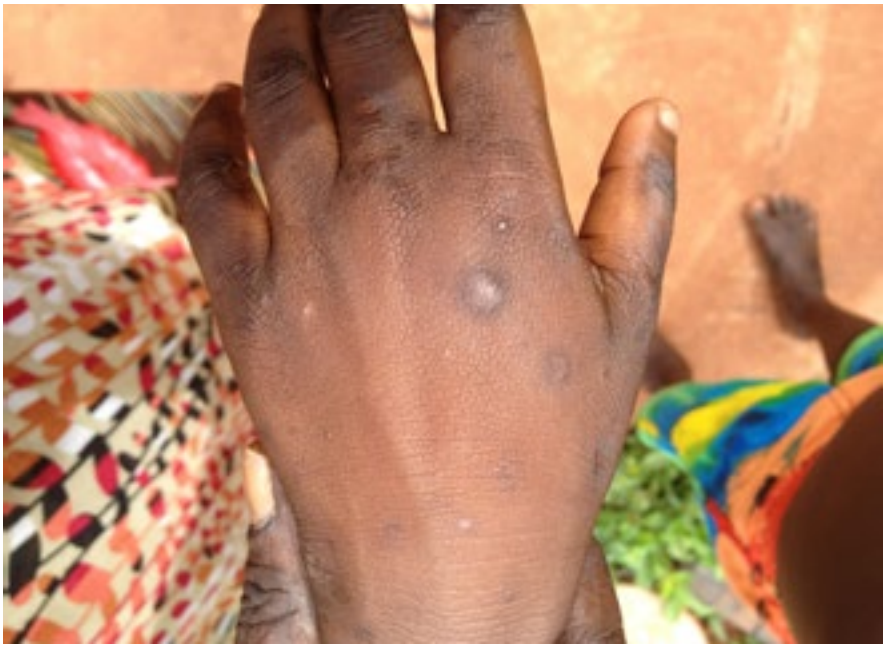
"This understanding helps us to think with communities about types of interventions that might be more effective at preventing repeated infections."

The researchers are hoping to quantify some of the transmission events to create meaningful advocacy and drive holistic models of change within communities.

The project has created new opportunities for collaborations including with One Disease, a not-for-profit organisation that aims to eliminate crusted scabies. Crusted scabies is a severe and highly contagious form of scabies present in some remote Indigenous communities across Australia.

"We're working with One Disease to quantify the contribution of crusted scabies to the overall risk of infection in households and communities. We'll use this information to inform future discussions around two main areas – mass drug administration and a vaccine for Group A Streptococcus – and how they might best be used as part of a suite of interventions," says Professor McVernon.

"There are a number of different vaccines at various points along the pipeline. We're working with others to understand how immunity from vaccines differs from natural immunity after infection, and how good natural immunity is at preventing repeat infections. Having that data and analysis will hopefully inform design and use of such vaccines."



RESEARCHERS WORKING HARD TO PUT VIRAL INFECTION ON THE GLOBAL RADAR

A virus related to HIV is affecting remote Indigenous communities and researchers are driving the global push to find a treatment.

There's no treatment or cure for HTLV-1, a virus related to HIV that causes a disproportionally high infection rate in remote Aboriginal communities.

HTLV-1 – Human T-cell lymphtrophic virus – is from a similar family of viruses as HIV, but its pattern of disease is very different.

While most people do not become sick from the virus, infection can lead to neurological diseases and blood cancers. Infection can also suppress the immune system, although how this works needs further study.

In Alice Springs hospitals, 34 per cent of Indigenous people have tested positive for HTLV-1, and this figure is almost 50 per cent in older men.

Following a special symposium on HTLV-1 at the Global Virus Network's 9th International Meeting at the Doherty Institute in 2017, University of Melbourne Professor Damian Purcell was one of a team of researchers and advocates from across the globe to pen an open letter to the World Health Organization, published in *The Lancet*, calling for an end to HTLV-1.

"There's an opportunity to prevent transmission of HTLV-1, but it's not even on the table in Australia or globally as a major issue," says Professor Purcell.

In addition to his advocacy for more research on this important virus, Professor Purcell is also studying the virus and pursuing treatments and the potential of a vaccine for HTLV-1.

Research conducted by Professor Purcell and his team has found that the virus infecting Aboriginal people is a unique strain, and they've identified opportunities to develop preventative drugs.

"We've got the first signs that some of the newer HIV drugs can also prevent transmission of HTLV in a mouse model, but we need to find out more," says Professor Purcell.

"We've also been able to identify that infected patients can harbour powerful antibodies that are able to block the infection process. That tells me we have the potential to develop a monoclonal antibody that can prevent transmission."

Professor Purcell is part of a $4.2 million long-term study funded by the Commonwealth Government, which will investigate the proportion of people in Indigenous communities with HTLV-1 infection. The researchers will study what percentage of cells are infected with HTLV-1 and if the amount of virus is related to poorer health outcomes or even death.

"We need to offer men and women in remote Australia the same opportunities that people living with HIV have been given in preventing a virus that could alter their health significantly."

ACHIEVING EQUALITY IN HEALTH FOR YOUNG ABORIGINAL CHILDREN

University of Melbourne Dr Sarah Hanieh, Post-Doctoral Research Fellow, Global Health group

I'll always remember the day that I met Lisa*. I had just flown into a remote community in Arnhem Land. A community synonymous with red dust, crystal blue waters, and baru (crocodiles).

As I held discussions with our recruited local community health workers about the new project on child nutrition we would be starting together, I remember seeing Lisa out of the corner of my eye.

Lisa was busy drawing in colourful texta pen all over the arm of one of our volunteer co-workers from Melbourne, who happily obliged as her human canvas with his outstretched arm. One of the community health workers told me that this was her adopted daughter, Lisa. She told me that Lisa was four years' old, she loved drawing, and she was 'a bit slow'.

Taking a closer look at Lisa, I could see that she was significantly short for her age. Her adopted mother told me she hadn't had breakfast, which was 'normal'. Lisa was chronically malnourished.

Over the next eight weeks of our field study, Lisa became an important part of our team. She joined us every morning at our group meeting, eating a bowl of Weetbix on the ground and charming us with her beautiful drawings, as we discussed our strategy for the day. Overtime, we began to gain a better understanding of all the factors (present and historical) that may have contributed to her poor growth.

It's a jarring experience to see chronic malnutrition right in front of your eyes, and realise that it still exists within our wealthy and 'lucky' country. A child who is chronically malnourished is likely to have impaired cognitive development resulting in poorer learning outcomes, reduced educational opportunities and reduced earning capacity as an adult.

They also have a significantly increased risk of developing chronic diseases in adulthood such as diabetes, obesity and heart disease.

My experience in Arnhem Land changed the focus of my research. My goal now is to contribute to achieving equality in heath for young Aboriginal children through a better understanding of all the many layers of factors contributing to chronic undernutrition. We know that environmental, socio-economic factors and dietary patterns have an important influence on a child's growth, however underneath these layers it is also important to acknowledge the contribution of some of the more hidden or 'invisible' pathways to malnutrition in Aboriginal Australia (for example the impact of structural violence). Secondly, to ensure that there is effective translation of research outcomes into sustainable, culturally safe and coordinated programs that provide ownership at the community level.

Because doesn't every child deserve the same opportunities in life?

FIND OUT MORE ONLINE

Scan the QR code to read more about our **Indigenous Health work.**

*name has been changed

EDUCATION AND PROFESSIONAL DEVELOPMENT


500 µm
Image represents all 3 lipid species in one
Blue to yellow hue represents the lowest
Significant increase in PC, PE and Lyso-PE

HOLISTIC SUPPORT FOR OUR NEXT-GENERATION INFECTION AND IMMUNITY WORKFORCE

The Doherty Institute provides students with career and personal development that expands beyond their research projects.

In any given year, the Doherty Institute is home to approximately 120 PhD students, but while many continue to travel the research career path, others have different career aspirations.

In recognition of this, the Doherty Institute PhD Program was established in 2017 to provide students with the opportunity to supplement their research training in their primary discipline with extracurricular professional development.

Since then, more than 140 graduate research students (MSc and PhD) have been enrolled and 30 workshops have been delivered. The workshops span topics such as science communication, bioinformatics, computer programming, curriculum vitae and interview preparation, and poster and abstract writing. Career events also help students explore different employment sectors.

"The PhD Program trains candidates in a broader sense than their chosen research project and we try to equip them with skills for various employment sectors," says Program Co-Leader, University of Melbourne Professor Dick Strugnell.

"These skill sets will give them a competitive edge that sets them apart from the crowd."

The Program is the only PhD Program across the Melbourne Biomedical Precinct that benefits from access to an Industry Advisory Committee made up of key partners working in biopharmaceutical-linked industries such as CSL Limited and GlaxoSmithKline Australia.

"The Advisory Committee expertise helps tailor the content of workshops to ultimately assist with employment beyond the pure research environment," says Program Co-Leader, University of Melbourne Professor Tim Stinear.

The Program closely engages and plans activities with the student representative group, SPASIM, and has collaborative relationships with Women in Science Parkville Precinct (WiSPP) and other PhD Programs across the Precinct, including at the Walter and Eliza Hall Institute and the Victorian Comprehensive Cancer Centre.

"Joining forces with the different PhD Programs and other professional development initiatives adds different layers of expertise that enable us to implement a wide range of program offerings, and to provide an inclusive and open learning environment where graduate researchers can network with others from similar disciplines," says University of Melbourne Dr Marie Greyer, PhD Program Officer.

Providing resources towards better mental health for graduate researchers, an issue for many PhD candidates, has been a key initiative of the Program.

SPASIM President and University of Melbourne PhD candidate, Ashley Hirons, notes that, "Support with mental health is immensely important, helping students to survive and thrive throughout their PhD."

MY EXPERIENCE OF THE DOHERTY INSTITUTE'S PHD PROGRAM

By Anjaleena Anthony, Applications Specialist/Territory Manager at Promega Corporation

I received my PhD from the Doherty Institute in University of Melbourne Professor Stephen Rogerson's laboratory, working on the immunology of malaria in pregnancy.

I'm now working as an Applications Specialist at Promega Corporation, a global leader with a portfolio of more than 4000 research and development products, that provides innovative solutions and technical support to life scientists in academic, industrial and government settings. My role is a perfect blend of scientific communications, administration, customer service and travel.

Participating in the Doherty Institute's PhD Program was an easy and an obvious decision for me because I was always interested in transitioning my career from academia to industry.

Throughout the Program, I attended several workshops that included learnings around intellectual property and business skills, but undoubtedly my most favourite was the session on interview/resume skills. This is because it was a one-on-one discussion with the invited industry experts and was a critical eye opener for students at an early career stage.

I learned a lot of important skills during the PhD program, including how to structure a CV correctly to industry standards and the language to use in a cover letter, how to deliver everything briefly on one page and still be able to tell your story. I also developed my communication skills and was made more aware of how to polish my soft skills.

My advice to students is that even if you're the best student in the lab, it's worth being exploratory, open-minded and flexible with your career. At least try and attend two to three career-building workshops a year, if not more. It's the best way to test your skills, because sometimes you don't know what you want to do next or what sort of skills you might develop. Be proactive, opportunistic and manage your time around your lab work and designing your next career steps.

WORLD HEALTH ORGANIZATION PROGRAMS TRAIN PEOPLE AND BUILD CAPACITY GLOBALLY

WHO influenza workshop in action at the Doherty Institute

World Health Organization (WHO) centres and laboratories based at the Doherty Institute are part of the global effort to enhance capabilities related to infectious diseases.

The Doherty Institute is home to three WHO Collaborating Centres and three WHO Regional Reference Laboratories. Each of these WHO-designated centres and laboratories have an important role to play in training and capacity building in the countries and regions they serve.

For influenza, the WHO relies on designated National Influenza Centres (NIC) across the globe to collect virus specimens and perform preliminary analyses. These data ultimately determine the composition of the seasonal flu vaccine for the Northern and Southern Hemispheres.

"In recent years, isolating and characterising some subtypes of influenza has become challenging using our standard laboratory tests," says Professor Patrick Reading, an Educator for the WHO Collaborating Centre for Reference and Research on Influenza.

"This prompted the Centre to develop initiatives to support and enhance the capabilities of the NICs in the Asia-Pacific region to generate and analyse viral isolates."

In late 2016, the Centre developed and organised an External Quality Assessment (EQA) program with the WHO Regional Offices for the Western Pacific and South-East Asia. The EQA tested the capacity of NICs in these regions and was followed by a week-long workshop the following May held at the Doherty Institute.

The EQA program has expanded to include NICs in the WHO Africa Region, Americas Region and Eastern Mediterranean Region and is now coordinated by the Doherty Institute-based Centre together with WHO Headquarters in Geneva.

The Centre regularly hosts staff from NICs and public health laboratories around the world for training in aspects of influenza detection and characterisation. In addition, Centre staff also travel to provide in-house training within overseas NIC laboratories.

As another example of global impact, the WHO Regional Measles and Rubella Reference Laboratory at the Doherty Institute also works to build capacity to fight measles. The Laboratory ran a workshop on the development of national proficiency testing schemes and the performance of measles enzyme immunoassays in May 2019. The objective of the workshop was to sustain the quality of measles and rubella laboratory networks in countries with multiple laboratories, including India, Indonesia and Thailand.

RESEARCH COLLABORATIONS BETWEEN AUSTRALIA AND GERMANY THRIVE AT THE DOHERTY INSTITUTE

An innovative international postgraduate training program enhances student opportunities and promotes ties between Europe and Australia.

The Bonn Melbourne Graduate School in Immunology is a joint PhD training program in immunology between the University of Melbourne at the Doherty Institute and the University of Bonn in Germany. Established in 2016, the program brings together scientists and students from both countries.

"Bonn University has expertise in innate immunity, while our Melbourne-based researchers complement this expertise as world leaders in the research of adaptive immunity," says Program Director, University of Melbourne Professor Sammy Bedoui.

"The ability to join forces provides an excellent opportunity to deliver basic and applied science, and to maximise our success in combatting infectious diseases or cancer."

The Graduate School currently has over 60 graduate researchers and more than 30 participating supervisors in both locations. PhD candidates typically spend two years of their PhD at their home institution and one year at their partner institution.

"Our students are highly competitive candidates and the research output in this program has been fantastic," says Melbourne Coordinator of the Program, University of Melbourne Dr Marie Greyer.

"We have had over 40 publications in high-ranking journals, more than 16 student awards, and most recently, the first cohort of doctorate students have also submitted their theses at the three-and-a-half-year mark. This is an important milestone and we are incredibly proud!"

In recognition of its innovation, international engagement and training of the next generation of scientists, the University of Melbourne awarded the Bonn Melbourne Graduate School in Immunology with the Excellence Award for Internationalisation of Research in 2018. In 2017, the Federal Ministry of Education and Research in Germany also awarded €650,000 to establish a second exchange program called "BM-AXIS" to encourage additional research collaborations in the clinical arena between Australia and Germany.

The Graduate School is supported by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) and the University of Melbourne through the International Research and Research Training Fund (IRRTF), with a total of AUD$10 million in funding until 2020, and a current bid to have this funding extended for another four-and-a-half years.

FIND OUT MORE ONLINE

Scan the QR code to read more about our **Professional Development work.**

Bonn Melbourne Graduate School in Immunology participants and supervisors in St. Goar, Germany

PHILANTHROPY

DONOR IN THE SPOTLIGHT - FIONA GEMINDER, VISY

WHAT INFLUENCED YOUR CAREER AND LED YOU TO PROFESSIONAL SUCCESS?

I grew up in a family business. My grandparents founded the business in 1948. My parents, most notably my father, took over the packing business in 1969 and now my brother, my sister and I own VISY; inheriting it when my father died in 2009.

I always knew I would go into the family business. Before I joined VISY, I worked in advertising and marketing in London, New York and Melbourne and I also completed a Law degree at Monash. I was born into business and I bring my own take on it to the executive team.

WHAT INSPIRES YOUR PHILANTHROPY?

Philanthropy runs in our family. My parents established the Pratt Foundation in 1978 when I was just a teenager. Like many immigrants who had become successful in Australia, they had a strong belief in giving back to the community. I was surrounded by this from a very young age and it is something that I instil in my own children who are already active philanthropists. It is in our DNA. VISY staff and customers are a constant inspiration to me. A big focus of my philanthropy are the VISY customer and employee's local and national philanthropic initiatives – from fun runs all the way up to medical research and legal aid.

WHAT INSPIRED YOU TO GENEROUSLY SUPPORT THE DOHERTY INSTITUTE?

Professor Sharon Lewin AO and I have been friends for decades. She is a remarkable medical researcher so this latest collaboration with the Pratt Foundation makes a lot of sense. We began the conversation over coffee and she spoke about the latest research she was doing in HIV cure, which sparked my interest. I then came to the Doherty Institute to see first-hand what she and her team were working on.

WHAT DO YOU HOPE TO ACHIEVE THROUGH YOUR SUPPORT OF THE DOHERTY INSTITUTE?

Once I saw first-hand what Sharon's team was doing, I wanted to support two projects in particular: New ways to 'shock' – a patent for latency-reversing drugs; and better ways to 'kill' by harnessing the immune system, moving these discoveries into clinical trials.

The reason a cure for HIV remains elusive is because the virus goes into hiding, what is termed, 'HIV latency'. One HIV cure strategy is called 'shock and kill', the philosophy of which is if you can 'shock' the virus out of its hiding place, you can then 'kill' it, resulting in a cure.

MILLERS SCHOLARSHIP IN INFECTION AND IMMUNITY

Through a generous donation to the Doherty Institute, the prestigious Millers Scholarship in Infection and Immunity was established to support postgraduate research students with demonstrated excellence in the areas of immunology or infectious disease research.

To date, seven students have been awarded the Scholarship. Here, four Scholars describe their projects.

JESSIE CHANG

I have been able to commence research in understanding a specific bacteria called Klebsiella and how it causes lung infections. I have established a laboratory model to perform the infections and then assess how the bacteria alters the genes in that cell, using an approach called dual RNA-sequencing. Following this, I will be able to work out how the bacteria hijacks the host cells during infections in order to develop new approaches to treating severe lung infections.

JOSHUA DEERAIN

I have been able to undertake my PhD with University of Melbourne Professor Jason Mackenzie. My research has focused on developing new laboratory models to grow and study human noroviruses, a major cause of diarrhoea. Through this work, I plan to understand how the virus causes cells to die during infection. I have had the opportunity to collaborate extensively within the Doherty Institute, with external colleagues and have presented my work at three international and three national conferences.

AMAYA ORTEGA

In my PhD, I have been studying pregnant women living in endemic areas with high transmission of malaria. Malaria can cause severe infection in the setting of pregnancy and my goal is to understand the role of different parts of the immune system in fighting malaria. I have been specifically interested in the role of a particular immune cell called a monocyte. I am trying to understand how antibodies interact with monocytes in the elimination of the malaria parasite. Hopefully, this will contribute to the design of a vaccine for pregnancy-associated malaria.

THE DOHERTY INSTITUTE WOULD LIKE TO THANK THE FOLLOWING GENEROUS DONORS:

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JARED STERN

My PhD studies focus on how HIV is controlled inside a cell. When a person living with HIV is taking suppressive antiviral therapy, HIV still persists long-term inside a cell and therefore current treatments are life-long. We previously found that HIV inside a cell increases and decreases with a 24 hour cycle, similar to many other biological processes that have a circadian rhythm. We are currently working to understand the mechanisms for this variation in HIV expression, with the overall aim to exploit these pathways to develop new approaches to eliminate long-lived forms of HIV that persist on antiviral therapy.

FIND OUT MORE ONLINE

Scan the QR code to read more about **philanthropy.**

From top left, clockwise: Jared Stern, Joshua Deerain, Jessie Chang and Amaya Ortega

ABOUT THE DOHERTY INSTITUTE

Finding solutions to prevent, treat and cure infectious diseases and understanding the complexities of microbes and the immune system requires innovative approaches and concentrated effort.

This is why the University of Melbourne – a world leader in education, teaching and research excellence – and The Royal Melbourne Hospital – an internationally renowned institution providing outstanding care, research and learning – partnered to create the Peter Doherty Institute for Infection and Immunity (Doherty Institute); a centre of excellence where leading scientists and clinicians collaborate to improve human health globally.

Located in the heart of Melbourne's Biomedical Precinct, the Doherty Institute is named in honour of Patron, Laureate Professor Peter Doherty, winner of the 1996 Nobel Prize in Physiology or Medicine for discovering how the immune system recognises virus-infected cells. Under the expert guidance of Director, University of Melbourne Professor Sharon Lewin, a leader in research and clinical management of HIV and infectious diseases, the Doherty Institute has more than 700 staff who work on infection and immunity through research, education and public health activities. Our work includes discovery research; diagnosis, surveillance and investigation of infectious disease outbreaks; and the development of ways to prevent, treat and eliminate infectious diseases.

THE DOHERTY VISION

To improve health globally through discovery research and the prevention, treatment and cure of infectious diseases.

THE DOHERTY MISSION

The Doherty Institute will be an inspiring, innovative and enabling environment. We are dedicated to identifying and addressing fundamental challenges in all aspects of infection and immunity. Through our leadership, advocacy and education we will shape policy, practice and research both nationally and internationally.

THE DOHERTY VALUES

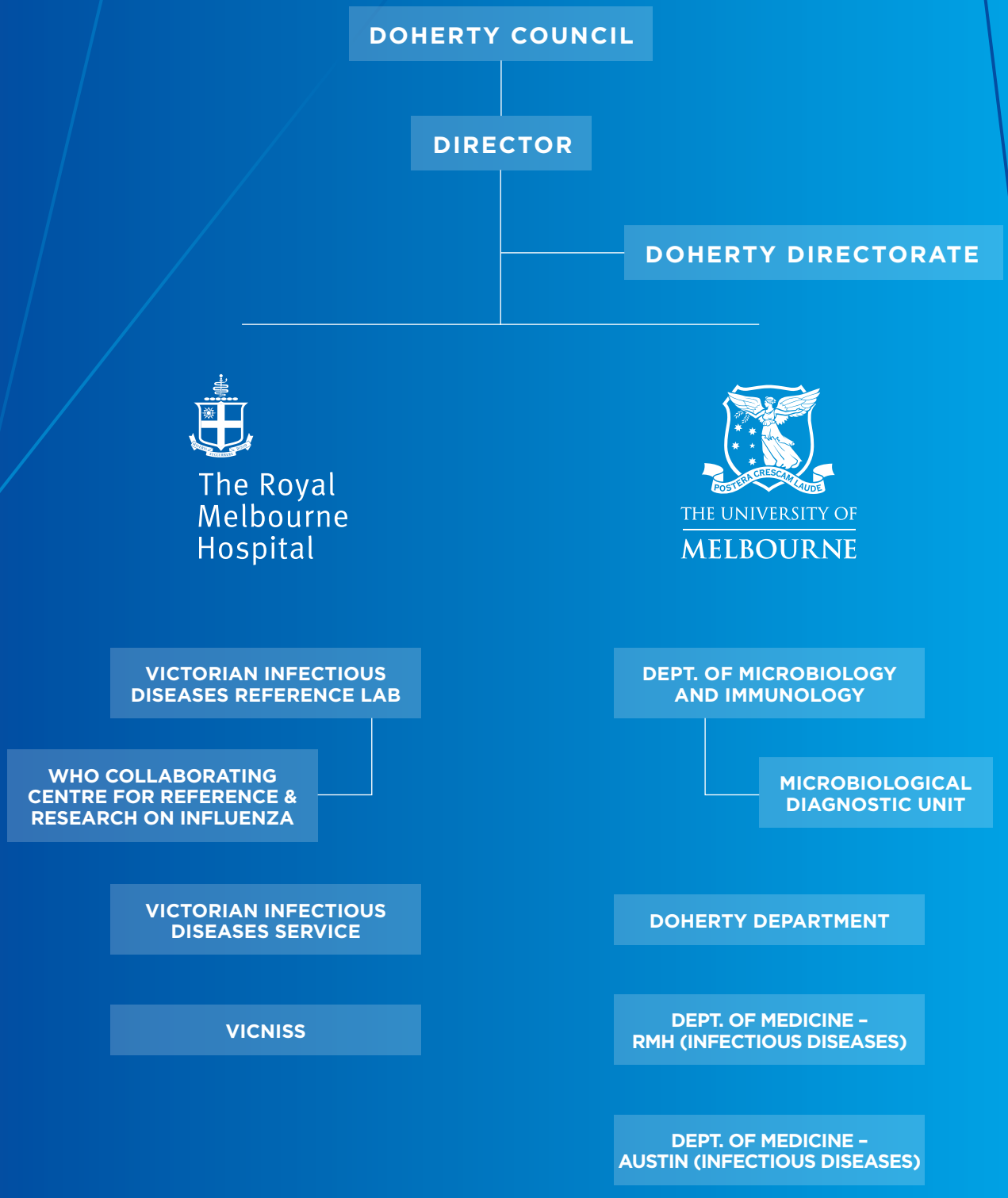
Discover: we break new ground and innovate

Deliver: we work to improve health practice and outcomes

Inspire: we develop the highest calibre people to achieve excellence

Connect: we engage locally and globally with our partners, stakeholders, colleagues and community

GOVERNANCE MODEL



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PROFESSOR SHARON LEWIN

Director of the Doherty Institute

OUR DEPARTMENTS

DEPARTMENT OF MICROBIOLOGY AND IMMUNOLOGY

The Department of Microbiology and Immunology is part of the School of Biomedical Sciences in the Faculty of Medicine, Dentistry and Health Sciences (MDHS) at the University of Melbourne.

The Department has a significant role in training the next generation of biomedical scientists, as well as being home to over 100 post-graduate research students. It also has internationally recognised research expertise, particularly in molecular and genetic analyses of bacterial and viral infections and in basic immunology.

"Working in an institute that is custom-designed for research into infection and immunity has been extremely beneficial for the Department. The Department is nearly double in size, now with 35 laboratories. In addition, while we have always had some co-appointments with other institutions or research entities, the co-location and proximity with other researchers has been transformational in our ability to share resources, creating greater efficiencies and better outcomes. Being part of the Institute has also facilitated greater community and government exposure, particularly in the area of public health." – University of Melbourne Professor Andrew Brooks, Head of the Department of Microbiology and Immunology

DOHERTY DEPARTMENT

The Doherty Department is a research only department of the University of Melbourne's Faculty of Medicine, Dentistry and Health Sciences.

The Doherty Department supports cross-Institute and multidisciplinary research at the Doherty Institute in infectious diseases such as HIV, viral hepatitis, tuberculosis, sexually transmitted infections, skin pathogens (Staphylococcus aureus, Group A Streptococcus) and emerging infectious diseases. Researchers work across many disciplines including epidemiology, genomics, global health, Indigenous health, public health, and translational and clinical research.

"The Doherty Department is truly multidisciplinary with a strong focus on translational and clinical research. Through our close collaborations with major teaching hospitals and diagnostic laboratories, our work can be rapidly translated into improved health outcomes for patients and communities both locally and globally." – University of Melbourne Professor Sharon Lewin, Head of the Doherty Department

DEPARTMENT OF MEDICINE (ROYAL MELBOURNE HOSPITAL)

The Department of Medicine at the Doherty Institute includes research teams working on global health, malaria, nutrition and antimicrobial resistance and stewardship.

Their research covers basic disease mechanisms through to clinical trials and operational research and social science research. It hosts two National Health and Medical Research Council Centres for Research Excellence - one in antimicrobial stewardship and another in malaria elimination.

"The new links we have made within the Doherty Institute have been really exciting; from sharing cutting-edge equipment to working with other disciplines on various projects. Being in the Institute has also fostered interactions with state and federal government, and with international organisations such as the World Health Organization (WHO), through research education, training and translational activities." – University of Melbourne Professor Stephen Rogerson, Interim Head of Department

MICROBIOLOGICAL DIAGNOSTIC UNIT PUBLIC HEALTH LABORATORY (MDU PHL)

The MDU PHL is a leader in public health microbiology which informs public health policy and practice. Serving the community since 1897, the MDU PHL is the longest continuously serving public health laboratory in Australia.

Its primary responsibility is to investigate the public health implications of certain bacteria from humans, animals, food, water and the environment. The MDU PHL is also home to the WHO Regional Reference Laboratory for Invasive Bacterial-Vaccine Preventable Diseases (IB-VPD).

"We've been able to very closely integrate research and public health services, particularly through genomics technology, which has been our key focus for the last five years. Establishing Doherty Applied Microbial Genomics has allowed us to form extensive collaborations across the Doherty Institute and externally in translational genomics for clinical and public health microbiology. In addition, we've transitioned MDU into an antimicrobial resistance (AMR)- savvy laboratory with reference activities in that space, while also working more closely with the Department of Health and Human Services to establish new surveillance systems for AMR." – University of Melbourne Professor Ben Howden, Director of MDU PHL

VICTORIAN INFECTIOUS DISEASES REFERENCE LABORATORY (VIDRL)

VIDRL is a public health reference laboratory which is part of The Royal Melbourne Hospital and also performs diagnostic testing, mainly in virology, for Victorian hospitals.

VIDRL's activities include surveillance, outbreak investigations, reference testing and research. VIDRL has national reference laboratory designations to the Commonwealth Government for polio and enteroviruses, measles, viral haemorrhagic fevers and smallpox. It also has a strong commitment to international health programs through the WHO spanning more than 50 years. VIDRL has WHO Collaborating Centre designations for Reference and Research on Influenza, Mycobacterium ulcerans, and Viral Hepatitis together with WHO Regional Reference Laboratory designations for poliovirus, measles and hepatitis B, and is a WHO National Influenza Centre.

"Being part of the Doherty Institute has connected VIDRL to staff who complement our skills and has provided new opportunities for us to enhance what we do. The Institute has quickly built considerable stature in public health, allowing us to walk a little taller than we did as VIDRL alone. I am inspired by the Doherty Institute, and I believe that as part of this Institute VIDRL's best days lie ahead of us." – Dr Mike Catton, Director of VIDRL

WHO COLLABORATING CENTRE FOR REFERENCE AND RESEARCH ON INFLUENZA

The WHO Collaborating Centre for Reference and Research on Influenza is part of the WHO Global Influenza Surveillance and Response System.

The network was established in 1952 to monitor the frequent changes in influenza viruses and reduce the impact of influenza. Together with the other four WHO Collaborating Centres in Atlanta, Beijing, London and Tokyo, the Centre is responsible for analysing influenza viruses circulating in humans across the globe. This information is used by the WHO to make recommendations on appropriate viruses to be included in annual seasonal influenza vaccines for the Northern and Southern Hemispheres. The Centre also undertakes research, training and regional capacity building activities related to influenza.

"Our collaborative research has increased significantly since becoming part of the Doherty Institute. We bring virology expertise to many of the influenza research programs, providing the investigators with the samples they need to study the virus, and we also often run assays or test compounds for them. The facilities in the Institute are outstanding and we have more room to do the types of work we need and want to do than we did previously." – Professor Kanta Subbarao, Director of WHO Collaborating Centre for Reference and Research on Influenza

OUR DEPARTMENTS

VICTORIAN INFECTIOUS DISEASES SERVICE (VIDS)

VIDS provides inpatient and outpatient care of patients with infectious diseases at The Royal Melbourne Hospital.

The service has a special focus on travel-related and tropical infections, HIV, hepatitis, tuberculosis, malaria, healthcare associated infections and refugee health. The VIDS team comprises more than 50 staff, including consultant physicians, junior doctors, nurses and research fellows, with an established record of clinical research, strong links to public health and a commitment to evidence-based practice. VIDS also includes the Victorian Tuberculosis Program, a multidisciplinary team providing state wide public health services relating to tuberculosis.

"As clinicians in The Royal Melbourne Hospital, we see patients presenting with infectious symptoms on a daily basis. If we observe a problem that we don't know the immediate answer to we bring it back to the expertise at the Doherty Institute where we discuss it in meetings, in the corridors, in the tearoom. Together, we find answers. It's these clinical questions that drive research where there is a gap in evidence, which in turn drives change and ultimately, better healthcare." – Associate Professor Kirsty Buising, The Royal Melbourne Hospital's Acting Director of VIDS

VICNISS COORDINATING CENTRE

VICNISS provides an integrated system in Victoria for the monitoring, analysis and reporting of infections in hospital and aged care settings.

Funded by the Victorian Department of Health and Human Services, the service includes senior infection prevention clinicians, epidemiology and biostatistics personnel and IT staff. Their work spans longitudinal studies of disease burden and severity, national epidemiological studies, 'big data' linkage with registries and contribution to international and national infection prevention standards, such as the Australian Commission on Safety and Quality in Healthcare.

"New links we have made within the Doherty Institute have enhanced and strengthened the national outlook of the program. For example, our group is collaborating with other staff in the Doherty to reduce infections and improve antimicrobial prescribing in residential aged care facilities. Being co-located in the Institute has also facilitated work with the MDU and Department of Health to ensure that monitoring of antimicrobial resistant organisms in hospital and other settings is coordinated to adequately inform timely public health responses." – Associate Professor Leon Worth, Acting Head of VICNISS

DEPARTMENT OF MEDICINE (AUSTIN HEALTH)

The Austin Health Infectious Diseases Department has an outstanding track record in clinical service, teaching, research and public health policy in infectious diseases, and are world leaders in antimicrobial resistance and stewardship, Mycobacterium ulcerans (Buruli ulcer), drug allergy and infection control.

The Austin Health Infectious Diseases Department is also the coordinating centre for Hand Hygiene Australia and has a very active research program aimed at addressing clinically relevant infectious disease problems.

"We were very pleased to formalise the long-standing collaborative research partnership between Austin Health Infectious Diseases and the Doherty Institute in March 2019. We look forward to continuing this collaboration, training the next generation of clinician scientists and expanding our joint research initiatives both nationally and internationally." - University of Melbourne Professor Lindsay Grayson, Director of Austin Health Infectious Diseases Department

FIND OUT MORE ONLINE

Scan the QR code to read more about our highlights over the last five years.

The Peter Doherty Institute for Infection and Immunity
CELEBRATING FIVE YEARS
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Doherty Institute

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