IMPACT

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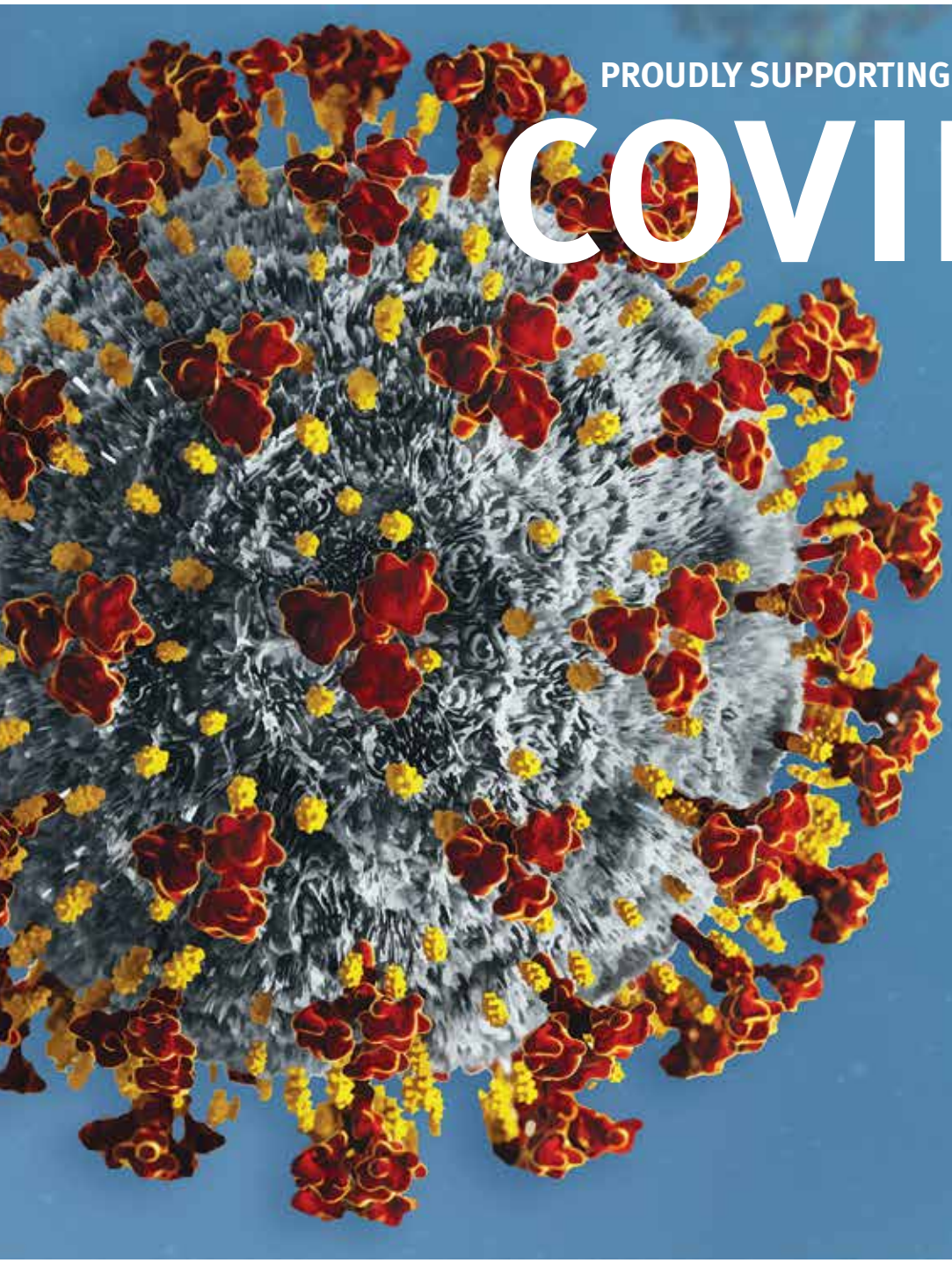

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COVID-19

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Burnet Institute is a leading Australian medical research and public health organisation focused on achieving better health for vulnerable communities in Australia and internationally by accelerating the translation of research, discovery and evidence into sustainable health solutions.

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DIRECTOR'S REPORT

Welcome to the SPRING issue of *IMPACT*.

As I write this column, more than five million Melburnians are in Stage 4 lockdown in the midst of the COVID-19 pandemic, one of the greatest challenges facing humanity in the last century.

Globally tens of millions have been infected and sadly more than a million have lost their lives. Unemployment has reached levels not seen since the Great Depression, and many businesses may never recover. Many resource-poor communities around the world that have poor health systems have been impacted most severely and, surprisingly, a number of Western countries with stronger health capacity have failed dismally in their response. The pandemic has been politicised in many countries and used as a means to strengthen control over populations.

Yet there is hope. We have seen scientific communities around the world coming together in a race to develop vaccines, diagnostic tests and therapeutics. Not since the onset of the HIV epidemic has there been so much effort to develop a vaccine, to find ways to test and detect infection, to develop and strengthen public health strategies to prevent and contain the spread of the virus. We are fortunate to be living in Australia where, for the most part, our governments have been working together, putting aside political differences to develop and implement the best possible approaches, and most importantly, they have listened and taken advice from the best scientific minds across the country.

Burnet Institute has been at the forefront of the response to COVID-19. It's in our DNA, it's really what we were founded on back in the 1980s at the start of the HIV epidemic. We have continued to build and strengthen our research and public health capacity in the areas of major global infectious diseases. While the pandemic has brought significant challenges to the Institute for the way we work and communicate, we have been able to pivot much of our work to addressing many aspects of the response, from rapid diagnostic test and vaccine development, to public health research and advice. We have been actively involved in developing strategies to influence behaviour change and uptake of interventions such as face masks, improve social distancing, and ways to better support people in home isolation and quarantine. A number of our staff have been seconded to health authorities at state, national and international levels to support and to provide the most up-to-date strategic advice, and to also support our country partners in Papua New Guinea and Myanmar.

Medical research has been, and will continue to be, front and centre in our approach to COVID-19 and to future pandemics in Australia and the region. Its importance to the health of the nation and the region cannot be underestimated and has finally been recognised.

I am very thankful for the incredible words of encouragement provided by our many supporters and also incredibly grateful for the financial support many have provided, which has enabled Burnet to be in a position to make a meaningful response to the pandemic. I am also incredibly thankful for the wonderful team of scientists, public health and support staff at the Institute who are all so committed and working incredibly hard to help get us through this challenging time.

Please keep safe and keep well.

Professor Brendan Crabb AC
Director and CEO

“The devastating impact of the global pandemic, COVID-19 has significantly raised awareness that the answer to any of these big health problems is science. There is no other answer. You can’t ‘clinical’ your way out of it, you’ve got to solve it, you’ve got to solve a complex problem.”

PROFESSOR BRENDAN CRABB AC,
DIRECTOR AND CEO, BURNET INSTITUTE

Know-C19

RESEARCH - INNOVATION - EVIDENCE - RESPONSE - RECOVERY

Burnet’s innovative and evidence-based public health and laboratory-based COVID-19 research initiatives are contributing to solutions to the global pandemic.

Since the start of the COVID-19 pandemic, Burnet has proactively contributed to the national and global response through public health and laboratory-based research, advocacy and the provision of high-level advice to government.

The Institute’s key programs are home to researchers with significant expertise and longstanding collaborations and networks that are critical to the response to COVID-19.

Our expertise in virology, rapid diagnostics, and in assessing and developing antiviral agents is well recognised internationally. Combined with our public health expertise in epidemiology, modelling, disease elimination and understanding human behaviours, Burnet is well positioned to provide a significant ongoing contribution to the COVID-19 response.

Professor Brendan Crabb AC and other researchers are involved in multiple COVID-19 response committees, such as the National Advisory Committee on COVID-19, and provide strategic advice to Australia’s Chief Medical Officer, state Chief Health Officers and Departments of Health.

The Know-C19 Hub is our gateway to research, policy and technical reports, addressing gaps in knowledge and providing novel information to inform the global response.

Diagnostics
Development of a rapid point-of-care test to identify people who have been infected and cleared the virus.

Advocacy
Providing strategic advice to Australia’s health authorities, and communicating with the general public.

Antivirals
Screening of novel drugs with antiviral action for their ability to prevent or treat COVID-19 infection.

Public Health
Improving our knowledge through public health measures to strengthen care and stop community transmission of COVID-19.

Vaccine
Development and evaluation of antibody assays to understand the immune response to COVID-19 in humans.

International Health
Supporting COVID-19 responses in Papua New Guinea, Myanmar and other countries through modelling and other strategies.

BURNET RESPONSE TO COVID-19 PANDEMIC: IT'S IN OUR DNA

By Jack Banister

Since the start of the HIV epidemic in the 1980s, Burnet has continued to build and strengthen our research and public health capacity in the areas of major global infectious diseases. Now, we are supporting the COVID-19 response across many areas – from rapid diagnostic tests and vaccine development to public health research and advice.

When the World Health Organization declared COVID-19 a global pandemic on 11 March 2020, Burnet Director and CEO Professor Brendan Crabb AC already had a clear understanding of the fundamental challenges facing Australia, and how Burnet was well positioned to assist.

The central dilemma was, and remains, how to lockdown as stringently as possible to suppress or eliminate the virus, without causing serious and lasting damage to the Australian economy and 'the social contract'.

To this end, Professor Crabb began collaborating with leading scientists, clinicians, researchers, policymakers and communicators to fine-tune Australia's response, before joining the National COVID-19 Health Research Advisory Committee as one of Australia's medical leaders feeding information to the Commonwealth's Chief Medical Officer and to National Cabinet.

Much of Australia's initial success in suppressing the virus, Professor Crabb said, can be attributed to that 'Team Australia' approach.

"Prime Minister Scott Morrison and the premiers functioned, to a large extent, as a team. And the most important thing they did, secondarily to that, is they listened to experts," he said.

"We're seeing some countries where that hasn't happened... There's no Team USA. There's no Team UK. And that's their failing."

Burnet, meanwhile, rapidly transitioned its research output to tackle the pandemic, something Professor Crabb believes is in its DNA.

"Burnet's origins are from an infectious diseases hospital, the Fairfield Hospital in Melbourne ... we became 'famous' on the back of the world's previous major epidemic/pandemic, and that was HIV and AIDS. We still work on HIV and AIDS, and if you interview me in 30 years' time, I suspect we'll still be working on COVID-19, because it's the next really big thing."

Like HIV and AIDS, Professor Crabb said that tackling COVID-19 requires a two-pronged approach – technical solutions, like vaccines and medicines, and behavioural ones, like physical distancing, hand washing, mandatory quarantining and wearing masks.

"Burnet is involved in all facets," Professor Crabb said, "both of tool development, and influencing social and community behaviour to influence uptake. The main people that are going to prevent COVID-19 are the public themselves. There's a social contract that needs to be developed. And that's a science."

Public and media attention has zeroed in on tool development, especially the search for a vaccine, which includes Burnet's own research, led by Professor Heidi Drummer. But Professor Crabb believes a vaccine is likely to take 12 to 18 months to develop from scratch, and when it arrives there is a possibility that there won't be enough doses, and that public perception issues around the use of vaccines will hamper uptake.

Above: *Burnet researchers have appeared prominently in Australian media since early 2020. Burnet's Dr Alyce Wilson was seconded to Victoria's Department of Health and Human Services in February.*

That's why he and Australia's key decision-makers are hungry for information about the second part of the equation – the social contract.

"We know that we need to have the mechanisms in Australia to keep the virus very low or to eliminate it altogether without going into lockdown again. But that does not mean that it's going to work," he said.

The question, Professor Crabb said, is about what behaviours effectively combat COVID-19, but also about how rates of compliance with those 'COVID-safe' behaviours can be pushed upwards.

"If the public is asked by governments: 'These are the things we want you to follow now', what does it take for people to actually follow those [directives]? What's the science behind influencing behaviour?"

Burnet quickly identified this gap in clear messaging and evidence-based advice influencing public behaviour, especially the test-treat-isolate strategy. A new flagship program, Know-C19, was launched and brought together the Institute's leading COVID-19 researchers. The Optimise Study began, led by Professor Margaret Hellard AM, focusing on two key intervention methods to restrict the spread of the COVID-19 virus – isolation/quarantine and physical distancing.

Professor Crabb was an early advocate of the initial nationwide lockdowns enforced in April, another learning from past epidemics and pandemics.

"Your best strategy is to act very fast and strongly. You don't wait until you've got 'all your ducks in a row' because it's too late. It's still evidence-based, but it's not evidence-based about COVID-19. In fact, we didn't know much about COVID-19. What we did know is what worked for other epidemics," he said.

So – will the world ever win when it comes to suppressing the virus, and protecting vulnerable people? For Professor Crabb this is a question that invites more questions.

"Science will solve this problem. There's no doubt about that. We will end up with top class therapies and preventions, hopefully the main one being a super effective vaccine," he said.

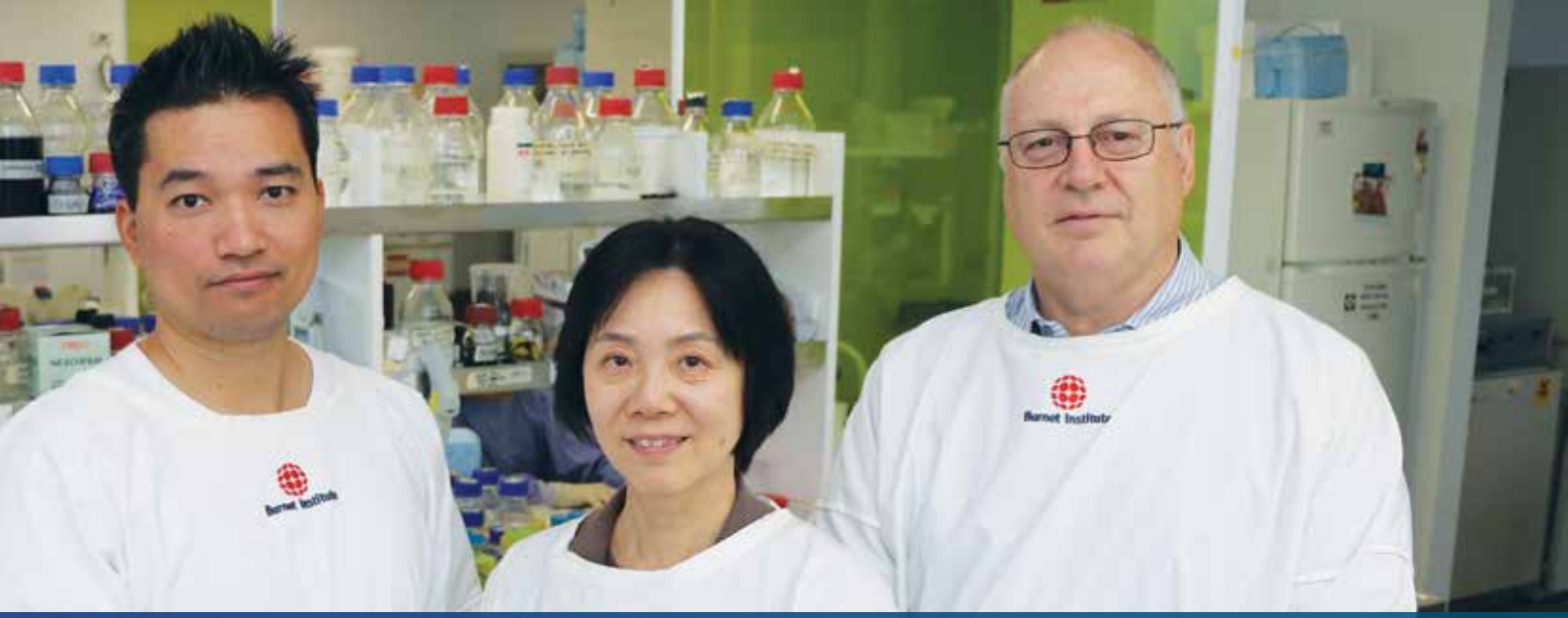
"But what human price will you pay? What societal price will you pay? What economic price will you pay? And those are interconnected things. The pandemic has happened. It's having a devastating effect. The question is, what's the price that we will have to pay for that victory?"

60+
Burnet COVID-19 R&D projects

41
reports advising government and policymakers

11
Burnet staff formally seconded to federal and state health departments

7
peer-reviewed COVID-19 publications, and counting



COVID-19 Diagnostic: a game-changer

Who has been infected with COVID-19, and may not even know it?

Answering this critical question is what drives Burnet's Global Diagnostic Development Group in developing a game-changing, rapid, point-of-care test that could become a vital tool in the management of COVID-19 globally.

Associate Professor David Anderson can recall precisely when he found out the first prototypes of a rapid point-of-care (RPOC) test for COVID-19 that he and his team had been developing, were likely to work.

It was 17 April 2020, his birthday, and the research breakthrough was a real cause for celebration.

Australia was in its first COVID-19 lockdown at the time, and as head of Burnet's Global Health Diagnostics Development Group, Associate Professor Anderson was focused on finding new diagnostic tools to identify people who had been infected with the virus, many without even knowing it but still having potential to spread the infection.

"Once the test is working a little bit, then you can systematically improve it," he said of the milestone, just one of many achieved in his 30 years of research discovery at Burnet.

His extensive body of work includes an RPOC test for hepatitis E in the 1990s that was far superior to existing tests, through to the VISITECT® CD4 Advanced Disease Test, which recently achieved World Health Organization prequalification. This test measures CD4 T cell levels in HIV-positive patients to determine whether they should be treated with antiretroviral drugs. Other work includes RPOC tests for active syphilis, liver disease and liver cirrhosis, and current research on new diagnostics for sepsis and measles.

"We learned a lot along that pathway about how to develop different reagents, and we developed some other proprietary technology. We got a really good understanding of how lateral flow tests, point-of-care tests, can work," Associate Professor Anderson said.

With the COVID-19 prototype in hand, the aim is to put to market a product that could be a game-changer because of its accuracy – in the order of 99 percent – far higher than the 91-95 percent accuracy of existing RPOC tests.

WHAT SETS IT APART?

What distinguishes Burnet's finger-prick blood sample diagnostic from the rest is a patented process to test for dimeric IgA, one of the antibodies the body makes in response to COVID-19, to indicate current or recent infection.

Other RPOC tests look for a different antibody, IgM, which is often cross-reactive to other viruses including many common cold viruses, which leads to a high proportion of false positive results.

Testing for dimeric IgA, Associate Professor Anderson said, was a "pre-COVID idea" his team has been working with since a PhD student, Khayriyyah Mohd Hanafiah, showed it could be useful around eight years ago.

"We now have all of the reagents dried down onto what looks exactly like a pregnancy test, and you just add patient blood and it goes through the device and gives you the colour reaction if there's antibodies present against the virus," he said.

The best option for a testing blitz would be to use the RPOC test and the familiar PCR laboratory test, using throat and nasal swabs, in tandem. Because the RPOC test doesn't require a lab, it can give a result within half an hour, and it can be used in settings where a lab-based test isn't feasible. It can also detect whether a person has had COVID-19 over a much longer time period, whereas the laboratory test relies on catching people when they're at the peak of their infection period.

"This test is probably most important in identifying contacts and asymptomatic cases," Associate Professor Anderson said.

RPOC TEST AS A COVID-19 MANAGEMENT TOOL

Detect sub-clinical infections in community screening for containment and contact tracing.*

Determine community rate of infection (prevalence) and identify new hotspots of infection.

Help manage isolation/quarantine requirements, i.e. tailor isolation periods to each individual.

In low- to middle-income countries diagnose acute infection where PCR is not available.

*High sensitivity for detecting incident infections within a few weeks of exposure with improved specificity compared to IgM.

Left: *Burnet's Global Health Diagnostics Group: Huy Van, Dr Fan Li and Associate Professor David Anderson.*

"The test can identify people who are very recently infected, enabling a closer look at their contacts. There is currently no way of telling where that person got their infection from, unless they're from a known cluster."

IDENTIFYING PEOPLE WHO HAVE CLEARED THE VIRUS

Containing Victoria's second COVID-19 wave in mid-2020 was difficult, and the source of nearly half the cases during that time eluded authorities. The RPOC test would have allowed for backward contact tracing, which is a real missing link in the response to new infections.

"So, if you were just positively diagnosed, we currently try and figure out which of your 20 possible contacts you got it (COVID-19) from," he said. "This antibody test would allow you to go and test all of your contacts, and figure out who among them actually had the infection. And then you can go to all of their contacts to see who you didn't have direct contact with, but other people they may have infected – who could be infectious right now without knowing it."

The test will also identify people who have been infected and cleared the virus, potentially enabling them to safely return to work post-infection. This will be vital for key services, in particular health workers who are disproportionately exposed to infection.

Another major advantage of Burnet's RPOC test, he said, would be its potential to help measure the effectiveness of COVID-19 vaccines once they are used in the community.

"No vaccine is 100 percent effective. If many people are immunised with a vaccine, it's unfeasible to follow up 10,000 or 100,000 and test everyone by PCR once a week to see if they have had the virus despite being vaccinated. But with our RPOC test, you could do this with monthly testing, for example."

BURNET'S CUTTING-EDGE RESEARCH ENVIRONMENT

Associate Professor Anderson credited the research environment at Burnet for many of the discoveries he's made. The Institute's focus, he said, is on identifying and addressing "unmet medical needs" and getting products to market to translate research into positive health outcomes.

"There's a phrase we use to describe what we're doing: the minimum viable product. MVP. What characteristics of a test would make it good enough that it could be useful?"

That's what his team are hoping to turn a prototype into. It took eight years to get a RPOC test onto the market for hepatitis E, and five years for the CD4 HIV test. But this time, Associate Professor Anderson is optimistic the new COVID-19 test can be fast-tracked.

Burnet's diagnostic development received initial funding from the Victorian Government.

BURNET'S TRACK RECORD IN PRODUCT DEVELOPMENT FOR GLOBAL HEALTH

HEPATITIS E

Assure™ HEV IgM
(CE Mark)

HIV

VISITECT® CD4
(CE Mark)

CD4 Advanced Disease
(CE Mark, WHO prequalified)

BioPoint® VL-Plasma
(CE Mark)

LIVER DISEASE

BioPoint® ALT1
(in clinical development)

SYPHILIS

Syphilis TP-IgA
(in clinical development)

Optimising behaviour to defeat COVID-19

> In the next 18 months, we're not going to get a vaccine or 'silver bullet' cure for coronavirus – COVID-19. The solution to how we manage this has to come from within the community."
>
> **PROFESSOR MARGARET HELLARD AM**

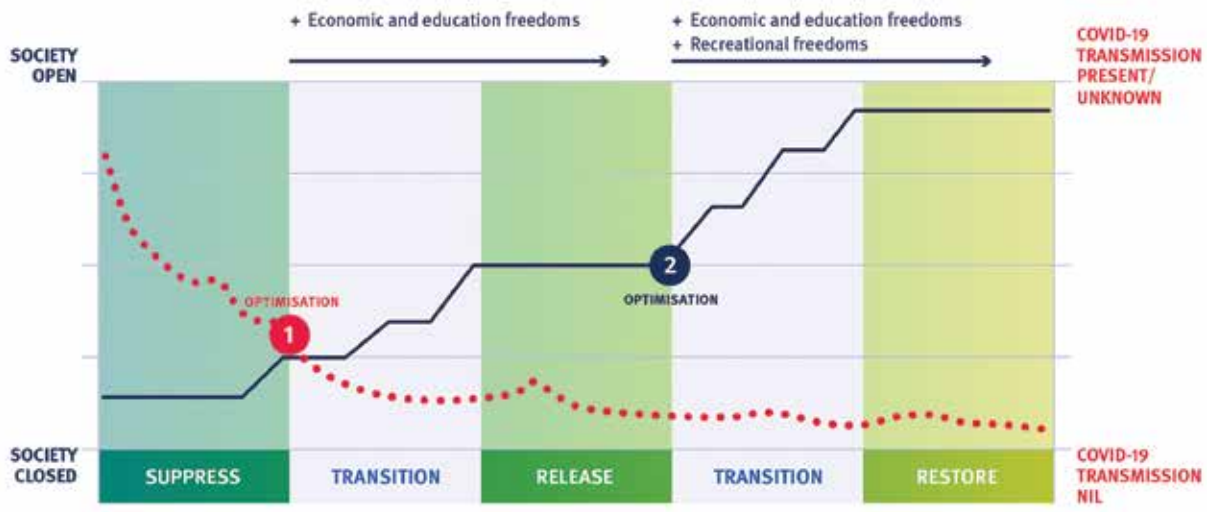
Although there are promising signs globally that an effective COVID-19 vaccine will be developed, Professor Margaret Hellard has spent much of 2020 focusing on another weapon against the virus.

"In my view, the 'silver bullet' of a vaccine or a cure won't be here for 12 to 18 months for the majority of people. Our one weapon is what I call 'the vaccine of human behaviour'," she said.

"Right now, we can work with the community around the behaviour change that is required to stop the ongoing transmission of infection. And that's a science."

Professor Hellard is leading the highly innovative Optimise Study, a partnership between Burnet Institute and Doherty Institute, in collaboration with The University of Melbourne, Swinburne University of Technology, Monash University, La Trobe University, the Victorian Government, Macquarie Group Foundation, the Centre for Ethnicity and Health, and the Health Issues Centre.

Recruitment has started, with study participants coming from a wide range of cultural and socio-economic backgrounds (healthcare and aged care workers, regional, metro, CALD community).



The research will try to answer key questions about how social, economic and structural factors affect compliance with restrictions, how social mixing patterns contribute to transmission, and the effectiveness of key messaging.

That information will be used to inform policy and practice on a national level, and to build and analyse mathematical models on the impact of isolation, quarantine and physical distancing measures.

Crunching the numbers has already led to some major discoveries. Modelling released in August 2020 showed that Victoria's Stage 3 lockdown restrictions in July prevented around 19,000 new infections that month. The same modelling indicated that the reproduction ratio (the R number) – the average number of people that one infected person will pass the virus on to – fell from 1.75 to 1.6.

But the most vital element of the study is its collaborative, circular approach to engage the community. Professor Hellard said her extensive work on eliminating viral hepatitis in Australia – which draws upon a deep understanding of people's social networks, contacts and how they interact – has informed her work on COVID-19.

"We know that 'optimising' the effectiveness of public health interventions will be critical to reduce transmission and restore society," she said. "Optimise is all about working with the community, especially the key vulnerable groups, to ask, 'how do we help you?'"

Aligning with community-driven organisations such as the Health Issues Centre, and the Centre for Culture, Ethnicity and Health will allow for key public health messages to be defined and refined via a co-design process. "That's crucial," Professor Hellard said, "because people do not engage with a 'top down' approach where they are told what to do without being consulted."

When it comes to understanding compliance with COVID-safe behaviour – such as self-isolating at home after a COVID-19 test – Professor Hellard said there are three elements to behaviour change to consider:

1. Do people know what they're being asked to do?
2. Do they agree and accept the need to change their behaviour?
3. Is it feasible to change?

"We have to understand that to change behaviour, you have to work on all those things," she said.

The aim is to produce messaging that isn't heterogenous and factors in all the different ways communication might break down.

"Two people who speak English can hear the same piece of information but interpret it quite differently. As soon as you bring in variants like language, culture, age differences, the messaging has to change. The nature of how I speak to an 80-year-old is different to how I would speak to someone in their 20s," she said.

As countries grapple with second and third waves of this highly communicable virus, it's crucial that communities understand the key role they play in suppressing transmission, until an effective vaccine is rolled out.

Initially, public health responses to COVID-19 were often made quickly and without behavioural data to guide effective messaging to communities and guide behaviour change. As Victoria emerges from the grip of a Stage 4 lockdown, finding a new weapon to suppress virus transmission rates and keep them low is not just a health issue, but an economic, social and mental health one.

As the race to discover an effective vaccine continues at pace, science is also helping refine the best weapon currently available: people's behaviour.

The Optimise Study is supported by the Victorian Government.

Thanks to the Macquarie Group Foundation

The Optimise Study has been made possible by the generous support of the Macquarie Group Foundation. Foundation Global Head, Lisa George, said the decision to support Burnet's research into optimising interventions that restrict the spread of COVID-19 was in recognition of the exceptional challenges that the disease is presenting now and will continue to present in the medium term.

"The COVID-19 crisis is placing sudden and significant human and economic stress on communities around the world," she said. "Burnet Institute has been at the forefront of infectious disease research and public health for over 30 years, so we're pleased to support the Optimise Study which aims to assist community organisations in restoring economic activity and recreational activities while keeping infection rates low.

"At Macquarie we're focused on empowering people to innovate and invest for a better future and we're confident the results of this study will support vulnerable communities both in Australia and abroad."

“It’s all-consuming”

Burnet’s role in COVID-19 vaccine quest

Researchers are manipulating the ‘key’ SARS-CoV-2 uses to break into our cells

Professor Heidi Drummer has always been fascinated by viruses – which is lucky, because now she spends up to 10 hours per day thinking about one virus in particular.

“I wake up thinking about SARS-CoV-2. The work on a vaccine has been really consuming,” Professor Drummer, Burnet’s most senior virologist, said.

While hundreds of research groups around the world are working frantically to create a vaccine against COVID-19, the disease caused by the SARS-CoV-2 virus, a team at Burnet is taking a unique approach guided by decades of research on other viruses.

“Several vaccines around the world have now entered human clinical trials, and all of them include the surface spike protein of the SARS-CoV-2 virus, which is the primary target of neutralising antibodies in our immune system,” Professor Drummer said.

The spike protein is particularly important because it acts like a key to unlock the ‘photocopy room’: it gets the virus into our cells, where it can hijack the machinery and copy itself over and over.

Professor Drummer said the other groups are using the spike protein in its natural form.

But Burnet’s COVID-19 Vaccine Development team of five researchers, led by Dr Andy Poumbourios and Professor Drummer, is tweaking the spike protein so it attracts more focused attention from the immune system, without sending the response into overdrive.

“Our approach is to change the structure of the spike protein into one that will generate an antibody response that will be protective, but have no ability to cause what’s called antibody-dependent enhancement (ADE), where the disease is worse in vaccinated people,” Professor Drummer said.

> **Burnet's COVID-19 vaccine development is working to re-engineer the spike protein (seen in red on the image) of the COVID-19 virus so that it generates a stronger immune response. It's important to get the balance right as too much immune response can cause the disease to be worse in vaccinated people. This halted vaccine development for SARS after the outbreak in 2002-04."**

PROFESSOR HEIDI DRUMMER
BURNET INSTITUTE

ADE halted the development of several vaccines against SARS (now SARS-CoV-1), when reports emerged that animals suffered worse disease when exposed to the virus if they had been vaccinated.

The Burnet team plans to put several of its best-performing spike proteins into animal trials in October 2020, with early results expected before year's end.

The work is a natural transition for Professor Drummer; for almost 20 years she has been studying what makes certain viruses so good at evading our immune systems.

"A major focus for my career has been understanding how viruses attach to receptors on our cells and then how they rearrange their structure to get into the cell," she said.

"The flip side is, how does the immune system see the virus? And how can we make better antigens – which stimulate an immune response – for vaccines?"

During her PhD, awarded in 1993, Professor Drummer helped to identify new parts of the influenza virus that T cells (a type of white blood cell) bind to when they attack.

She later studied the role of various adjuvants (substances added to vaccines to boost the immune response) for the influenza vaccine, and the proteins on the surfaces of human immunodeficiency virus (HIV) and human T cell lymphotropic virus (HTLV).

Professor Drummer and Dr Poumbourios have been working for years on a vaccine to protect against all eight of the circulating genotypes of hepatitis C virus (HCV), securing three patents on their technology. This has included re-engineering the protein that helps the virus enter our cells.

"If you just immunise people with the 'native' HCV glycoprotein, it's incredibly hard to get a protective immune response because HCV has immune-evasion mechanisms that minimise the amount of neutralising antibodies our bodies make, and restrict the ability of those antibodies to recognise other strains of virus," Professor Drummer said.

"This has been a really intractable problem for HCV vaccine research. A lot of my work has been on trying to re-engineer those HCV surface proteins so they better stimulate these broadly reactive neutralising antibodies, which are effective against lots of different strains of HCV. Hopefully then we can use one antigen to protect against many different strains of the virus.

"When COVID-19 happened, we saw an opportunity to transfer what we've learned from HIV, HTLV, and HCV, to see if we can generate really strong, long lasting neutralising antibodies."

Despite the intense focus, securing a vaccine will be a long process, she said.

"There has been an incredible, unparalleled global response to this pandemic, even going beyond what we did for HIV, but I think we're still a couple of years away from a vaccine.

"What happens in the next 18 to 24 months in vaccine development will be really interesting: they're going to require big phase III studies, to prove that ADE doesn't happen, and to manufacture and distribute it."

As to whether Australia will have the necessary manufacturing capacity will depend on the type of vaccine that performs best in clinical trials, Professor Drummer said.

"Then we'll need to find a way of immunising everyone. Even with vaccines currently available, it's hard to vaccinate people – you can't just say 'come and get it', because people don't behave that way."

And while each team wants to be first, others' successes will not mean the work stops.

"Several international research groups have published early results of COVID-19 vaccines tested in humans and the results look promising, with all generating an immune response and most having excellent safety profiles," Professor Drummer said.

"But large, multi-country trials will be needed to fully examine their safety in diverse populations and ability to protect from infection and disease. As such, it's essential that as many vaccine candidates are progressed as possible, so we have multiple options to augment the international vaccine effort and provide new knowledge about SARS-CoV-2 vaccine design and immunity."

In the meantime, their team is happy to be contributing, Professor Drummer said.

"As a virologist, you almost have a duty to help in some way. Everybody in the lab is inspired to work on it – we feel we've got to do something, to lend our expertise to find a solution for this."

HOW DIFFICULT IS IT TO ATTRACT FUNDING?

"Some organisations were already working in epidemic preparedness, whereas for groups like us who've come from a different field and perhaps come into it from a different angle, it's been much harder to get funding," Professor Drummer said.

"We're basically running on limited funds and applying for every grant opportunity to progress this work."

Young school kids say thanks to our scientists!

Scientists overwhelmed with heartfelt expressions of gratitude from the next generation

Burnet's scientists were thrilled to receive over 100 letters from students at Malvern Primary School in Melbourne, thanking them for their efforts to find a vaccine and cure for COVID-19, and for their contributions to science.

The letters, organised by Malvern Primary mum, Dr Sarah Meachem, were written by children of all ages, from Prep to Grade 6.

Dr Meachem, who also works in Victoria's medical research sector, was inspired to create the 'Gratitude Project' after hearing about a similar idea in Canada.

"I'm a science advocate and I'm very passionate about getting the message out there about how important science is. I just want scientists to feel valued," Dr Meachem said.

"As I was sitting in lockdown I felt so helpless. Across the country many scientists are really facing uncertain times. I thought it would be great to hear thanks from the next generation of scientists. Kids just say it how it is."

For our scientists working so hard to find a solution to COVID-19, the letters were especially touching, coming at a time when many were also dealing with Stage 4 lockdown.

"They made me laugh and they made me cry. Kids are so insightful. It was unbelievably impressive and I can't believe how the kids understand how important scientists are," Dr Meachem said.

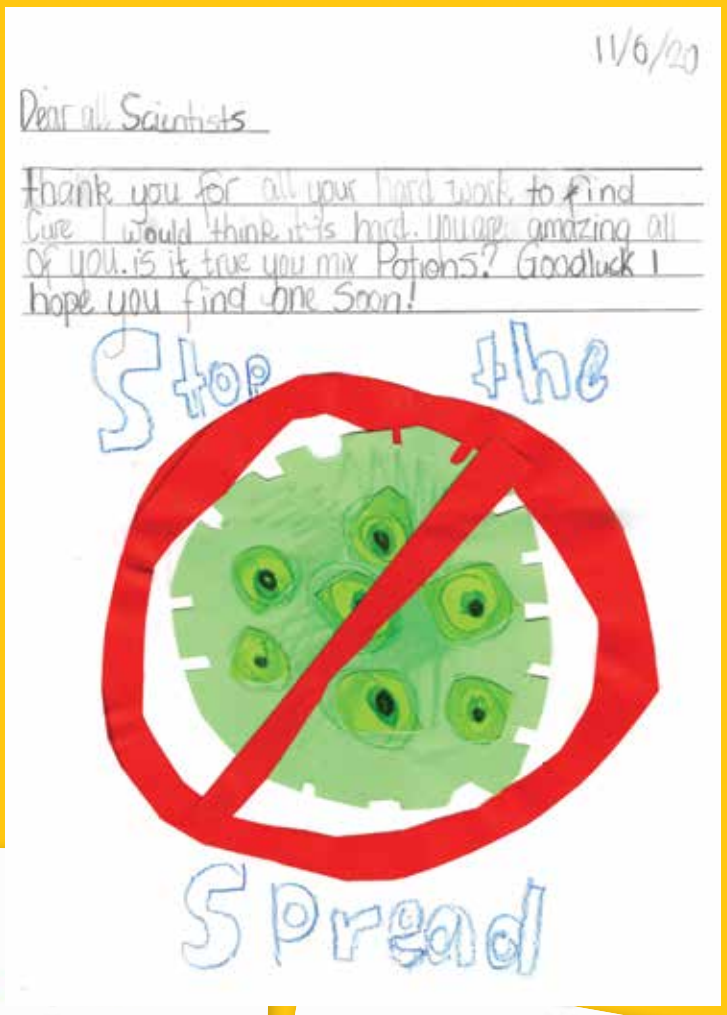
Malvern Primary students were particularly thankful and concerned that some of the scientists were not able to spend time with their own families while they work tirelessly on finding a vaccine.

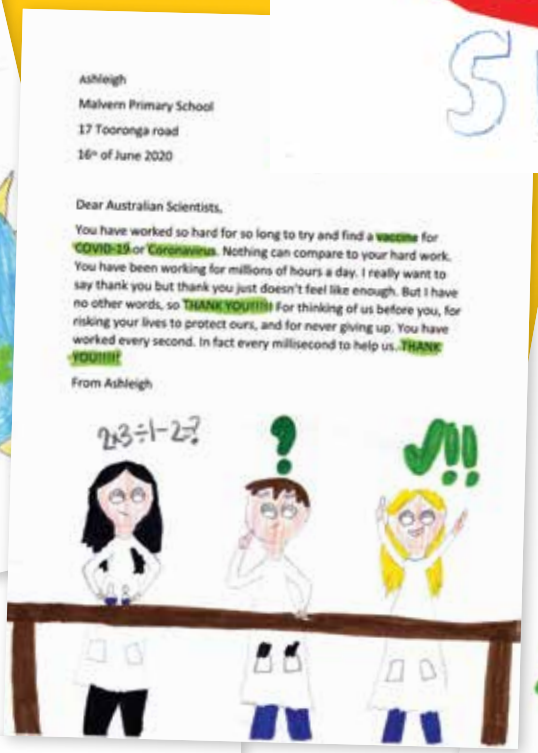
Emily wrote: *"How important must you feel," but assured scientists she was not trying to put them under additional pressure.*

Young Charlie asked *scientists to ensure a vaccine could be made available for everyone in the world, "otherwise the whole thing will just be another huge argument. Anyway, keep persisting, you'll get there."*

Lola wrote: *"Your job is so cool and you are cool too."*

The reaction to the letters was very positive when first shared with Burnet's scientists and staff at a weekly Zoom session. Nearly 20 staff have promised to become pen pals.





"It is a fantastic initiative and all our scientists were so appreciative of the uplifting support from these young students, and we hope some are budding scientists of the future," Burnet scientist and Director and CEO, Professor Brendan Crabb AC said. "The reaction was so positive and I know many of our scientists are super keen to thank the children and Malvern Primary School too."

Mobile Immunisation Clinic supporting homeless during COVID-19

Taking health care to Melbourne's at-risk homeless populations amidst the COVID-19 pandemic is the focus of an important new service funded by the Department of Health and Human Services and supported by Burnet resources and expertise.

Since May 2020, teams of two – a social worker from the Salvation Army's ACCESS Health, and vaccination nurse from St Vincent's Melbourne – have criss-crossed Melbourne in Burnet's mobile clinic, visiting emergency accommodation, homeless services, drop-in centres and hotels made available to the homeless during the COVID-19 lockdown.

Their initial idea was to offer vaccinations for hepatitis A following a serious outbreak among people experiencing homelessness in Melbourne in late 2019, but the brief was expanded to include influenza and hepatitis B vaccinations, overdose education, naloxone training, housing and family violence referrals, COVID-19 screening referrals, even toiletry packs and comfy clothing.

"In this particular time lots of services have changed the way they operate, and lots of people, including the homeless are not necessarily accessing their usual services," ACCESS Health Program Manager, Bec Thatcher said.

"This is about filling the gaps to provide information on hepatitis A and free immunisations, where to get a meal, or access to health care for particular needs, and it's been going very well."

As well as our 'clinic on wheels', Burnet is providing project management support and evaluation. So successful has the service been that initial funding through to the end of July 2020 was extended a further three months.

Above: *ACCESS Health social worker, Isi Palone working on the project to support people affected by homelessness in Melbourne.*

Burnet studies COVID-19 impact on drug markets

March 2020 saw Australia close its borders for the first time in history.

For those with a dependence on illicit drugs it is a time of uncertainty, with COVID-19 restrictions and an unsettling of supply chains disrupting the sourcing and purchasing of substances such as methamphetamine and heroin.

Burnet Program Director, Behaviours and Health Risks, Professor Paul Dietze, and collaborators have been speaking to cohorts of people who inject drugs in Victoria since the first wave of restrictions, to gather insights on supply, pricing and uptake of support services.

"As things have been going on for longer, we're seeing an increase in prices and starting to see people use a little less in some instances," Professor Dietze said.

Professor Dietze said uptake of support services to date had not declined significantly. More concerning was the potential for drugs like illicit fentanyl to enter the market. The potent substance is responsible for a surge in overdose deaths in the USA and Canada, but hasn't yet reached Australia.

"It's easily transportable, and in the context of this change in supply routes and mechanisms we could expect fentanyl to start showing up on Australia's streets," he said.

Burnet's cohort studies, which interview people who use heroin or methamphetamine in Victoria, have monitored changes to drug markets for many years and informed policies in many Australian states. During COVID-19 the studies have kept going, but Burnet researchers and participants have had to adapt.

"We have stopped face-to-face, field-based data collection. Everything is done by phone or video. It's been a remarkable reflection of our project team and staff group to make that transition because it's been challenging at times," Professor Dietze said.

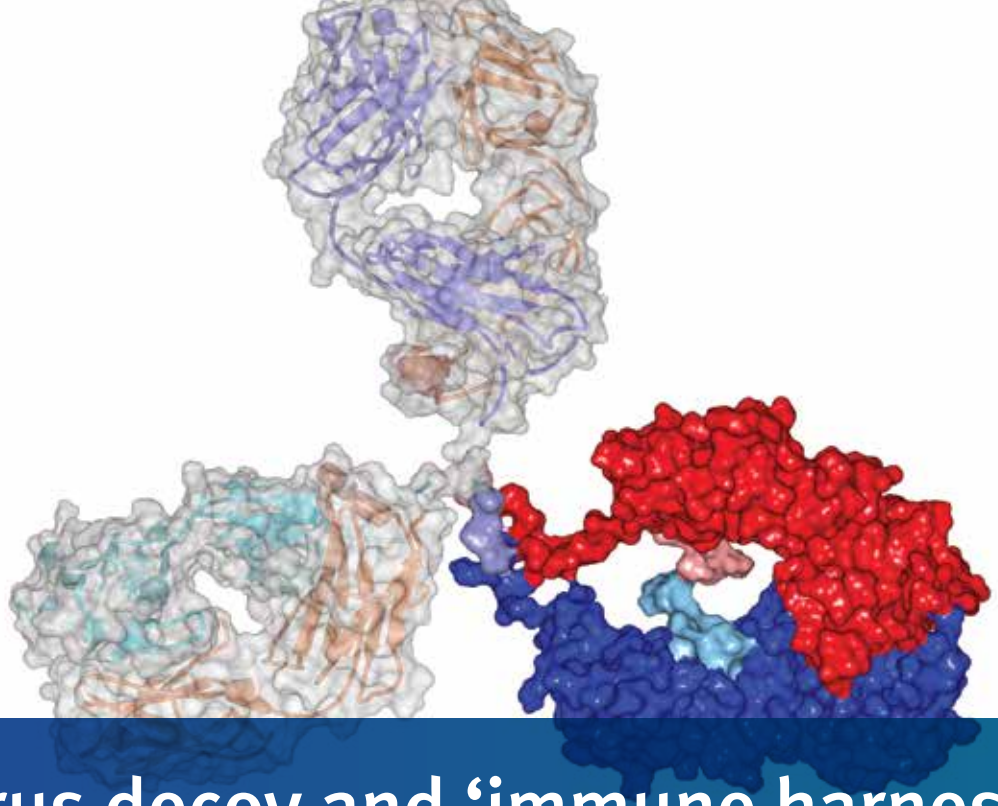
Looking ahead, he said a heightened risk of overdose could stem from a large increase in supply and purity, particularly if a person's tolerance is reduced from using less.

"We're positioned to be monitoring what happens as changes occur, like when restrictions are lifted," he said.

While 2020 is a year like no other, Professor Dietze said the heroin drought that began in late 2000 may provide some indication of what happens with the drug market.

"There was a really big change in supply, and a reduction in harms. It did take a long time before we ended up with similar levels of things like overdose deaths," he said. "Fortunately we have a range of new responses in place to ameliorate any harms as things change."

Professor Dietze said the advent of take-home naloxone, as well as the Victorian Government's support of a Medically Supervised Injecting Room in North Richmond, would reduce the impact of changes in heroin purity and tolerance.



Virus decoy and ‘immune harnessing’ trialled for COVID-19

Burnet adds antibody expertise to hunt for drugs against coronavirus

Understanding how immune cells rally against a threat – and settle down again – is crucial in developing treatments that fight disease but don’t cause damage themselves.

It’s an area of expertise that Burnet researchers are bringing to a multi-organisational search for medicines for COVID-19, supported by almost AUD$2m from the Australian Government’s Medical Research Future Fund.

Head of Burnet’s Immune Therapies Group, Professor Mark Hogarth is leading the development of a series of unique biological drugs (which mimic naturally occurring proteins) in the consortium, of which three will enter preclinical trials by the end of 2020.

“Our commitment to understanding how antibodies stimulate the immune system through receptors called Fc receptors has been a three-decade effort, during which we pioneered much understanding of the ‘immune harnessing’ work of antibodies,” Professor Hogarth said.

He and colleagues from The University of Melbourne discovered several Fc receptors in humans in the 1980s and have worked on them ever since – research with broad applications including cancer, autoimmune diseases, and infections.

“Everybody’s got a particular expertise and class of biological drug they are bringing to the COVID-19 testing table. We will also provide input into the selection process, so the biologicals that will be trialled are the best virus-neutralising entities, and the best immune function stimulating entities.”

Professor Hogarth’s lab has engineered two human proteins into the one molecule in a bid to both prevent and treat COVID-19.

One end of their ACE2-Fc drug is a clone of the human ACE2 receptor – the ‘entry point’ that the SARS-CoV-2 virus uses to get into our cells.

This clone acts like a decoy, stopping the virus entering and replicating within host cells, and has performed successfully in in vitro studies, Professor Hogarth said.

This decoy will also be effective against any other coronavirus that uses ACE2 as its receptor, including the virus that causes SARS and any future coronaviruses, Professor Hogarth said.

An important aspect of the drug’s Fc component is its ability to dial down an over-stimulated immune response, which caused worse disease in several animal trials for a SARS vaccine.

“We have a unique set of modifications that controls the immune-stimulating potential of the ACE-2 Fc and of antibodies,” he said.

“We’re one of few groups in the global research community that’s worked for so long on how antibodies and their Fc receptors really control the immune system. We are applying this experience from our cancer and inflammation studies to the prevention and cure of COVID-19.”

Above: *The x-ray crystal structure of an antibody. The immune stimulating Fc portion is composed of two chains shown in red and or blue. The virus neutralising Fab portions are uncoloured.*

Tracking down outbreaks and causes of fever in Papua New Guinea

Surveillance and response tool for vector-borne disease now also being used for COVID-19

By Lydia Hales

Above: PNGIMR staff working on the project: Sausi Research Nurse, Madang Province, Francis Kenuwai and STRIVE Health Systems Research Officer, Zebedee Kerry

In a remote clinic in Papua New Guinea (PNG), fever can be a slippery thing. Viruses, parasites, and bacteria are just some of the culprits that can increase a patient's body temperature. But patches of fever across a population – as well as the pathogens in each person's blood – can reveal outbreaks of potentially preventable, deadly disease.

Deputy Director of the PNG Institute of Medical Research (IMR) Dr Moses Laman and Burnet's Co-Program Director of Health Security, Associate Professor Leanne Robinson are co-leading an innovative, DFAT Indo-Pacific Centre for Health Security-funded project. Partnering with Beyond Essential Systems, a group that provides Tupaia data aggregation and visualisation for Asia-Pacific countries, the STRIVE group has created a real-time 'heat map' of febrile illness (a temperature of 38°C or higher for two days or more).

Customisable layers of the map include patient gender or age, cases per week, molecular diagnostics, mosquito abundances, and areas where malaria parasites are showing notable mutations.

"We are piloting a surveillance and response system that brings this data together in an accessible platform," Associate Professor Robinson said.

A member of the World Health Organization Vector Control Advisory Group, she has spent more than 10 years in PNG, including five years as Head of the IMR Vector Borne Diseases Unit.

"Everybody in PNG's National Department of Health and the provincial health authorities can log in and look at data at the national or local level – for example, to see what proportion of febrile illnesses were malaria, and what proportion were caused by *Plasmodium falciparum* or *Plasmodium vivax*," she said. "Crucially, you can see which cases might be due to any other vector-borne disease outbreaks, like dengue."

Before COVID-19, research nurses in PNG triaged out cases that were clearly pneumonia or influenza-like illness to focus on fevers with unclear cause. These patients received a Rapid Diagnostic Test (RDT) for malaria, sent with a blood sample to the molecular hub in Port Moresby. Tests were run for all species of malaria parasite and priority viruses including chikungunya, Murray Valley encephalitis, Ross River virus, and the four strains of dengue, and the molecular data uploaded into the platform.

"A key aim of the platform is to allow the real-time visualisation of data, such that if you start seeing a RDT-negative fever rate of more than double what you saw in the past month, it can allow earlier investigation of possible outbreaks of other pathogens," Associate Professor Robinson said.

"This addressed a need that was identified and prioritised by PNG partners at both the national and provincial level, for ready access to more timely and in-depth information for diseases spread by mosquitoes in key sentinel sites throughout the country."

STRIVE monitors parasite markers associated with resistance to antimalarial drugs

The STRIVE researchers have helped identify areas where parasites have a mutation that may increase their resistance to antimalarial drugs.

STRIVE PNG
STRONGER SURVEILLANCE FOR VECTOR BORNE PATHOGENS

"Our surveillance has shown a higher prevalence of a particular mutation in the *P. falciparum* parasite that in other places has been associated with delayed parasite clearance for the patient," she said.

"This information is considered very useful by the National Malaria Control Program to guide where they will decide to inform where they will conduct their studies to monitor the clinical efficacy of the first-line treatment."

Impact of COVID-19

Amidst the COVID-19 pandemic, some of the six facilities in the STRIVE network have expanded testing to capture cases of acute respiratory illness, expanded data collection, and are providing weekly and monthly summaries to the PNG Provincial Health Authorities. COVID-19 has reinforced the importance of strengthening health systems of developing countries against threats from increasing international travel.

"It has highlighted how we can better support health workers – not only for diseases they know well like malaria, but for the next emerging pathogen like SARS-CoV-2," Associate Professor Robinson said.

"IMR has led the diagnostic testing of COVID-19 in PNG, and the STRIVE molecular hub has been able to support the response as one of the testing sites. They're getting through enormous numbers of tests in a week that would normally exceed capacity, because everybody was already working together.

"It's of no value to implement a program that's going to stop after three years without having embedded tools, skills and processes to outlive it."

For example, the team is working with the provincial health teams and National Agriculture Quarantine and Inspection Authority at STRIVE sites to build local capacity for long-term mosquito monitoring.

"The project has strong leadership and engagement at the national and provincial level in PNG – they know which approaches will have a meaningful and sustainable impact,"she said.

"We're operating in what is often a dynamic and changeable environment in terms of politics and health systems, so working at both the national and the provincial level is critical for having – we hope – a lasting impact on the country's disease surveillance and response systems."

PAPUA NEW GUINEA INSTITUTE OF MEDICAL RESEARCH

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Thanks to the June Canavan Foundation

'Abrusim COVID-19'

Strengthening outbreak response and reducing the impacts of COVID-19 in East New Britain, Papua New Guinea (PNG).

Burnet Institute, in partnership with the East New Britain Public Health Authority has developed the 'Abrusim COVID-19' project, which, in the local language of Tok Pisin, means to 'avoid' or 'prevent' COVID-19.

This is a collaborative ongoing project, working with healthcare professionals, technical experts, community and government to strengthen and support the province's response and preparedness for COVID-19.

Thanks to the support of the June Canavan Foundation, the project has created COVID-19 information and communication tools for community leaders to use and refer to when talking about COVID-19.

The Burnet team in East New Britain has also been distributing posters and flyers in English and in Tok Pisin, speaking to locals and travellers from nearby islands to promote the 'Abrusim COVID-19' message.

Dr Johanna English, from the Board of the June Canavan Foundation, has had a family connection with PNG for close to 40 years.

"When I read the Abrusim proposal, my first reaction was this was a great opportunity to grow sustainable change, especially in two of the June Canavan Foundation focus areas: health and education," Dr English said.

"The tools being developed now have future currency in a wide range of health applications.

"The impacts of COVID-19 are so widespread. PNG is one of our closest neighbours and we must do much more to help – with access to good health and education opportunities the country can work to reach its full potential."

Burnet has long had a strong connection with PNG and is committed to supporting PNG communities and government in their response to COVID-19.

With thanks to the June Canavan Foundation. Successful applications to Trusts and Foundations are a major source of income for Burnet's research and public health programs.

Insect repellent's surprising role in malaria elimination

Repellents to be included in Myanmar's malaria policy to prevent new infections, in response to world-first Burnet study.

Despite strong evidence demonstrating that topical insect repellent protects against mosquito bites, the World Health Organization is yet to endorse deployment of repellents for malaria prevention as an intervention with public health value.

In a world-first, Burnet Institute researchers established the real-world effectiveness of repellent distribution in the context of large-scale disease prevention programs in Myanmar, and demonstrated that it can prevent a third of new malaria infections. Their findings were published in the international journal *PLOS Medicine*.

Burnet Head of Malaria and Infectious Disease Epidemiology and principal investigator, Professor Freya Fowkes, said that to achieve malaria elimination in the Greater Mekong Subregion the toolbox for the malaria elimination agenda needs to be expanded, because the efficacy of endorsed vector control interventions is under threat.

"Establishing that repellent can significantly reduce the burden of malaria is incredibly important for the region, given that rates of insecticide resistance are increasing and changes in mosquito composition and behaviour can reduce the effectiveness of cornerstone vector control interventions, such as bed nets and indoor residual spraying," Professor Fowkes said.

Importantly, using novel analyses, the researchers established that repellent was equally effective across a variety of transmission intensities and high-risk populations. Study statistician and first author, Mr Paul Agius, said there was very little variation in the impact of repellent on reducing sub-clinical malaria across different villages and high-risk populations.

"This suggests that repellent distribution may be an effective intervention across a range of transmission settings and populations," Mr Agius said.

Senior Program Manager of Health Security in Burnet Myanmar, Dr Win Han Oo, said that findings from the study conducted in collaboration with the Myanmar National Malaria Control Programme have provided evidence for the change in Myanmar's malaria policy to include repellents, and will also be invaluable to inform Regional Malaria Elimination policies.

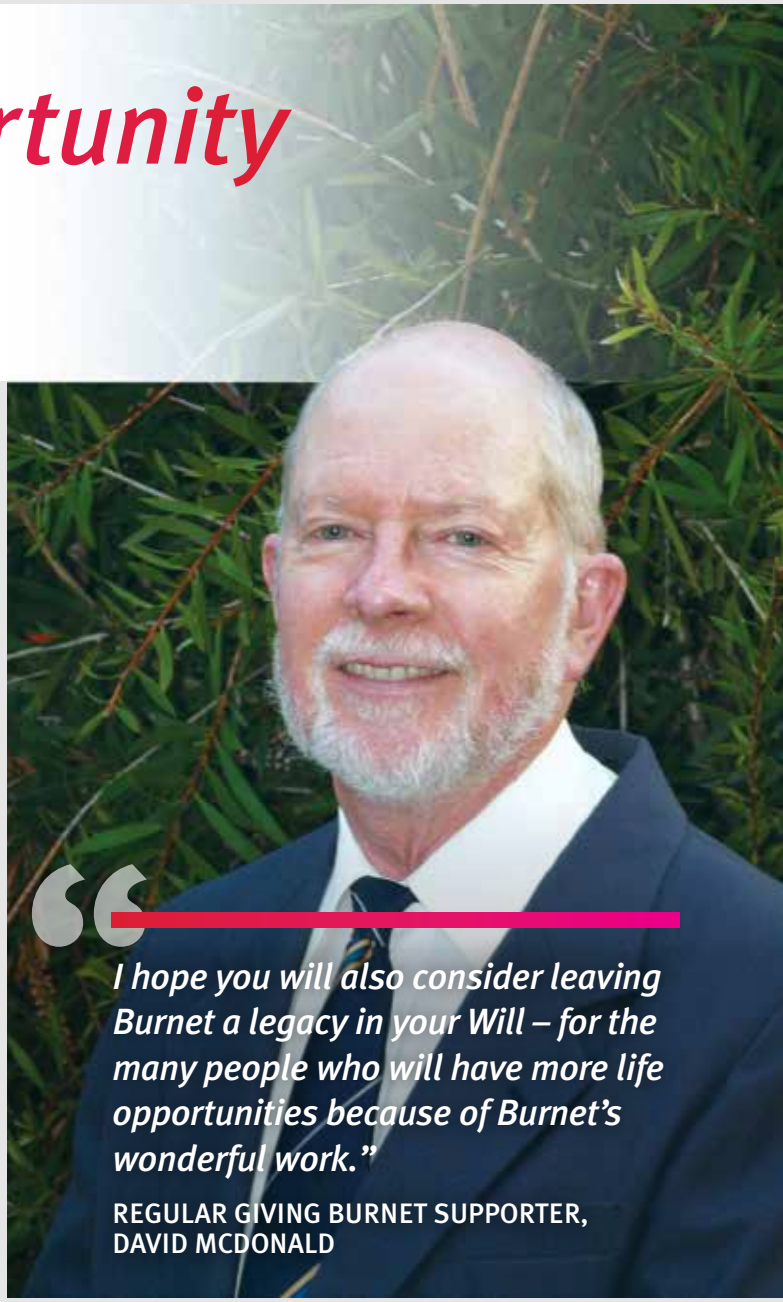
"Incorporation of repellent into the National Strategic Plans for malaria elimination may advance achieving the Greater Mekong Subregion elimination target of 2030," Dr Win said.

Burnet Director and CEO, and co-author on the paper, Professor Brendan Crabb AC, applauded the team behind the study.

"Not only is this one of the highest quality pieces of work Burnet has been involved in, the result is actually a surprise. There were reasons to doubt effectiveness of repellents but this study shows they can actually have a role in shifting the dial of this insidious disease," he said.

Giving the opportunity for a better life

Recently, David McDonald, 74, increased his support of Burnet Institute by commencing regular monthly donations and by including a gift in his Will.



"I have had the good fortune of working closely with Burnet scientists on a number of research projects," David said.

"This gave me a unique insight into the Institute's operational philosophy and I was very impressed by the high calibre of scientists and the organisation's focus on assisting vulnerable communities. I quickly decided that Burnet Institute was worthy of my support."

David lives with his wife on a five-acre bush block 30km from Canberra. He is a keen bird observer and also enjoys researching and documenting the local community's history. David maintains a long-term interest in social development and population health, with a particular focus on alcohol, tobacco and other drug matters. With almost 50 years experience in that field, backed by several tertiary and related qualifications, he continues to consult to governments, universities and other organisations.

Early in his career, David worked in community development in Papua New Guinea (PNG). This experience opened his eyes to the unique challenges facing this developing nation – from local community isolation due to rugged terrain and poor roads; to sparse medical infrastructure and services; to communication problems because of the many local languages/dialects. David is a supporter of Burnet's work in developing countries, and in particular the Institute's Healthy Mothers, Healthy Babies (HMHB) program in PNG.

"The HMHB program illustrates one of Burnet's finest attributes – its focus on what I call implementation research," he said.

"To be successful, health programs need to understand local issues such as culture, family customs, education, medical service availability, etc. Burnet takes the time to carefully address such issues. I wish that more other research institutes understood the importance of this approach."

During 2013-15, David was a member of a team of social scientists evaluating an Australian Capital Territory trial that permitted people other than health professionals to administer the drug naloxone – used to reverse opioid overdose. The team found that the trial was a success (many lives were saved) and recommended the practice continue and be scaled up. He also worked with Burnet scientists during this evaluation.

"This evaluation project highlighted another Burnet attribute – its willingness to focus on improving the lives of people who are vulnerable and too often stigmatised. My experience is that Burnet scientists are not only skilled but also compassionate and non-judgemental – qualities that are not always abundant in an organisation. This makes Burnet special," he said.

"Many people who are disadvantaged, vulnerable or simply lack sufficient voice, would be left behind, or perish, if it were not for organisations like Burnet. That is why I have left a gift in my Will for Burnet Institute."

If, like David, you can support Burnet Institute through a gift in your Will please contact Mr Arnis Stonis on +61 3 8506 2338 or arnis.stonis@burnet.edu.au.

“For over 30 years, with your generous support, Burnet Institute has been at the forefront of infectious disease research, public health and national health security.

COVID-19 is an unprecedented and complex global health challenge. Burnet is uniquely placed to contribute to the response with our technical skills, and a strong track record of leading large collaborative initiatives in partnerships with government, community, health services and other researchers, to improve the health of the community.

Our COVID-19 response is focused on six areas, each of which, working together, are critical to successfully fighting COVID-19 and saving lives.”

PROFESSOR BRENDAN CRABB AC,
DIRECTOR AND CEO, BURNET INSTITUTE

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