



# Lab+Life SCIENTIST

COVID-19  
**VACCINE TRIAL**

**TRACKING**  
INFECTIOUS DISEASES

**MORE EFFICIENT**  
MICROSCOPY

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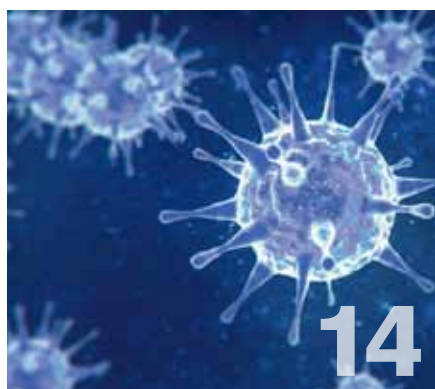


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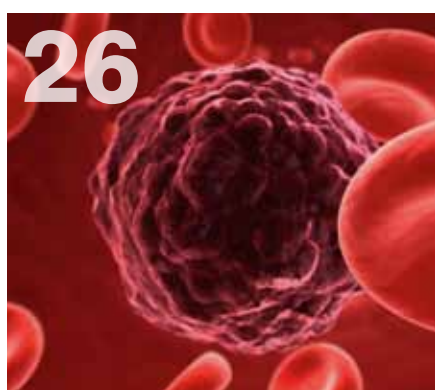
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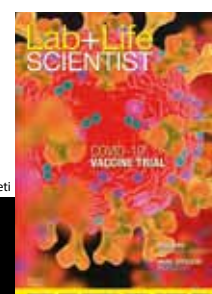
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The new diagnostic approach has the potential to enhance infectious diseases surveillance, and so is now being adapted to track immunity to COVID-19.



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## (Not) working from home

Welcome to another issue of *Lab+Life Scientist* — working from home edition. At the time of writing, restrictions are still very much in place all around Australia, though they have been lifted more in some states than in others. You may even be back in the office by the time this issue reaches you, and it looks like Australia will be well on its way to getting back to some level of normality soon. Unfortunately, the research workforce is likely to take longer to recover.

The Rapid Research Information Forum (RRIF) recently produced the report ‘Impact of the pandemic on Australia’s research workforce’, which details how a dramatic drop in international student fees (estimated at \$2.2–2.5bn for 2020) and business research spending will impact the sector significantly in the six months from May and beyond. University job losses of up to 21,000 full-time equivalent (FTE) positions are projected over six months, of which an estimated 7000 could be research-related academic staff. Research interruptions and travel and visa restrictions meanwhile suggest that more than 9000 international research students will not resume their research in 2020. As a result, industry sectors may experience a reduced capacity to innovate given that universities perform approximately 43% of all applied research in Australia.

The report’s authors are concerned that women, early-career researchers and recent graduates will

disproportionately experience negative impacts. Indeed, a second RRIF report, ‘The impact of COVID-19 on women in the STEM workforce’, indicates that hard-won gains for women’s advancement in the sector are now at risk of a major setback. This is because women — who were already under-represented in STEM — have suffered even greater job losses than men, as well as carrying a greater share of responsibilities for caring and distance learning duties during isolation. Australia’s scientific and technical services industry recorded job losses of 5.6% from mid-March to mid-April 2020, with jobs down 6.3% for women compared with 4.8% for men in this field. And with casual and short-term contract jobs likely to be the first to go — and, of course, unlikely to be covered by JobKeeper — women are at particular risk of missing out.

For those whose work is more directly involved in the eradication of COVID-19, the news is more promising, with an array of funding opportunities available for projects looking to cure or protect against the virus. In this issue of *LLS* we speak to Dr Paul Griffin, whose company is conducting the first human trial of a COVID-19 vaccine in the Southern Hemisphere. We also check in with an additive manufacturer that has found a way to 3D print antimicrobial copper onto metal surfaces, enabling them to kill 96% of SARS-CoV-2 in the process.

Other highlights include a look at the microbiomes of plants — yes, plants have them too — and tips for how you can use LC-MS/MS for therapeutic monitoring of immunosuppressant drugs (ISD).

I would like to conclude by noting my genuine surprise at how well the Australian population has bounced back from the threat of COVID-19 since we last spoke. I know this is my first pandemic, but I guess things seemed pretty dire just a couple of months ago — our way of living had changed so much. It really is a testament to the medical and scientific community that they were able to mobilise so quickly to discover so much about this virus, and that we have been able to fight back as a result. Here’s hoping that the next time we speak, things will be looking even better.

Regards,  
Lauren Davis  
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Liquid chromatography-tandem mass spectrometry (LC-MS/MS) is potentially the new gold standard for therapeutic monitoring of immunosuppressant drugs (ISD).

**H**owever, for this technology to become widely adopted, the methodology needs to be standardised globally, including addressing bottlenecks both at the pre-analytical stage of sample preparation and within the process itself. Here we take a look at the top four pitfalls to avoid when implementing LC-MS/MS for ISD monitoring.

ISDs have massive potential to decrease patient morbidity and mortality, despite their inherent risks. Recent developments include patient-friendly sample submission (eg, dried blood spots and micro sampling), higher sample throughput and standardisation via automation, and the ability to quantify and multiplex ISD monitoring assays.

However, during its evolution from research to clinic, LC-MS/MS has had a lot of limitations to overcome, including specific matrix interferences, high purchase and maintenance costs, the need for trained staff, complex method validation, limited robustness and minimal automation. Given the progress we have seen over the last decade, let's take a closer look at some of the main bottlenecks in the LC-MS/MS workflow that are particularly relevant to the design of ISD monitoring protocols.

The four most commonly prescribed immunosuppressive medications are: cyclosporine A, tacrolimus, sirolimus (rapamycin) and everolimus.<sup>1</sup> Recent developments, some of which are described below, indicate that LC-MS/MS is now sufficiently standardised for therapeutic drug monitoring (TDM) of the major ISDs that have

# Considering LC-MS/MS for therapeutic drug monitoring?

Avoid these four common pitfalls





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been studied and can now replace immunoassays, but only if the caveats below are taken into account.<sup>1</sup>

### 1. Have you optimised your sample type?

The challenges related to the accurate monitoring of ISDs revolve around sample type and quality, and the relative stability of the drug in question throughout the LC-MS/MS process. Fresh blood is the most common sample type used in ISD analysis, in part because it is the circulating concentration of a specific ISD that is important. However, recent studies using dried blood spots show that they could also be considered as a sample type for monitoring ISDs ahead of LC-MS/MS.<sup>2</sup>

#### *Is dried blood spot sampling viable?*

The use of dried blood spots (DBSs) and other micro sampling approaches could allow patients to prepare their own samples at home and send them to the laboratory. In terms of convenience, this would be a major step forward, since it would also eliminate the need for sample collection by a phlebotomist. A recent study looked at the impact of DBS methods on TDM of the three ISDs: tacrolimus, sirolimus and everolimus. Considering pre-analytical factors, the study found that differences in blood spot volume, degree of homogeneity, drug stability, hematocrit (Hct) effects and drying time were all important.

Tacrolimus is not significantly influenced by these factors. However, sirolimus and everolimus are more prone to heat degradation and exhibited variations in recovery that were dependent on Hct and drying time. Tacrolimus can thus be considered a viable candidate for DBS sampling, but sirolimus or everolimus will require further validation. However, application of 2019 guidelines regarding standardisation of DBS parameter validation for use in TDM should help overcome the current limitations with stability of ISDs and self-sampling.<sup>3</sup>

#### *What about sample types other than blood?*

A recent study demonstrated the validation of an LC-MS/MS method for mycophenolic acid, tacrolimus, sirolimus, everolimus and cyclosporin A for use with oral fluid (OF), as an alternative to blood or plasma.<sup>4</sup> The method validation met all

the acceptance criteria, with limits of detection (LOD) and quantification (LOQ) of 0.05–1 ng/mL and 0.1–5 ng/mL, respectively. Silanised tubes offered the best recoveries. The method was successfully applied to 31 OF specimens, describing everolimus detection in OF for the first time, and it was concluded that the method is sensitive enough for the detection of OF trough concentrations in patients receiving immunosuppressants when using an appropriate OF collector.

### 2. Is your sample collection and handling standardised?

#### *Sample handling and storage ahead of LC-MS/MS*

In a comprehensive review of the state-of-the-art of TDM for ISDs, it was found that the time taken from sample collection to analysis varied from a couple of hours to one week.<sup>5</sup> Many laboratories did not control the temperature during this time, and 15% of the laboratories had no specific procedures for temperature control of samples during transport and storage. A large percentage of laboratories did not reject partially clotting whole blood samples (29%), those collected using an incorrect anticoagulant during sample acquisition (43%) or those that did not meet requirements for a minimal sample volume (53%). Sample preparation was mostly manual (72%). The extraction procedures were often poorly controlled and standardised. It was concluded that validation/verification of methods for ISDs should be performed on samples based on the same matrix and anticoagulant intended to be used in routine services. Whole blood samples were recommended for the TDM of cyclosporine, tacrolimus, sirolimus and everolimus, whereas plasma is preferred for mycophenolic acid. Ethylene-diamine-tetra-acetic acid (EDTA) is the anticoagulant of choice because (i) it minimises problems with clotting and (ii) its use allows for the quantification of multiple immunosuppressive drugs in the sample.

The review goes on to recommend that LC-MS/MS method validation/verification should also include experiments with actual patient samples because they reflect the relevant proportions of

LC-MS/MS method validation/verification should also include experiments with actual patient samples because they reflect the relevant proportions of free and bound drug, and of parent drug and drug metabolites.

free and bound drug, and of parent drug and drug metabolites. Spiked samples can be used to supplement the experiments, but they may not provide an accurate assessment of the performance characteristics and demonstrate the robustness of the method only if used as the sole matrix. Furthermore, the use of fresh patient materials is recommended because frozen samples do not allow for the full testing of the sample pretreatment procedure. Sample pretreatment for analysis of cyclosporine, tacrolimus, sirolimus and everolimus, for example, must be quality controlled to ensure complete hemolysis of fresh whole blood samples, but these quality control procedures will be compromised if hemolysis has already occurred due to the freezing of the whole blood samples after collection.

### 3. Do you need to push your detection limits?

ISDs are present in such low concentrations that standard LC-MS/MS techniques are sometimes insufficient to attain the required LOQs, or the method becomes too impractical for routine use.<sup>6</sup> To this end it is possible to use signal summing, an underutilised, easy-to-apply practice to increase LOQs for immunosuppressant LC-MS/MS methods.

In one such study, the limits of signal summing for everolimus were tested by running samples of everolimus at three concentrations in triplicate programming, increasing amounts of identical transitions in a constant cycle time up to the maximum number the software permitted to sum. The increase in peak area and the signal-to-noise ratio were then determined. The imprecision, LOQ and recovery were compared for a routine everolimus method (using one transition for everolimus and one for d3-everolimus) and an adapted method that summed three identical transitions for everolimus (and one for d3-everolimus).

The increase in signal was close to that theoretically expected, with a larger experimental spread for everolimus once more than five transitions were used. There was no clear beneficial effect of summing on imprecision. The adapted everolimus method showed a lower LOQ, but comparable imprecision and recovery as the routine method. It was concluded that quantification levels can indeed be improved by signal summing, such that it could indeed be considered for TDM of immunosuppressants.

### 4. Is proactive training part of your lab's DNA?

In the aforementioned state-of-the-art TDM review, it was noted that on average, 65% of the individuals performing immunosuppressant TDM assays in the laboratory had less than one year of experience. Of these, 20% had less than three months' experience, whether for immunoassays or for LC-MS/MS.<sup>5</sup> Also, instead of proactively maintaining an adequate educational and training level, most laboratories (71%) retrained their personnel only 'after the fact' — that is, after problems had already occurred. Taken together, the three main reasons for variability of ISD results in TDM were all essentially training-related:

- Lack of standardisation of analytical methods and sample testing practices.
- Inadequate use of appropriate reference materials, calibrators and control samples.
- Inconsistency in knowledge of regulatory requirements and in the level of compliance with internationally accepted laboratory practice guidelines.

Continuous education and training of TDM laboratory personnel must be an integral part of ensuring a high level of analytical quality. Therefore, the establishment of proactive training programs to maintain an adequate and up-to-date level of knowledge of the LC-MS/MS ISD assays used is strongly recommended for all personnel involved in

analysis and reporting, or in interpreting the results. Also, because the clinical effectiveness of TDM (and ISDs in particular) depends to a large extent on timely sample collection and treatment, and correct sample storage and transport, the education program should ideally include the nursing staff and healthcare professionals who are responsible for taking patient samples in the first place, right at the start of the LC-MS/MS workflow.

Taking into account the recent work and reviews on the standardisation and optimisation of LC-MS/MS sample prep and the processes outlined above, you will now be able to think about setting up, optimising or validating your own ISD assays, according to the infrastructure and instrument needs for your specific laboratory.

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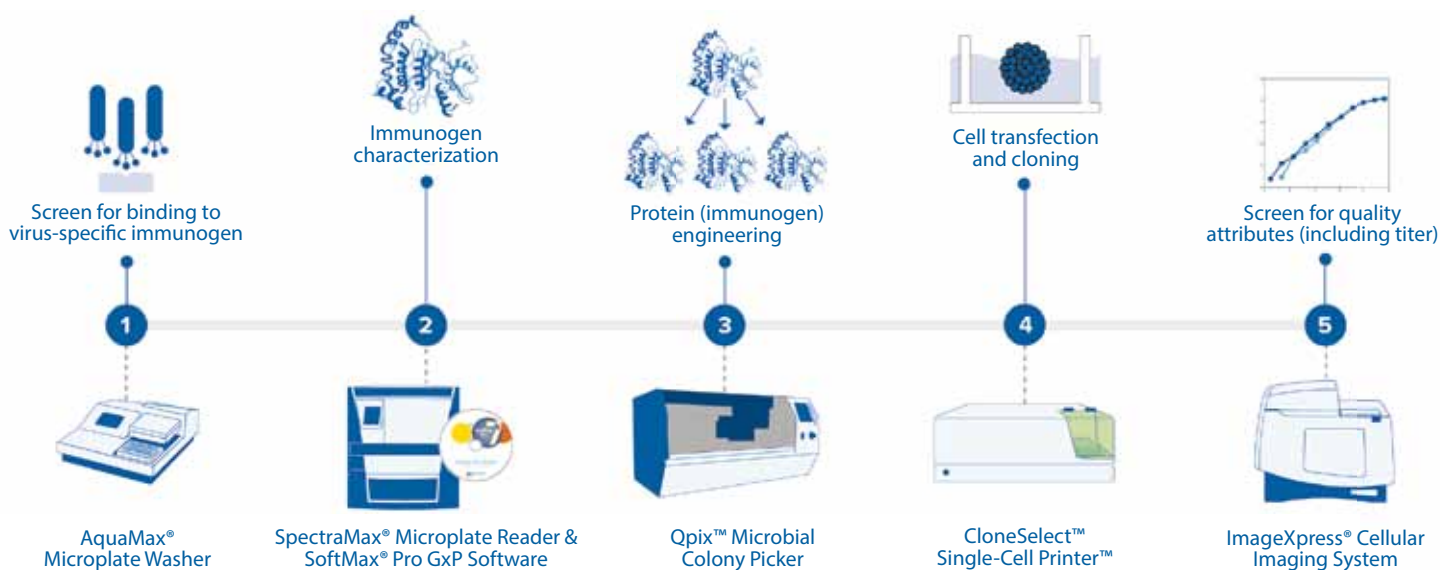
# Coronavirus SARS-CoV-2 (COVID-19) Research

Accelerate your COVID-19 research



Vaccine development workflows vary depending upon the platform (e.g. inactivated virus vs. DNA vaccine) chosen, each having its own advantages. In order to increase the likelihood of success against the infectious agent, CEPI, the Coalition for Epidemic Preparedness Innovations, and many other organizations promote diverse approaches during a pandemic.

Molecular Devices have created a variety of virus-related workflows – from antigen/immunogen and antibody discovery to stable cell line development. Below is a general workflow for vaccine development using recombinant proteins as the immunogen, referencing the systems to aid in your research.



1. **Screen for binding to virus-specific immunogen** – Screen virus-specific immunogens through binding using phage display
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## The secret behind virgin birth in South African bees

Researchers from The University of Sydney have identified the single gene that determines how South Africa's Cape honey bees reproduce without ever having sex. Writing in the journal *Current Biology*, the scientists revealed that the gene GB45239, on chromosome 11, is responsible for the virgin births. Reversions to asexual reproduction are rare in nature, so this may be the first time that the genetic basis of such a phenomenon has been discovered.

"It is extremely exciting," said behavioural geneticist Professor Benjamin Oldroyd.

"Scientists have been looking for this gene for the last 30 years. Now that we know it's on chromosome 11, we have solved a mystery."

In the Cape honey bee (*Apis mellifera capensis*), GB45239 has allowed worker bees to lay eggs that only produce females instead of the normal males that other honey bees do. "Males are mostly useless," Prof Oldroyd said, "but Cape workers can become genetically reincarnated as a female queen and that prospect changes everything."

But this also causes problems: "Instead of being a cooperative society, Cape honey bee colonies are riven with conflict because any worker can be genetically reincarnated as the next queen. When a colony loses its queen, the workers fight and compete to be the mother of the next queen."

The ability to produce daughters asexually is restricted to this single honey bee subspecies. Several other traits distinguish the Cape honey bee from



Cape honey bee workers laying parasitic eggs on a queen cell.

other subspecies; in particular, the ovaries of worker bees are larger and more readily activated and they are able to produce queen pheromones, allowing them to assert reproductive dominance in a colony. These traits also lead to a propensity for social parasitism — a behaviour where Cape bee workers invade foreign colonies, reproduce and persuade the host colony workers to feed their larvae. Every year in South Africa, 10,000 colonies of commercial beehives die because of the social parasite behaviour in Cape honey bees.

The existence of Cape bees with these characteristics has been known for over a hundred years, but it is only recently, using modern genomic tools, that we have been able to understand the actual gene that gives rise to virgin birth. According to Prof Oldroyd, "Further study of Cape bees could give us insight into two major evolutionary transitions: the origin of sex and the origin of animal societies."

Perhaps the most exciting prospect arising from this study is the possibility to understand how the gene actually works functionally, with Prof Oldroyd saying, "If we could control a switch that allows animals to reproduce asexually, that would have important applications in agriculture, biotechnology and many other fields. For instance, many pest ant species like fire ants are thelytokous, though unfortunately it seems to be a different gene to the one found in *capensis*."

Image credit: Benjamin Oldroyd

## Molecular reagents used to treat Alzheimer's disease

South Korean researchers have developed redox-active aromatic molecular reagents with a simple structural composition that can simultaneously target and modulate various pathogenic factors in complex neurodegenerative disorders such as Alzheimer's disease. Published in the *Journal of the American Chemical Society*, the redox-based strategy has been described as effective and efficient.

Alzheimer's disease is one of the most prevalent neurodegenerative disorders, affecting one in 10 people over the age of 65. A number of pathogenic elements such as reactive oxygen species, amyloid-beta and metal ions have been suggested as potential causes of Alzheimer's disease; and while each element itself can lead to Alzheimer's disease, interactions between them may also aggravate the patient's condition or interfere with the appropriate clinical care. For example, when interacting with amyloid-beta, metal ions foster the aggregation and accumulation of amyloid-beta peptides that can induce oxidative stress and toxicity in the brain and lead to neurodegeneration.

Because these pathogenic factors of Alzheimer's disease are intertwined, developing therapeutic agents that are capable of simultaneously regulating metal ion dyshomeostasis, amyloid-beta agglutination and oxidative stress responses remains a key to halting the progression of the disease. Now, researchers from the Korea Advanced Institute of Science and Technology (KAIST) have demonstrated the feasibility of structure-mechanism-based molecular design for controlling a molecule's chemical reactivity towards the various pathological factors of Alzheimer's disease by tuning the redox properties of the molecule.



Professor Mi Hee Lim and her collaborators rationally designed and generated 10 compact aromatic molecules presenting a range of redox potentials by adjusting the electronic distribution of the phenyl, phenylene or pyridyl moiety to impart redox-dependent reactivities against the multiple pathogenic factors in Alzheimer's disease. During the team's biochemical and biophysical studies, these designed molecular reagents displayed redox-dependent reactivities against numerous desirable targets that are associated with Alzheimer's disease such as free radicals, metal-

free amyloid-beta and metal-bound amyloid-beta.

Further mechanistic results revealed that the redox properties of these designed molecular reagents were essential for their function. The team demonstrated that these reagents engaged in oxidative reactions with metal-free and metal-bound amyloid-beta and led to chemical modifications. The products of such oxidative transformations were observed to form covalent adducts with amyloid-beta and alter its aggregation.

Moreover, the administration of the most promising candidate molecule significantly attenuated the amyloid pathology in the brains of Alzheimer's disease transgenic mice and improved their cognitive defects.

"This strategy is straightforward, time-saving and cost-effective, and its effect is significant," Prof Lim said. "We are excited to help enable the advancement of new therapeutic agents for neurodegenerative disorders, which can improve the lives of so many patients."





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## Scientists could sabotage bacteria's cell wall

Scientists from the University of Leeds have pieced together how bacteria build their outer, defensive wall — in essence, the cell's armour plating — thus heralding a new strategy in the hunt for antibiotics. Their findings have been published in the journal *Nature Communications*.

The research focused on the role of a protein called SurA. Known as a chaperone, the job of SurA is to marshal other proteins from where they are made, at the centre of the cell, to where they are needed — in this case, to bolster the bacterium's outer wall.

Proteins are long chains of amino acids that must adopt a defined structural shape in order to function effectively. Without the chaperone SurA, the essential proteins needed to build the cell wall run the risk of losing their structural integrity on their journey to the outer membrane.

Using advanced analytical techniques, the scientists mapped how the chaperone SurA recognises proteins to transport them to the bacterial outer membrane.

"For the first time we have been able to see the mechanism by which the chaperone, SurA, helps to transport proteins to the bacterial outer membrane," said Dr Antonio Calabrese, University Academic Fellow in The Astbury Centre for Structural Molecular Biology, who led the research. "In effect it does this by cradling the proteins, to ensure their safe passage. Without SurA, the delivery pipeline is broken and the wall cannot be built correctly."

The research team focused on *E. coli*, a bacteria found in animal and human intestines. But the process they discovered is shared by many pathogenic gram-negative bacteria, a number of which are becoming resistant to antibiotics.

"Understanding that process of how bacteria build their cell wall in greater detail may identify ways we could intervene and disrupt it," Dr Antonio Calabrese said.

"In doing so, we can either destroy the bacteria altogether or reduce the rate at which they divide and grow, making bacterial infections less severe."

Professor Sheena Radford, Director of The Astbury Centre for Structural Molecular Biology, said, "This is an exciting discovery in our quest to find weak spots in a bacteria's armoury that we can target to stop bacterial growth in its tracks and build much-needed new antibiotics."

"It's early days, but we now know how SurA works and how it binds its protein clients. The next step will be to develop molecules that interrupt this process, which can be used to destroy pathogenic bacteria."

Dr Calabrese concluded, "We are at the start of a quest that could result in new, drug-based therapies that work either alone or with existing antibiotics to target these disease-causing bacteria."

## New influenza treatment found to reduce spread of virus

Australian and UK researchers have shown that a new antiviral drug for influenza can treat the infection at the same time as reducing the risk of transmission to others, offering the potential to change the way we manage influenza outbreaks — particularly in vulnerable groups.

The antiviral drug, baloxavir (trade name Xofluza), is said to be the first treatment for influenza with a new mode of 'action' to be licensed in nearly 20 years. It was approved in Australia in February 2020 by the Therapeutic Goods Administration (TGA) and has been used to treat influenza in Japan, the US and several other countries since 2018.

Researchers at the WHO Collaborating Centre for Reference and Research on Influenza at Melbourne's Peter Doherty Institute for Infection and Immunity and Imperial College London tested whether baloxavir could prevent the spread of influenza virus in an animal model in conditions that mimicked household settings, including direct and indirect contact. They also compared the treatment to oseltamivir (trade name Tamiflu), a widely prescribed influenza antiviral. Their study was conducted in ferrets — considered the gold standard animal model for evaluating influenza — and published in the journal *PLOS Pathogens*.

The study found that baloxavir reduced the transmission of influenza across all settings, and did so immediately. Conversely, oseltamivir did not reduce the transmission of influenza to other ferrets. As explained by first author Leo Yi Yang Lee, a medical scientist at the WHO Collaborating Centre for Reference and Research on Influenza, "Our research provides evidence that baloxavir can have a dramatic dual effect: a single dose reduces the length of influenza illness, while simultaneously reducing the chance of passing it on to others. This is very important, because current antiviral drugs only treat influenza illness in the infected patient. If you want to reduce the spread of influenza to others, people in close contact need to take antiviral drugs themselves to stave off infection."

Senior author Professor Wendy Barclay, from Imperial College London, said if the results of the study were replicated in humans, the discovery could be a game changer in stemming outbreaks of influenza. A clinical trial is currently underway to test the effectiveness of baloxavir in reducing transmission amongst human household contacts by treating individuals infected with influenza and monitoring for infection in household members.

"If further trials prove successful, baloxavir could dramatically change how we manage seasonal influenza outbreaks and pandemic influenza in the future," Prof Barclay said.



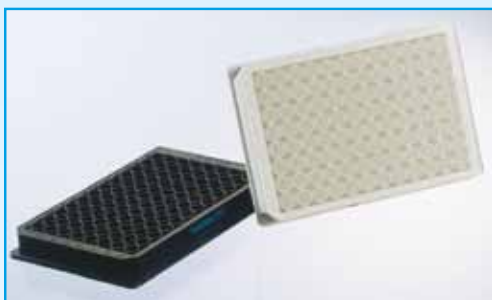
# The Power of Research



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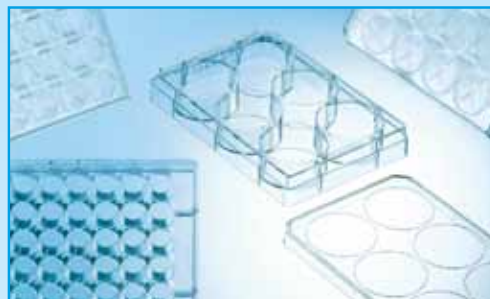
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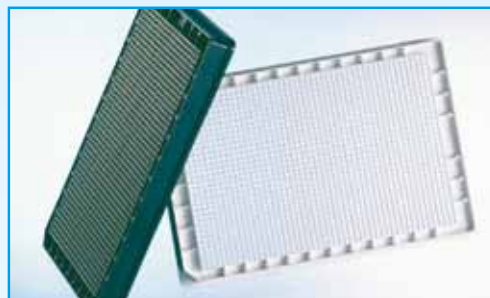
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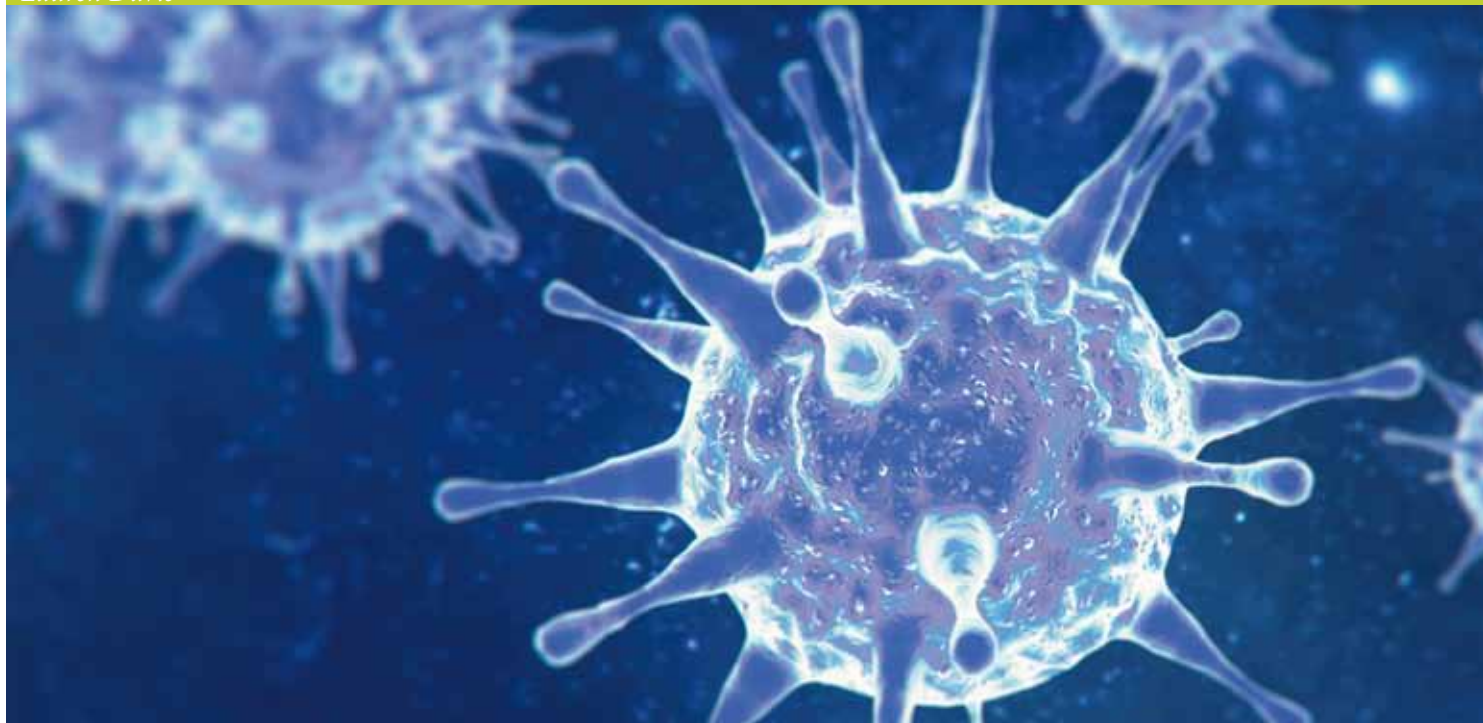


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# COVID-19 vaccine trialled in Australian volunteers

Australia's largest Phase 1 clinical trials specialist, Nucleus Network, has reached a milestone in the race to eradicate COVID-19, having begun dosing participants in the first human trial for a COVID-19 vaccine in the Southern Hemisphere.

and microbiologist Dr Paul Griffin. Dr Griffin told *Lab+Life Scientist* that Australia was singled out as an ideal location to conduct the vaccine trial, in part due to our low number of COVID-19 cases and our global reputation for successfully delivering Phase 1 trials.

"We need people that are immunologically naïve and not exposed to coronavirus, and in Australia that's a relatively easy thing, whereas in a lot of other parts of the world that would be a challenge," he said. And with Novavax having a pre-established relationship with Nucleus Network's Brisbane clinic, the companies knew they would be able to successfully collaborate on this most important trial.

Novavax identified NVX CoV2373 as its lead SARS-CoV-2 candidate following preclinical testing that demonstrated high immunogenicity and high levels of neutralising antibodies, with the product efficiently binding with receptors targeted by SARS-CoV-2 — a critical aspect for effective vaccine protection. These results provide strong evidence that the vaccine candidate will be highly immunogenic in humans, potentially leading to protection from COVID-19 and thus helping to control the spread of this disease.

**T**he Phase 1 trial of NVX CoV2373, a SARS-CoV-2 recombinant spike protein nanoparticle vaccine candidate, is being carried out at Nucleus Network's Melbourne and Brisbane clinics. The trial is being conducted on behalf of biotech company Novavax, the developer of NVX-CoV2373 and sponsor of the trial, with additional funding support from the Coalition for Epidemic Preparedness Innovations (CEPI). Approximately 130 healthy participants, aged 18 to 59 years of age, have been screened to take part.

The study is being held under the guidance of some of Nucleus Network's leading medical experts in clinical trials, including Chief Medical Officer Dr Jason Lickliter and infectious diseases physician

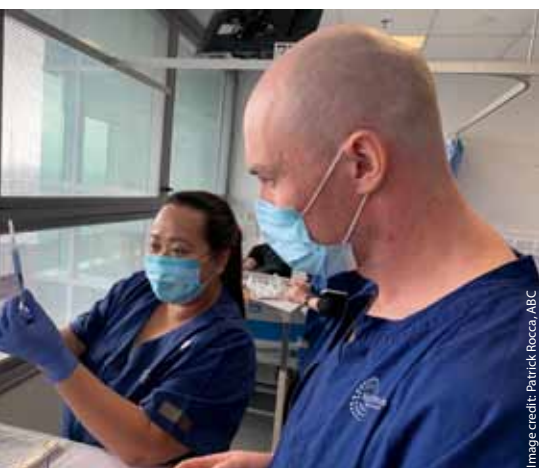


Image credit: Patrick Rocca, ABC





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The candidate is a stable, prefusion protein made using Novavax's proprietary nanoparticle technology, including the company's Matrix M adjuvant to enhance immune responses and stimulate neutralising antibodies. Novavax has already utilised its nanoparticle technology in other vaccine candidates, trialled in around 15,000 volunteers, giving the company what Dr Griffin called "a proven track record of both safety and efficacy".

"Novavax have obviously done significant preclinical work to be ready for human trials," he said. "And that preclinical work is very promising. So on all fronts that we like to see potential efficacy measured in preclinical studies, their results were very impressive."

The Phase 1 portion of the study is a randomised, observer-blinded, placebo-controlled trial designed to evaluate the immunogenicity and safety of NVX CoV2373, both adjuvanted with Matrix M and unadjuvanted. The protocol's two-dose trial regimen assesses two dose sizes (5 and 25 micrograms) with Matrix M and without, with 21 days in between doses. Regular blood tests will be conducted throughout the trial, with preliminary immunogenicity and safety results expected towards the end of July 2020.

"Nucleus Network will collect that data as quickly as we can and, if it supports it, allow Novavax to progress as quickly as possible to Phase 2," Dr Griffin said. This portion is expected to be conducted in multiple countries, including the United States, and would assess immunity, safety and disease reduction in a broader age range.

Should the trial ultimately prove a success, Novavax anticipates having 100 million doses available by the end of 2020, and being in a position to manufacture 1.5 billion doses in 2021 — an incredibly fast-tracked trajectory for vaccine development.

"Given the investment requirement, you typically don't see scaling up of manufacturing until Phase 2 or even Phase 3 data is finalised; these are obviously exceptional circumstances," Dr Griffin said. "With this situation, there's the additional funding support available [from CEPI] to progress of all those steps essentially in parallel. Usually that would come after all the different clinical trial phases had been done sequentially, so usually that's not something that's considered until four, five, six years down the track."

So what's it like conducting a clinical trial in the middle of a pandemic? Dr Griffin said Nucleus Network has made it a priority to progress as quickly as possible, while being careful not to compromise on any of the usual steps.

"The rigour around preclinical assessments and the regulatory environment with this vaccine trial has probably been more, rather than less," he said. "So while we've done things a lot quicker, we've not skipped any steps, to make sure we're as confident as ever, if not more so, that it's the right time for the human trials based on us being confident of the safety and the efficacy. To have done that so quickly has been a little bit of a challenge, but fortunately the regulatory environment has supported that with much faster turnaround times for processes and reviews."

Importantly, Nucleus Network has implemented extensive safety measures in all clinics to ensure compliance with COVID government restrictions; protection of both staff and participants remains vital. Dr Griffin revealed, "We've actually implemented very strict policies, procedures and processes to make sure all of our staff and all of our volunteers are protected. And that includes temperature screening, risk assessments, use of PPE, in-house hygiene practices and all of those things in our clinical trials unit."

Of course sceptics have noted that a vaccine for any type of coronavirus has never been previously achieved, so why should SARS-Cov-2 be any different? According to Dr Griffin, this line of thinking is actually the result of a few misconceptions.

"With the common cold, obviously the number of people that get that is very high, but that's a mixture of coronaviruses, it's not just one, and the impact of those is fairly mild," he said. "The mortality directly associated with those cold viruses is incalculable — so the return on investment, the motivation for people to devote their careers scientifically to those viruses, but moreover the ability to get funding for those, it just would never happen."

"The other thing that people talk about is that we didn't get a vaccine for SARS in the early 2000s. And the main thing there is that the magnitude of that outbreak was very different. We didn't even have 8000 cases, and that outbreak was controlled through good infection control and hygiene practices. So there were a lot of really good vaccine candidates that were developed, but again, the funding and ongoing support to continue that work when that virus was essentially eradicated didn't lend itself to those vaccines making it all the way to market. In fact, a lot of those vaccines did look quite promising and have been the platform for a lot of our vaccine development for SARS-Cov-2."

It's clear that Dr Griffin is cautiously optimistic that a vaccine for COVID-19 is on the horizon, and perhaps even a bit closer to reality than the estimates suggest. Indeed, he suggested that we don't even need to aim for a "perfect" vaccine that provides lifelong immunity — something along the lines of the flu vaccine could be sufficient to start with, then scientists could refine it in time. And with around 13 vaccine candidates for COVID-19 in human trials at the time of writing — and Nucleus Network the only Phase 1 clinical trials specialist to conduct multiple COVID-19 studies simultaneously — there's a small chance that one of those might be the key to ending this once-in-a-century pandemic.

"Even if one of those isn't the candidate that's taken forward to be the vaccine that's used, every trial that's done in humans gives us really important information upon which all the people developing vaccines will be able to use to improve the product," Dr Griffin said. "So every human trial for vaccines is a really important step, and will help everybody else. So that's why we'll get there."

## 3D-printed copper kills SARS-CoV-2 on contact surfaces

Australian additive manufacturer SPEE3D has developed a fast and effective way to 3D print antimicrobial copper onto metal surfaces. Laboratory tests have shown that a touch surface modified by this process 'contact kills' 96% of SARS-CoV-2, the virus that causes COVID-19, in just two hours.

The process, known as ACTIVAT3D copper, was developed by modifying SPEE3D's 3D printing technology, using new algorithms for controlling the company's metal printers to allow existing metal parts to be coated with copper. Copper parts are difficult to produce using traditional methods, and thus 3D printing may be the only tool available to rapidly deploy copper; SPEE3D technology makes this possible.

SPEE3D developed the technique to harness copper's ability to eradicate bacteria, yeasts and viruses rapidly on contact by breaking down the cell wall and destroying the genome. This is compared to traditional surfaces like stainless steel and plastic, with recent studies showing that SARS-CoV-2 can survive on these materials for up to three days. And while stainless steel and plastic surfaces can be disinfected, it is impossible to clean them constantly. When surfaces become contaminated between cleans, touching them may contribute to superspreading events.

360biolabs, a NATA-accredited clinical trial speciality laboratory, tested the effect of ACTIVAT3D copper on live SARS-CoV-2 in its Physical Containment 3 (PC3) laboratory. The results showed that 96% of the virus is killed in two hours and 99.2% of the virus killed in five hours, while stainless steel showed no reduction in the same time frame. Stainless steel is currently the material typically used in hygiene environments.

To further validate its ability to kill SARS-CoV-2, the SPEE3D team developed a process to coat a stainless steel door touch plate and other handles in just five minutes. The digital print files were then sent to participating partners around the globe,

allowing the simultaneous installation of newly coated parts in buildings in the USA, Asia and Australia.

A trial at Charles Darwin University's (CDU) Casuarina campus, for example, involved the coating of a touch plate and door handle. CDU Director of Research and Innovation Dr Steve Rogers said the results were promising and he was excited that this innovative technology could help reduce the survival of the virus on high-traffic surfaces.

"Using the LightSPEE3D 3D printer on our campus, the SPEE3D team have trialled this innovative engineering solution," Dr Rogers said. "Working with our facilities staff

they installed the first door plate on one of our buildings in late March. The results suggest that it is possible to copper coat further items using the LightSPEE3D machine to help reduce the survival of the virus on surfaces."

Meanwhile, Swinburne University of Technology trialled copper door push plates at its Hawthorn campus. Swinburne Associate Professor Suresh Palanisamy said, "Using the LightSPEE3D printer in our Factory of the Future, we have successfully coated a number of existing stainless steel plates and confirmed the speed and ease of this coating process. Further, trial installations have clearly demonstrated the simplicity and practicality of replacing conventional stainless steel with the new ACTIVAT3D plates."

SPEE3D CEO Byron Kennedy said his company was focused on developing a solution that can be rapidly deployed and is more efficient than printing solid copper parts from scratch. He said, "The lab results show ACTIVAT3D copper surfaces behave much better than traditional stainless, which may offer a promising solution to a global problem. The technology can be used globally addressing local requirements, be they in hospitals, schools, on ships or shopping centres."

With laboratory testing complete, it is hoped that the technique can be applied to common touch items like door handles, rails and touch plates in public places.



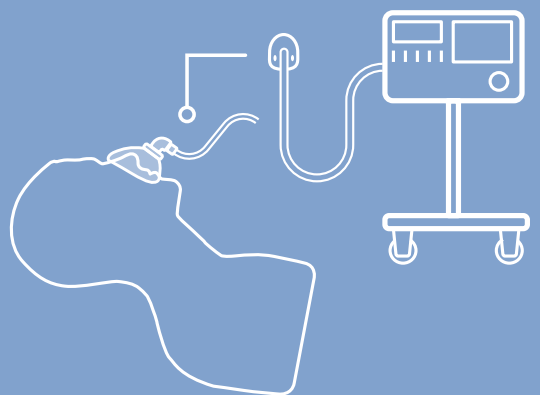
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## Particle size analyser for aerosol and spray characterisation

The nasal passage, commonly used to deliver decongestants and anti-inflammatory steroids, can provide a direct route

for fighting infection from disease-causing pathogens like viruses, including SARS-CoV-2. The nasal route offers a possible alternative to oral or injection methods for the delivery of vaccines. The large surface area for absorption in the nose and lungs, coupled with the high density of blood vessels, allows for rapid onset of action as well as avoiding enzyme degradation within the GI tract.

The droplet or particle size delivered by the spray pump is an important parameter in defining the drug deposition site within the lung and nasal passages. The design of the pump as well as drug formulation properties like viscosity, rheology and surface tension can influence the droplet size produced. If the droplet size is too fine, there is a possibility that the particles will pass through the nasal passages and deposit in the lungs. On the other hand, if the droplet size is too large, the spray may be trapped in the nostrils.

The Malvern Panalytical Spraytec is a laser diffraction-based particle size analyser and is designed with a measurement rate fast enough to characterise sprays and aerosols in real time. Used to investigate the performance of nasal sprays, nebulisers and inhalers, it is designed to provide accurate data for even highly concentrated spray plumes.

The Nasal Spray Actuator accessory can help in the elimination of operator bias during bioequivalence studies. Monitoring the effect changes in the force applied during actuation of a device can aid in the development of new efficient devices and formulations.

The Spraytec system is easy to use with single-click, SOP-driven operation and user-friendly software for effective data interpretation.

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## Viral RNA extraction kit

Beckman Coulter's RNAAdvance Viral XP Reagent Kit enables the extraction of high-quality RNA from universal transport media (UTM) collection devices for use with PCR-based applications.

Built on SPRI (solid phase reversible immobilisation) paramagnetic bead-based technology, the reagent kit is a ribonucleic acid (RNA) isolation process that enables users to purify high-integrity RNA for pathogen or infectious disease research. The kit is demonstrated on PCR applications and shows a limit of detection (LoD) of 1 copy/μL for viral RNA. It offers automation-friendly chemistry that is quickly adaptable to liquid handling platforms used in high-throughput research workflows.

For research use only.

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## Image analysis software for life science

Bitplane Imaris 9.5 is a software solution for correlative microscopy, enabling the possibility of opening multiple 2D, 3D or 4D datasets of differing spatial and temporal resolutions in the same scene. The product is designed to let the image tell its story with aesthetic rendering tools as well as improved quantitative analysis for calculating the relative distance between pairs of object populations.

The latest release has improved surface (reconstructions) rendering to catch the eye of the audience while showing more information so the presenter can spend more time discussing what the results mean rather than what the results are. It includes Surfaces and Spots material options including semi-transparent ones to help the user make eye-catching animations and snapshots.

For every Surfaces and Spots object, the software natively calculates the shortest distance to any other surfaces or spots. The edge of surfaces and the centre of spots are used for these calculations. The computation is fast and capable of running on large images. Calculations can also be performed on multiple datasets at once in Batch mode.

Distance applications include: immunology; organoid studies; tumour microenvironment; bone marrow stem cell niche; organelle distribution inside the cell; and 3D nucleus organisation.

Fast visualisation of terabyte-sized images is possible due to saving the image as a multi-resolution pyramid. The software renders the image in blocks where only the resolution blocks that are required for good-quality rendering on the screen are used. That is, higher resolution data are used when blocks that are closer to the camera (or zoomed in) are rendered and lower resolution data are used when blocks are farther away.

The dynamic volume rendering during rotations and fast zooming are improved in Imaris 9.5 because each block is rendered as a mixture of two resolution levels and this mixture changes with the distance from the camera. In prior versions each block was rendered in one of the discrete resolutions available in the pyramid.

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# 3D imaging tech makes fluorescence microscopy more efficient



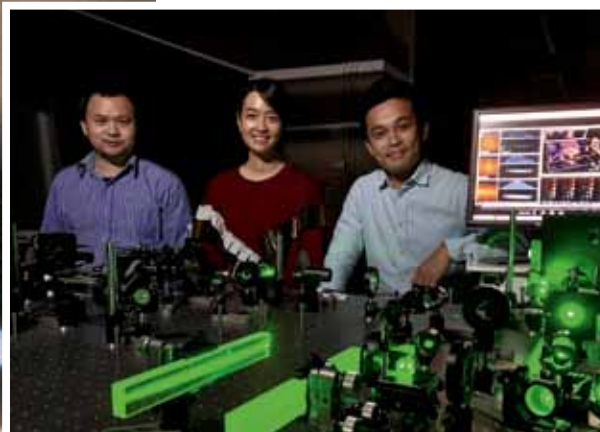
Hong Kong researchers have developed a new optical imaging technology that they believe will push the boundaries of living cells research.

Scientists have been using fluorescence microscopy to study the inner workings of biological cells and organisms for decades. However, many of these platforms are often too slow to follow the biological action in 3D, and too damaging to the living biological specimens with strong light illumination.

To address these challenges, researchers from The University of Hong Kong (HKU) developed coded light-sheet array microscopy (CLAM), which can perform 3D imaging at high speed and is said to be power efficient and gentle to preserve the living specimens during scanning at a level that is not achieved by existing technologies. Their breakthrough has been described in the journal *Light: Science & Applications*.

“CLAM allows 3D fluorescence imaging at high frame rate comparable to state-of-the-art technology (~10 volumes per second),” explained





Dr Kevin Tsia (right) and his team developed a new optical imaging technology to make 3D fluorescence microscopy more efficient and less damaging.

often illuminated for thousands to million times more intense than the sunlight. It is likely to damage the specimen itself, and thus is not favourable for long-term biological imaging for diverse applications like anatomical science, developmental biology and neuroscience.

Moreover, these platforms often quickly exhaust the limited fluorescence ‘budget’ — a fundamental constraint that fluorescent light can only be generated upon illumination for a limited period before it permanently fades out in a process called ‘photo-bleaching’, which sets a limit to how many image acquisitions can be performed on a sample.

“Repeated illumination on the specimen not only accelerates photo-bleaching, but also generates excessive fluorescence light that does not eventually form the final image,” Dr Tsia noted. “Hence, the fluorescence budget is largely wasted in these imaging platforms.”

The heart of CLAM is transforming a single laser beam into a high-density array of ‘light-sheets’ with the use of a pair of parallel mirrors, to spread over a large area of the specimen as fluorescence excitation. As explained by postdoctoral researcher Dr Yuxuan Ren, “The image within the entire 3D volume is captured simultaneously (ie, parallelised), without the need to scan the specimen point by point or line by line or plane by plane as required by other techniques. Such 3D parallelisation in CLAM leads to a very gentle and efficient 3D fluorescence imaging without sacrificing sensitivity and speed.”

CLAM also outperforms common 3D fluorescence imaging methods in reducing the effect of photo-bleaching.

To preserve the image resolution and quality in CLAM, the team turned to code division multiplexing (CDM), an image encoding technique which is widely used in telecommunication for sending multiple signals simultaneously. Postdoctoral researcher Dr Queenie Lai, who developed the system, said, “This encoding technique allows us to use a 2D image sensor to capture and digitally reconstruct all image stacks in 3D simultaneously. CDM has never been used in 3D imaging before. We adopted the technology, which became a success.”

As a proof-of-concept demonstration, the team applied CLAM to capture 3D videos of fast microparticle flow in a microfluidic chip at a volume rate of over 10 volumes per second comparable to state-of-the-art technology. Dr Jianglai Wu, the postdoctoral research who initiated the work, noted, “CLAM has no fundamental limitation in imaging speed. The only constraint is from the speed of the detector employed in the system, ie, the camera for taking snapshots. As high-speed camera technology continually advances, CLAM can always challenge its limit to attain an even higher speed in scanning.”

The team has taken a step further to combine CLAM with HKU’s newly developed tissue clearing technology to perform 3D visualisation of mouse glomeruli and intestine blood vasculature in high frame-rate. Dr Tsia said, “We anticipate that this combined technique can be extended to large-scale 3D histopathological investigation of archival biological samples, like mapping the cellular organisation in brain for neuroscience research.

“Since CLAM imaging is significantly gentler than all other methods, it uniquely favours long term and continuous ‘surveillance’ of biological specimen in their living form. This could potentially impact our fundamental understanding in many aspects of cell biology, eg, to continuously track how an animal embryo develops into its adult form; to monitor in real-time how the cells/organisms get infected by bacteria or viruses; to see how the cancer cells are killed by drugs; and other challenging tasks unachievable by existing technologies today.”

CLAM can be adapted to many current microscope systems with minimal hardware or software modification. Taking advantage of this, the team is planning to further upgrade the current CLAM system for research in cell biology, and animal and plant developmental biology. An US patent application has also been filed for their innovation.

Dr Kevin Tsia, who led the research. “More importantly, it is much more power efficient, being over 1000 times gentler than the standard 3D microscopes widely used in scientific laboratories, which greatly reduces the damage done to living specimens during scanning.”

Existing 3D biological microscopy platforms are slow because the entire volume of the specimen has to be sequentially scanned and imaged point by point, line by line or plane by plane. In these platforms, a single 3D snapshot requires repeated illumination on the specimen. The specimens are

## Perth laboratory reimagined for phenome researchers

National design practice Hames Sharley has designed the Australian National Phenome Centre (ANPC), located within the research and education precinct of Perth's Fiona Stanley Hospital (FSH). Hames Sharley had originally designed the Harry Perkins Institute of Medical Research at FSH, which was completed in 2013, and was invited to return to the building to reimagine an existing laboratory that would serve as home to the ANPC.

By analysing the molecular, physical and biochemical characteristics of biological tissue and fluids such as blood and urine, researchers at the ANPC aim to predict the complex genetic, environmental and lifestyle interactions causing disease and develop personalised treatments. As arguably the only centre of its kind, the ANPC positions Perth and WA as a global leader in precision medicine, enabling leaps in predicting, diagnosing and treating disease.

Hames Sharley's design for the specialist research laboratory occupies 1400 m<sup>2</sup> of PC2 laboratory space, office space and data visualisation facilities, and can accommodate up to 60 researchers. The laboratory is said to house the largest collection of mass spectrometers in the Southern Hemisphere, combined with several nuclear magnetic resonance spectroscopy instruments (NMRs) and advanced data modelling equipment. Deployed to analyse samples, these instruments emit a significant amount of heat and noise that often precludes researchers from prolonged laboratory access due to the uncomfortable conditions.

Hames Sharley Director James Edwards said the design team rose to the challenge by prototyping a laboratory furniture system for on-site testing with actual instruments, which allowed modifications and important refinements.

"The final design comprises movable benches, upon which the large and heavy instruments are located," Edwards said. A central fixed spine of bespoke cabinetry houses electrical and gas distribution services and allows easy connection to the instruments. Additionally, the spine contains an exhaust system that extracts hot air from the instruments before it enters the lab.

Traditionally, the loud pumps associated with these instruments are positioned on the laboratory floor. "To insulate the noise, the central spine of the cabinetry incorporates acoustic enclosures for the pumps — essentially forming a barrier between the

noise and the researchers," Edwards said.

The result is that researchers have the opportunity to converse in their workplace without shouting — a rare occurrence in this type of research facility. Another welcome outcome of the design is the reduction in energy consumption thanks to the extraction of hot air at its source, which minimises the need for air conditioning. Likewise, waste reduction was top of mind as Edwards and his team redeployed some of the existing lab's glass splashbacks to be incorporated into a new dividing wall.

Because the laboratory sits within an existing building, the team had to be mindful of minimising disruption

to nearby offices and other neighbouring facilities. Planning travel routes for the instruments — some of which weigh up to two tonnes — was a key consideration.

"We liaised closely with the manufacturers of the instruments, together with our builders and engineers to plan transportation of equipment and, upon arrival, to ensure our configuration evenly distributed weight across the floor plate," Edwards said.

The new design also incorporates a long corridor which serves as a viewing gallery from which visitors can safely observe researchers at work. Given the significant interest and profile of the research being undertaken at the ANPC, this visibility is another welcome feature.

ANPC Senior Operations Manager Sze How Bong said the response to Hames Sharley's design has been overwhelmingly positive. "The facility's functionality and architectural integrity have surpassed our expectations," he said.

"We're exceedingly grateful for Hames Sharley's well-considered approach, which has resulted in an outstanding laboratory that continues to impress our team and our aligned networks of researchers, both locally and internationally."



Image credit: Douglas Mark Black

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## Focused ion beam scanning electron microscope

The Thermo Scientific Helios 5 Laser PFIB system is an advanced focused ion beam scanning electron microscope (FIB-SEM) with a fully integrated femtosecond laser that quickly characterises millimetre-scale volumes of material in 3D with nanometre resolution. The product combines the Thermo Scientific Elstar SEM Column for ultrahigh-resolution imaging and advanced analytical capabilities with a plasma FIB column for high performance at all operating conditions, and a femtosecond laser that is said to enable in situ ablation at material removal rates not previously obtained by a commercially available product.

The system is designed to accelerate the pace of research for both academic and industrial users, allowing them to characterise materials in a matter of minutes as opposed to days. Not only can researchers quickly image statistically relevant, site-specific, millimetre-size cross-sections at nanoscale resolution, they can also set up large-volume 3D analyses to be automatically completed overnight, freeing up the microscope for other uses.

The device allows researchers to obtain large-volume 3D and subsurface data up to 15,000 times faster than a typical gallium ion source focused ion beam (Ga-FIB). For many materials, a large cross-section of hundreds of microns can be milled in less than 5 min. Serial-section tomography is now possible with this combination of laser and plasma FIB, and can be extended to 3D elemental and grain orientation analysis at the millimetre scale when combined with EDS and EBSD detectors.

The product makes it easy for academic and industrial labs to process challenging non-conductive, air-sensitive and beam-sensitive materials. They can also expedite failure analysis while obtaining fast access to buried subsurface layers often inaccessible with traditional FIB. The FIB-SEM can be used to analyse a variety of materials, including metals, batteries, glass, ceramics, paint coatings, polymers, biomaterials and graphite.

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## Suction system for cell culture and laboratory waste

The Rocker Lafil 300-Bio-Dolphin provides an all-in-one, space-saving solution for the suction of cell culture and laboratory waste.

The complete system integrates a vacuum source, waste bottle and suction kit.

The Lafil 300 is a compact vacuum pump, including an autoclavable PES waste bottle. The incorporation of the bottle and pump together is designed to ensure the bottle is always secure and reduces the risk of spills. The maximum vacuum and flow rate are 105 mbar and 20 L/min respectively. The pump is driven by piston, so there is no need for regular oil changes and maintenance.

The BioDolphin suction kit offers quick connection to ensure adapters can be replaced fast. With its innovative tip ejection design, changing tips is easily done single-handedly. The suction kit also features a lock switch, so users don't need to continuously press the button to maintain suction. Once it's locked in, it can be unlocked when complete. The kit also conveniently comes with a multifunctional storage rack, with an inbuilt liquid collection tray.

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## Cell culture microplates

Greiner Bio-One has various microplates available, including tissue culture microplates, with a wide variety of surface treatments that suit every need. The spectrum ranges from tissue culture plates for classic and sensitive cells to ELISA/immunology and biochemical assay plates.

The portfolio includes 96-well plates, 384-well plates and 1536-well plate formats in clear, black and white opaque or  $\mu$ Clear ultrathin film bottom, and a full range of polypropylene microplates for sample storage and dilution. Specialty microplates — such as glass bottom microplates, ultralow well base SCREENSTAR microplates for imaging and/or high content screening and UV-Star products for transmittance in the lower UV wavelength range — are also available.

Manufactured under DIN ISO 9001 guidelines without the use of silicon-based mould release, the microplates can be traced all the way back to production through a defined lot number system. They are free of detectable endotoxins (0.03 EU/mL), biozides and antistatics.

The microplates are manufactured out of raw materials tested for leachables and footprint compatible with automated systems. They are analysed for detectable DNase, RNase and human DNA, and regularly tested using an FDA-approved kinetic turbidimetric LAL test (limulus amoebocyte lysate assay). Barcode labelling is available on request.

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# AI blood test can detect over 50 types of cancer

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US researchers have developed a blood test that can accurately detect more than 50 types of cancer and identify in which tissue the cancer originated, often before there are any clinical signs or symptoms of the disease. It has been described in the journal *Annals of Oncology*.

**T**umours shed DNA into the blood, and this contributes to what is known as cell-free DNA (cfDNA). However, as the cfDNA can come from other types of cells as well, it can be difficult to pinpoint cfDNA that comes from tumours. The new blood test analyses chemical changes to the DNA called 'methylation' that usually control gene expression. Abnormal methylation patterns and the resulting changes in gene expression can contribute to tumour growth, so these signals in cfDNA have the potential to detect and localise cancer.

The blood test targets approximately one million of the 30 million methylation sites in the human genome. A machine learning classifier (an algorithm) was used to predict the presence of cancer and the type of cancer based on the patterns of methylation in the cfDNA shed by tumours. The classifier was trained using a methylation database of cancer and non-cancer signals in cfDNA. The database is believed to be the largest in the world and is owned by Californian company GRAIL, which funded the study.

"Our earlier research showed that the methylation approach outperformed both whole-genome and

targeted sequencing in the detection of multiple deadly cancer types across all clinical stages, and in identifying the tissue of origin," said Dr Michael Seiden, President of The US Oncology Network and senior author of the paper. "It also allowed us to identify the most informative regions of the genome, which are now targeted by the refined methylation test that is reported in this paper."

Blood samples from over 4000 participants were used for training and validating the machine learning classifier as part of the Circulating Cell-free Genome Atlas (CCGA) study — 3052 in the training set (1531 with cancer, 1521 without cancer) and 1264 in the validation set (654 with cancer and 610 without cancer). The algorithm analysed these blood samples to identify methylation changes and to classify the samples as cancer or non-cancer, and to identify the tissue of origin.

The researchers found that the classifier's performance was consistent in both the training and validation sets, with a false positive rate of 0.7% in the validation set, meaning that less than 1% of people would be wrongly identified as having cancer. As a comparison, about 10% of women are wrongly identified as having cancer in national breast cancer screening programs, although this rate can be higher or lower depending on the number and frequency of screenings and the type of mammogram performed.

The classifier's ability to correctly identify when cancer was present (the true positive rate) was also consistent between the two sets. In 12 types of cancer that are often the most deadly (anal, bladder, bowel, oesophageal, stomach, head and neck, liver and bile duct, lung, ovarian and pancreatic cancers, lymphoma, and cancers of white blood cells such as multiple myeloma), the true positive rate was 67.3% across clinical stages I, II and III. These 12 cancers account

for about 63% of cancer deaths each year in the US and, at present, there is no way of screening for the majority of them before symptoms show. The true positive rate was 43.9% for all cancer types in the study across the three clinical stages.

Detection improved with each cancer stage. In the 12 pre-specified cancers, the true positive rate was 39% in stage I, 69% in stage II, 83% in stage III and 92% in stage IV. In all of more than 50 cancer types, the corresponding rates were 18%, 43%, 81% and 93%, respectively. The test was also consistent between the training and validation sets in its ability to identify the tissue where cancer had originated, with an accuracy of 93% in the validation set.

"These data support the ability of this targeted methylation test to meet what we believe are the fundamental requirements for a multicancer early detection blood test that could be used for population-level screening: the ability to detect multiple deadly cancer types with a single test that has a very low false positive rate, and the ability to identify where in the body the cancer is located with high accuracy to help healthcare providers to direct next steps for diagnosis and care," Dr Seiden said.

"Considering the burden of cancer in our society, it is important that we continue to explore the possibility that this test might intercept cancers at an earlier stage and, by extension, potentially reduce deaths from cancers for which screening is either not available or has poor adherence. To our knowledge, this is the largest clinical genomics study, in participants with and without cancer, to develop and validate a blood test for early detection of multiple cancers."

Researchers are continuing to validate the test in large, prospective studies in the USA (STRIVE and PATHFINDER studies) and the UK (SUMMIT study), and to examine its feasibility for screening populations.





## Automation solutions for coronavirus research and detection

Tecan's DreamPrep solutions provide ready-to-go workflows for nucleic acid extraction and NGS library prep, helping to boost the productivity of labs investigating the SARS-CoV-2 virus — the causative agent of COVID-19.

DreamPrep NAP workstation featuring Zymo Research is designed to simplify nucleic acid extraction workflows by providing a pre-programmed, optimised workflow for the Quick-DNA/RNA Viral MagBead kit, which was recently evaluated

as part of a SARS-CoV-2 detection workflow. This set-up allows purification of up to 96 samples in less than 2 h, by combining the Fluent Automation Workstation and Fluent Gx Assurance Software for regulated environments.

Tecan is also helping to accelerate research into the COVID-19 pandemic with the DreamPrep NGS and Trio RNA-Seq library preparation kits for liquid biopsy, FFPE and other challenging samples. This approach to pathogen identification from low-input samples delivers insights into viral abundance, mutation rates, spectrum surveillance and gene expression. The valuable information gathered is helping researchers around the world to determine disease incubation times, quarantine periods, and the risks and impact of healthy carriers on the general population, epidemiology and viral evolution.

For research use only. Not for use in clinical diagnostics.

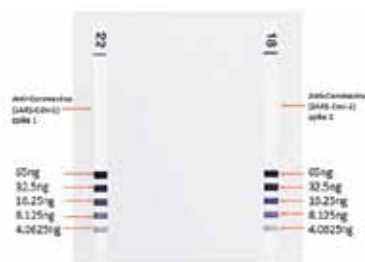
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## SARS-CoV-2 recombinant antigens and antibodies

To join the fight against the 2019 novel coronavirus (COVID-19), MP Biomedicals now offers three monoclonal antibodies from mouse and five recombinant antigens for SARS-CoV-2, expressed in *E. coli* and HEK293.

Recent scientific studies have discovered heightened affinity of the SARS-CoV-2 spike (S-protein) to the human ACE2 cellular receptor. The spike protein (S-protein) contains two subunits, S1 and S2. S1 defines the range of hosts and specificity of the virus, and thus recognises and binds with the cell surface receptor. The S2 subunit contains basic elements needed for membrane fusion. MP Biomedicals now offers three monoclonal antibodies from mouse with high affinity to the SARS-CoV-2 spike (S1 and S2) proteins for

use in various applications, including western blot, immunoprecipitation, ELISA tests, rapid tests and flow cytometry.

In addition to antibodies, a selection of recombinant protein antigens for SARS-CoV-2 expressed in *E. coli* and HEK293 cells are also available. These include not only the spike protein, but also the nucleocapsid protein and host receptor ACE2. The company's in-house validation (slot blot analysis) has observed high sensitivity and affinity for SARS-CoV-2 spike antibodies (4.06-67.5 ng) when tested against SARS-CoV-2 spike protein (S1+S2) (see image).

The company's anti-coronavirus antibodies include: (i) anti-coronavirus (SARS-CoV-2) spike S1, mouse, mAb; (ii) anti-coronavirus (SARS-CoV-2) spike S2, mouse, mAb; and (iii) anti-coronavirus (SARS-CoV-2) (B) spike S2, mouse, mAb.

The company's SARS-CoV-2 recombinant antigens include: (i) SARS-CoV-2 Nucleocapsid Protein, His tag (*E. coli*); (ii) SARS-CoV-2 Nucleocapsid Protein, His tag (HEK293 cells); (iii) SARS-CoV-2 Spike Protein (S1+S2), His tag (HEK293 cells); (iv) ACE2, His tag (*E. coli*); and (v) ACE2, His tag (HEK293 cells).

**MP Biomedicals Australasia P/L**

[www.mpbio.com](http://www.mpbio.com)

## TOC analyser

The 1080 TOC Analyzer from OI Analytical processes aqueous samples for analysis of the total organic carbon (TOC), total inorganic carbon (TIC) and non-purgeable organic carbon (NPOC) content. Supporting USEPA-approved methods, Standard Methods, ASTM, DIN/ISO/CEN and EU Methods, the product can analyse up to 300 samples per 24 h period.

The device employs a multistep analysis technique to distinguish and quantify different forms of carbon present in sample matrices and determine TOC content. The value reported as TOC is the non-purgeable organic carbon (NPOC) content. NPOC is derived by first determining, or sparging, the TIC content of a sample and then introducing the TIC-free sample into the combustion reactor to oxidise organic compound constituents.

TIC-free samples are pulse-timed injected into the reactor to perform high-temperature (680°C) combustion over a platinum catalyst. Organic compounds are oxidised and converted into CO<sub>2</sub>, which is then quantified by the SSNDIR detector. The result is reported as the TOC content in both mass and concentration of carbon. The

1080 TOC Analyzer also supports other analytical approaches — including TC, TOC by subtraction (TC-TIC) and simultaneous determination of total bound nitrogen (TNb) using the optional TNb analysis module.

Other features include: a wide operational range (50 ppb–2000 ppm C); a patented Smart Slide injector that extends O-ring life and reduces maintenance; and patented Tube Guard that extends furnace tube life and reduces maintenance.

**Walker Scientific Pty Ltd**

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## Containment filtration systems

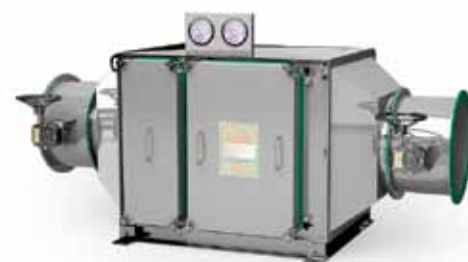
Meeting the critical standards required of negative pressure isolation rooms, quarantine isolation rooms, pandemic wards, TB wards, PC3 level biocontainment laboratories and cyclotron/nuclear medicine areas is a task for an experienced specialist in HEPA filtration systems and airborne isolation and containment technologies. Airepure specialises in developing and maintaining air filtration regimes for medical environments and laboratory exhaust systems, with the ability to design air filtration systems that meet the most exacting specifications and, once they are commissioned, to keep them functioning continuously.

Airepure's airborne containment and isolation filtration solutions include: terminally mounted HEPA containment housings and systems; inline containment exhaust filtration systems; bag-in bag-out (BIBO) style containment systems with bubble-tight isolation dampers, decontamination/fumigation ports, a remote scan arrangement for testing and BIBO arrangements for filter change out; and custom-engineered HEPA (particulate) and HEPA (gaseous) containment filtration systems. The company's NATA certified on-site technicians can also service customers' existing exhaust filtration containment systems through the replacement and testing of HEPA filters to meet Australian Standards and state healthcare regulations.

Airepure is a national air filtration company providing powerful and integrated air filtration solutions, ranging from basic HVAC filtration through to high-end HEPA/ULPA filtration and custom airborne containment technologies.

**Airepure Australia Pty Ltd**

[www.airepure.com.au](http://www.airepure.com.au)





### Microinjector

Designed to simplify intracellular injection and a variety of other microinjection tasks, the MICRO-ePUMP from WPI uses carefully regulated air pressure for injecting cells with fluid. Injected volumes range from microlitres to nanolitres. The port supplies positive pressure for high-pressure ejection. The pressure port maintains a low positive 'compensation' pressure to the injecting pipette between injection pulses to prevent fluid uptake through capillary action.

The product is designed to inject very small quantities of fluids, such as drugs, into cells or small organelles. Pressure injection is an especially useful alternative to electroionophoresis, since it does not mandate the use of charged ions. The compensation pressure is a constant low pressure that eliminates any capillary action front-filling of the pipette and then the precise burst of regulated higher pressure is activated with the foot switch that is included.

WPI's MICRO-ePUMP Pinpoint Cell Penetrator technology is embedded inside the MICRO-ePUMP. When the researcher enables the MICRO-ePUMP, it delivers a highly localised voltage signal to a targeted injection site to facilitate penetration with minimal trauma. The researcher determines the amplitude and frequency of the signal that best suits the application. The signal originates in the control box, and it is transmitted through the electrode interface cable to the microelectrode holder. A silver wire is used to transmit the signal into the electrically conductive substance being injected. A reference electrode is used to place the media at 0.0 V potential with reference to the generated voltage.

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# The S-Monovette® is the revolution in blood collection.

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When used as a syringe, the phlebotomist has full control over the speed at which the blood is drawn into the tube. This is particularly useful for patients with fragile veins, such as the very young or elderly, where the use of the aspiration technique prevents even the most fragile veins from collapsing. When the tube has been filled, the plunger is simply snapped off to leave a primary sample tube which can be centrifuged and is compatible with all major analysers.

The S-Monovette can also be used as an evacuated tube by drawing the plunger fully down and snapping it off immediately

prior to blood collection. This creates a fresh vacuum and ensures a precise filling volume, ensuring a correct dilution ratio.

The reduced vacuum pressure in the S-Monovette drastically reduces the rate of haemolysis and vein collapse, meaning increased sample quality and reduced costs associated with repeat collections. Furthermore, unlike pre-evacuated tubes, the S-Monovette does not have to hold a vacuum for many months after manufacture, which allows the membrane stopper to be thinner and more easily penetrated by the needle sheath. This minimises the movement of the needle in the vein when attaching the tube, ensuring optimum patient comfort.

The S-Monovette needle is ready to use so that there is no need for assembly to

a holder. The needle is of a compact, low profile design, which reduces the chance of haematoma by allowing for a reduced angle of puncture and eliminates the possibility of needle stick injury caused by assembly of the needle and holder. The compact design also results in approximately one sixth of the sharps volume caused by using a pre-evacuated system, giving significant cost savings.

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\* Lippi et al. Prevalence of haemolysis in blood samples collected from intensive care patients. Clin Biochem 2013;48(10):101-104

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# Plants control their own microbiome diversity

New research led by Michigan State University (MSU) has revealed how plants use their genes to select which microbes get to live inside their leaves in order to stay healthy.

Published in the journal *Nature*, this is said to be the first study to show a causal relationship between plant health and assembly of the microbial community in the phyllosphere — the total above-ground portions of plants. The work also suggests that plants and animals may share a similar strategy to control their microbiomes.

When scientists mention that human ‘gut bacteria’ should be well balanced, they refer to the gut microbiome — the genetic material of all the microbes living in human digestive

systems. And with large-scale study of the plant microbiome only around a decade old, the MSU team wanted to know if plants need a properly assembled phyllosphere microbiome.

“In nature, plants are bombarded by zillions of microbes,” explained MSU’s Sheng Yang He, lead co-author of the new study. “If everything is allowed to grow in the plants, it would probably be a mess. We want to know if the numbers and types of microbes matter; if there is a perfect composition of microbes. If so, do plants have a genetic system to host and nurture the right microbiome?”





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It seems plants do, with the researchers discovering a mechanism that involves two genetic networks: one involves the plant immune system and the other controls hydration levels inside leaves. Both networks work together to select which microbes survive inside of plant leaves.

“When we remove both networks from a plant, the microbiome composition inside the leaves changes,” He said. “The numbers and mix of bacteria types are abnormal, and our team sees symptoms of tissue damage in plants.

“The symptoms are conceptually like those associated with inflammatory bowel disease in humans. This is probably because the genes involved are ancient, in evolutionary terms. These genes are found in most plants, while some even have similarities to those involved in animal immunity.”

According to scientists in the He lab, this may be the first time that sickness associated with dysbiosis, or microbial imbalance, has been formally described in the plant kingdom. The fact that it seems conceptually similar to human health suggests a fundamental process in life.

### Determining causality

The reason it is difficult to find causality in microbiome studies is because it is practically impossible to cut through the noise of zillions of microbes. The He lab worked around this problem by developing a germ-free growth chamber they call the gnotobiotic system — an environment for rearing organisms in which all the microorganisms are either known or excluded.

“Very few people have grown a sterile plant in sterile, organic-rich material,” He said. “Our system uses a peat-based soil-like substrate; basically greenhouse potting soil. We use heat and pressure to kill all the germs in the soil, and the plants can grow under this germ-free condition.”

Researchers can then introduce microbes in a controlled fashion, into this environment.

“You can add one, two, or even a community of bacteria,” He said. “In our study, we extracted a community of bacteria from dysbiotic, or sick, plants and introduced them to our healthy plants, and vice versa. We found that both the microbiome composition and the plant genetic systems are required for plant health.”

For example, a plant with defective genetics could not take advantage of a microbiome transplanted from a healthy plant — the microbiome slowly reverted to the state that caused sickness. On the other end, a healthy plant exposed to a sick plant’s microbiome also suffered. Although it had the genetic tools to select the right microbes, microbe availability was limited and abnormal. The plant couldn’t fix the situation.

### Microbe levels and composition matter

It turns out that increased microbiome diversity correlates with plant health. Somehow, plant genes are gatekeepers that encourage this diversity.

The sick plants in the study had 100 times more microbes in a leaf, compared to a healthy plant. But the population was less diverse. To figure out why, the scientists did thousands of

one-on-one bacteria face-offs to tease out which strains were aggressive.

In the sick plants, proteobacteria strains — many of which are harmful to plants — jumped from two-thirds the composition of a healthy microbiome to 96% in the abnormal population. Firmicutes strains, many which may be helpful to plants, went down in numbers.

“Perhaps, when the population of microbiome is abnormally higher in that sick plant, the microbes are physically too close to each other,” He said. “Suddenly, they fight over resources, and the aggressive — in this case harmful — ones unfortunately win. Healthy plants seem to prevent this takeover from happening.”

### Supporting plant health

The study is an example of how diversity is important to support healthy living systems. Each type of microbe might impart different benefits to plants, such as increased immunity, stress tolerance or nutrient absorption.

Scientists such as He want to be able to manipulate the plant genetic system to reconfigure the plant microbiome. This would enable plants to become more efficient at selecting their microbial partners and experience improved health, resilience and productivity.

“Our field is still young,” He said. “Microbiome research tends to focus on human gut bacteria. But many more bacteria live on plant leaves, the lungs of our planet. It would be wonderful to understand how microbes impact the health of the phyllosphere in natural ecosystems and crop fields.”



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## SARS-CoV-2 IgG ELISA kit

The characterisation of the SARS-CoV-2 virus is critical for understanding the mechanisms of action of the virus, including the viral entry into the host cells, the replication cycle and the viral spread into human body. A better understanding of those biological processes is key for a better diagnosis and treatment of the disease.

Enzo Life Sciences provides a full range of tools including antibodies, antigens and assay kits that help investigate different aspects of the biology of the SARS-CoV-2 virus. The company now offers a SARS-CoV-2 IgG ELISA Kit for in vitro diagnostic use under the FDA's Emergency Use Authorization (EUA).

Enzo's ELISA assay is a qualitative assay, optimised to provide accurate and sensitive detection of IgG antibodies to SARS-CoV-2 in human serum, with high throughput testing capabilities for the clinical laboratory setting. The ELISA kit is a colorimetric immunoassay kit with results in under 2 h. Absorbance is read at 450 nm and can be used to measure up to 86 samples per kit, with all necessary reagents supplied.

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## Micropipettes

The Precise range of micropipettes from Capella Science provides a good combination of ergonomics and precision. Reduced operating force via a magnetic-assisted piston and ultrasmooth action are said to provide improved accuracy and comfort. The advanced design should also ensure the user's hands won't get tired even during extended bench work.

Tip ejection is said to be almost effortless, via the corrosion-resistant ejector with shock-absorbing mechanism. The tip cone is highly durable PVDF and the large 4-digit display has a lock setting. There are nine variable-volumes models, 14 fixed volumes and 12 multichannel models available. All are calibrated in an ISO-accredited lab and in-house recalibration is easy.

The comprehensive range of tips, from 10  $\mu$ L to 10 mL in plain or filter-tip format, is manufactured in a human-touch-free cleanroom. All are certified DNase, RNase, pyrogen, endotoxin, Human DNA and PCR inhibitor-free, and non-cytotoxic.

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## Precision compact balances

Fast and precise, Highland precision compact balances have many features. With strong ABS construction, an audible alarm that warns users if capacity is exceeded and its ShockProtect feature that offers advanced overload protection, the Highland is suitable for rigorous weighing demands in laboratories or in the field. The stainless steel pan is resistant to corrosive materials and easy to clean.

Percentage weighing simplifies formulation applications for creating ointments, medical compounds or chemical mixtures, while the accumulation feature allows users to keep a running total of the weight. Parts counting can streamline compounding tasks or pill packaging for pharmaceutical applications. Below-balance weighing allows for density measurements and specific gravity calculations.

HandiCal ensures internal calibration can be done without external weights, which can come in handy in busy labs. The draft shield helps prevent samples from being moved due to vibrations and air currents, and the balances can be stacked during storage without damaging the load cells. For true portability, the balance's internal battery can last up to 24 h.

RS-232 and USB interfaces allow for data communication with computers, printers and data collection software like AdamDU. They are frequently used in material testing, manufacturing, jewellery and education. Like all Adam balances and scales, Highland balances are compliant with the latest NRCS regulations regarding electrical safety standards.

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## Knockout cell lines and lysates

CRISPR-Cas9 knockout cell lines from Abcam provide scientists with off-the-shelf, single-gene knockouts so the user can confidently interrogate the relationship between genotype and phenotype without having to establish their own knockout cell line. The company provides a large and expanding range of knockouts in immortalised mammalian cell lines, such as HeLa and HEK293T. All knockout cell lines are Sanger sequenced and many have additional western blot data to confirm knockout at the proteomic level.

Additionally, users can access over 2700 diploid knockout cell lysates, generated from commonly used cancer cell lines. They can select from a large library of immortalised diploid knockout cell lines including HeLa, HEK293T, A549, HCT116, Hep G2 and MCF7, derived from single-cell clones. Each knockout cell line is individually cloned and validated by Sanger sequencing. The knockout cell lysates are provided lyophilised with the parental wild-type lysate to allow the biological impact of the knockout to be assessed within a consistent cellular background.

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## Fume cupboard

Fume cupboards are an essential part of many Australian labs, but are large energy users and can be a key contributor to running costs of large laboratory buildings. In recent years two technologies have become popular in reducing fume cupboard running costs: variable air volume (VAV) technology and the automatic closing sash.

When combined, these two features can significantly reduce the cost of conditioned make-up air, due to the fume cupboard airflow being reduced to reflect the actual sash opening and the sash being closed more often. But fume cupboards with VAV airflow control and auto sash were typically a luxury item, limited to top-end manufacturers or as an add-on to basic models, limiting the number of new projects that can afford to install energy-efficient fume cupboards.



G3Lab recognised the benefits of bringing these features to a wider range of lab users and has now introduced its own fume cupboard which includes VAV and auto sash features at a lower installed cost, according to the company. The fume cupboard also uses Accuvalve technology to measure actual airflow, which makes it 100% compliant to AS2243.8.

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## Gas mixtures

BOC's HiQ Environmental Standard gas mixtures are designed for laboratory applications such as air quality research, measuring stack emissions and environmental emissions testing according to the US EPA protocol. Typical components include nitric oxide, nitrogen dioxide, carbon monoxide and sulfur dioxide, with mixtures made to the specifications required to meet local environmental regulations or research needs. Alternative components are available with calibration gases made to meet the user's specific requirements. The gas mixtures are used daily to ensure emissions compliance from energy and chemical producers, while also being used to verify air quality results across Australia by state environmental bodies.

The traceability chain for HiQ Environmental Standards is sound, providing users with a high level of quality assurance and compliance to US EPA-600/R-12-531 G1 and G2 procedures for the Assay and Certification of Gaseous Calibration Standards. Mixtures are created in BOC's special gases facility in accordance with ISO 17034.

**BOC Limited**  
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## NGS library preparation

The epMotion 5073m NGS solution has everything required for small-scale NGS library preparation. It combines automated liquid handling and useful software features with high-quality consumables and space-saving accessories to optimise the library preparation of up to 24 samples.

The product is equipped with two single-channel and one multi-channel dispensing tools to give users the flexibility to work with different plate or tube formats, and provides uninterrupted library preparation by automatically switching between the single- and multi-channel dispensing tools when needed.

A Reservoir Rack Module NGS allows consumables, reagents and tips to be stored on one deck position and, when combined with the Reservoir Rack Module Tips, further increases tip capacity. The epMotion 5073m has a gripper tool for transporting labware, and comes with a TipHolder 73 to enable the stacking of 5 x 96 tips on just two positions. All labware, tips and liquid levels are checked prior to each run by the contact-free optical sensor.

The product also comes with an integrated magnetic finger, plate magnet and Eppendorf ThermoMixer to enable upstream nucleic acid purification, and can be used to automate clean-ups and set-ups as well as take on small incubations.

All methods can be easily designed, optimised and implemented using the epBlue software on either the Easy-Con, touch screen tablet or Multicon touch PC.

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## Laboratory washer

Miele Professional's PG 8583 laboratory washer is able to fit under a bench in a 600 x 600 x 835 mm (w x d x h) space. Its laser-welded, crevice-free chamber facilitates easy surface cleaning, while spray pressure and spray arm monitoring helps avoid poor cleaning results.

Rear docking enables efficient use of the internal space, allowing washing of narrow-necked glassware with 128 injector nozzles on two levels. This is also designed to improve water pressure for better cleaning performance.

A variable speed pump provides good spray pressure in all program phases. Integrated heating elements within the pump housing remove the elements from the wash chamber for enhanced safety. The product is supplied with two internal dispensing pumps for liquid detergent and liquid neutraliser dispensing.

The PG 8583 features 14 programs, including the 'Mini' program for slightly soiled loads. This program is designed to provide energy savings and shorter cycle times, using up to 45% less water. The 'Touch on Steel' control panel is meanwhile integrated into the angled door handle and incorporates a three-line, easy-to-read text display.

**Bio-Strategy Pty Ltd**  
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# Recent advances in microbial air sampling

*Joe Cardamone, General Manager, Cell Biosciences*

**Microorganisms that can cause infections in healthcare facilities and product spoilage in both a pharmaceutical and food setting include bacteria, fungi, and viruses. Typically the source of these microorganisms can include environmental sources, and for this reason, environmental monitoring protocols should include strategies to reduce the incidence of these organisms.**

Through air sampling, it is possible to evaluate the level of microbial contamination in the environment. Active monitoring and passive monitoring techniques are available.

In active air monitoring an impactor style microbial air sampler, such as the Orum TRIO. BAS device, is placed into the environment under test and draws in a known volume of air over a petri dish that is contained within the device. Different culture media can be used depending on the types of microorganisms being investigated. The quantity of microorganism present is measured in colony forming units (CFU) per m<sup>3</sup> of air.

Examples of passive monitoring include 'settle plates' which are standard petri dishes containing culture media that are exposed to air for a given period. Organisms which 'fall' on the surface of the agar plate can be counted to determine in level of bacteria in air. Only larger particles (greater than 10 µm) are likely to land on plates. Results are expressed in CFU/plate/time or in CFU/m<sup>2</sup> /h. Settle plates are not likely to be validated as a recovery method as there is no accurate measurement of the volume of air sampled.

## The Microbial Air Sampler

The impactor style air sampler dates to the 1860s, when researchers used these devices to study the relationship between dust and disease. Today's devices use the same

general principle — a jet of particle laden air impacting on a plate.

The original devices were bulky and industries' requirement for portable devices saw an influx of new models in the 1980s. The first of these new generation devices had a single sampling head, with the Orum TRIO. BAS MONO being a modern interpretation of the original devices. The device allows the addition of a single agar plate within the unit.

Recent advances have seen Orum introduce models containing two (TRIO. BAS DUO) and three (TRIO. BAS TRIO) sampling heads, allowing for more complex sampling plans with less user intervention. The benefit of a two-sampling head unit is that two different culture media can be utilised simultaneously: for example, Tryptone Soya Agar for total aerobic bacterial count and Sabouraud Dextrose Agar for counting yeasts and moulds. In addition, as the multi-head units allow for less user intervention, multiple plates can be tested simultaneously with a reduced risk of microbial contamination coming from the operator during setup rather than the test environment.

To illustrate the benefit of a three sampling head unit, Roberto Ligugnana from Orum presented a poster at the 14th Annual PDA Global Conference on Pharmaceutical Microbiology showing that, when comparing a single-head unit that needed to be accessed



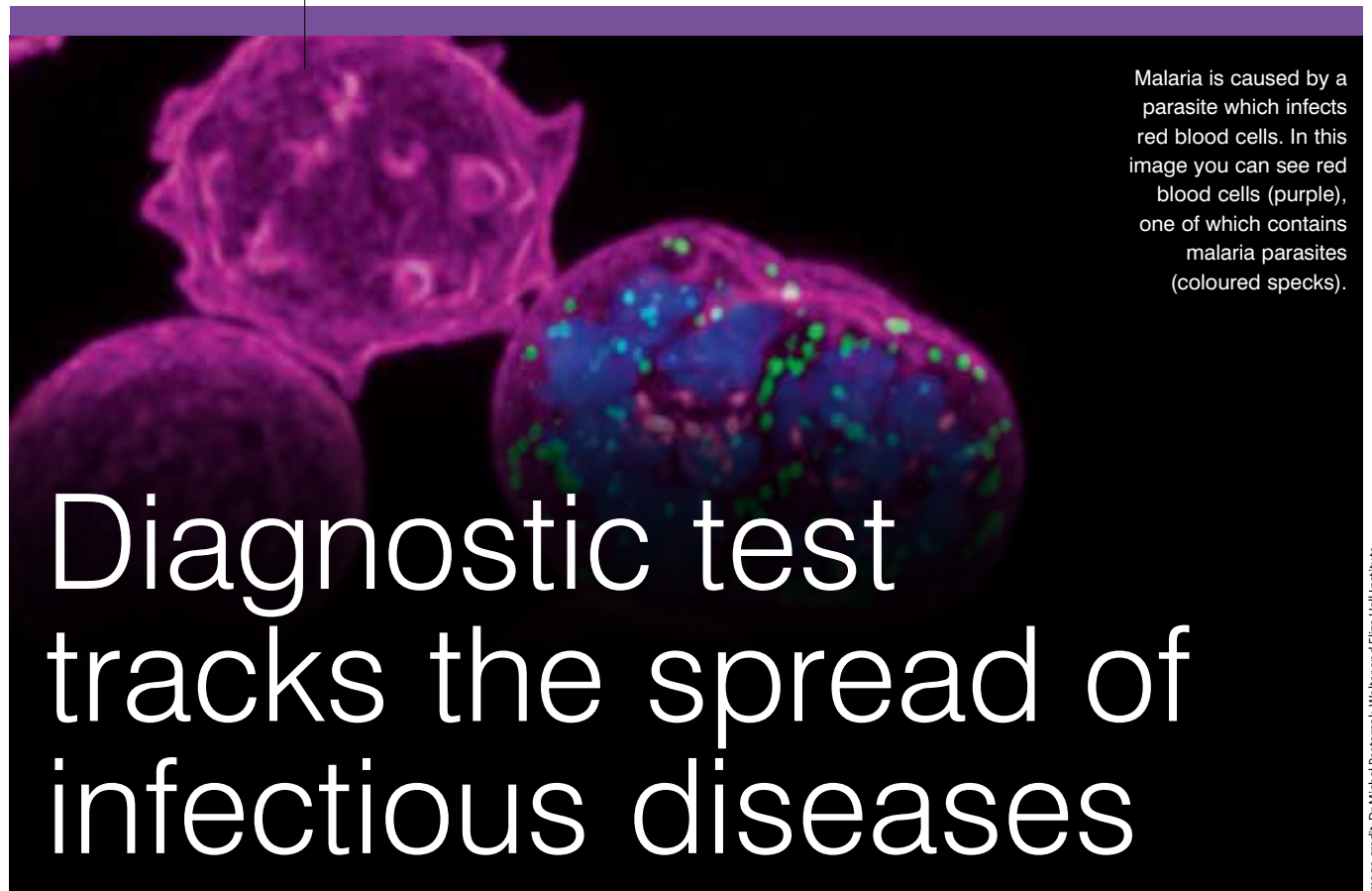
three times during its run to a three-head unit that was accessed only at the start of the run, and programmed such that each head ran at a different time, the CFU counts on the single head unit were higher, suggesting that the operator, and not the environment, was actually contributing to the total CFU counts. This artificially elevated count could result in a product failing QC when in fact the environment was within acceptable limits.

## The Microbial Monitoring of Compressed Gas

The microbial monitoring of compressed gas used in cleanrooms is an important requirement of the pharmaceutical production facility. The high-pressure gases that are in contact with pharmaceutical products during production and application include air, argon, carbon dioxide and nitrogen. They are stored in special containers or tanks and delivered in high-pressure cylinders or cryogenic vessels. Although the presence of active microorganisms in compressed gas is unusual due to the harsh environment, nutrients such as water and oil droplets are available to allow for the growth of biofilms. Orum supplies attachments for impact air samplers that allow for the testing of compressed gases. The air flow from the compressed supply is regulated through a flow valve before entering the aspiration head of air sampler.

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Malaria is caused by a parasite which infects red blood cells. In this image you can see red blood cells (purple), one of which contains malaria parasites (coloured specks).

# Diagnostic test tracks the spread of infectious diseases

Image credit: Dr Michal Pasternak, Waller and Eliza Hall Institute.

An international research team has developed a new diagnostic test to track the spread of infectious diseases such as malaria in populations and target resources where they are most needed.

**T**he new diagnostic approach has the potential to enhance infectious diseases surveillance, and so is now being adapted to track immunity to COVID-19. Development of the technique was led by the Walter and Eliza Hall Institute (WEHI, Australia), the Pasteur Institute (France) and Ehime University (Japan), and has been described in the journal *Nature Medicine*.

Exposure to viruses, parasites or bacteria triggers immune responses that lead to antibodies circulating in the blood. These antibodies can remain for years, but over time the amount of different types of antibodies changes.

The new diagnostic technique allows researchers to look in detail at the amounts of different antibodies in the blood, to pinpoint whether — and when — a person has been exposed to a particular infection. That's according to Professor Ivo Mueller, who led the research and has joint appointments at WEHI and the Pasteur Institute.

"Many tests for immunity give a simple 'yes or no' answer to whether someone has antibodies to the infectious agent," he said. "In contrast, our test — which was initially developed to look at malaria infections — can pinpoint how long ago a person was exposed to an infection.

"This information is extremely valuable for tracking the spread of an infection in a population. Particularly in lower income countries it may not be possible to monitor the actual spread of the infection, but it is very helpful to look retrospectively at whether the infection has been spreading — and to monitor the effectiveness of infection control programs, and respond to disease resurgence."

The technique was initially established to understand the spread of relapsing *Plasmodium vivax* malaria. The parasite causing this form of malaria — the most widespread malaria parasite in the world — can be carried in a dormant state by people and later reawaken to continue to disease spread, causing significant challenges for malaria control.

WEHI researcher and joint lead author Dr Rhea Longley said the malaria blood test had been validated using samples contributed by people living in malaria-endemic regions of Brazil, Thailand and the Solomon Islands, noting, "Our investigations confirmed that the test could detect people who had been infected with *P. vivax* in the preceding nine months — and who would thus be at risk of recurring malaria infections.

"This information will enable better surveillance and deployment of resources to areas where malaria remains, and targeted treatment of infected individuals. This could be a huge improvement in how vivax malaria is controlled and eventually eliminated."

Further development of the malaria blood test received a recent boost with funding from an NHMRC Development Grant, which commenced in 2020.

"We will be working with the Australian biotech company Axxin to develop a diagnostic test for malaria that can be deployed in the field, based on the immune markers our laboratory testing identified," Prof Mueller said. "We plan to continue clinical trials investigating how our test can guide malaria elimination efforts, and having a rapid field test will be an important aspect of this."

Prof Mueller added that his team is now applying the systems they have established for malaria to detect immunity to the coronavirus that causes COVID-19.

"We have already started to study the blood of people who have had COVID-19 infections to document the types of antibodies they carry. In the next six months we hope to have discovered how these antibodies change over time, meaning we can use this information to explore immunity in wider groups in the community.

"This is not a tool for diagnosing individual people, but rather for monitoring COVID-19 disease spread in populations. In countries in the Asia-Pacific, Africa or Latin America, it is possible that COVID-19 will be spreading undetected in some regions for the coming year — especially as governments try to loosen shutdown restrictions. This test could be invaluable for informing these decisions."





### ICP-OES platform for analysis of trace elements

The Thermo Scientific iCAP PRO Series ICP-OES platform is designed to provide a fast, sensitive range of trace element analysis solutions capable of capturing the complete spectrum of high matrix samples in a single run, improving workflow productivity and reducing analysis costs.

From standby to start-up in just 5 min, the inductively coupled plasma optical emission spectroscopy (ICP-OES) instruments reduce gas consumption within a vertical dual-purged optical pathway interface that has low installation requirements due to its standard wall socket and low extraction flow rate. They are suitable for food and beverage, consumer safety, industrial, environmental and pharmaceutical laboratories.

The analysis of trace elements in high matrix samples is essential for laboratory teams across a number of sectors to assure the quality, consistency and safety of products and the environment we live in, but it traditionally presents acute analytical and resource challenges that limit routine deployment. The ICP-OES platform helps laboratories bypass traditional sample preparation requirements and the need to undertake multiple measurements, providing a range of trace element analysis solutions that should enhance workflow productivity and reduce cost per sample.

Laboratories are set to reduce the number of measurements per run to obtain a complete spectrum through the combination of a single optical slit and a charge injection device detector, delivering increased analysis speeds and readout in a reduced time frame. Fast start-up makes analysis possible after just 5 min, and minimal recalibration of the instrument is required as a result of stable optics and polychromator.

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## ACE2 and lung stable cell lines for COVID-19 research

GeneCopoeia offers collections of cell lines expressing human host factors needed for SARS-CoV-2 infection as well as labelled cancer cell lines, which include five lung cancer cell line derivatives.

Angiotensin-converting enzyme 2 (ACE2) has been identified as a functional receptor for SARS-CoV1 and a potent receptor for 2019-nCoV2. ACE2 is a carboxypeptidase that potently degrades angiotensin II to angiotensin 1-7, playing a key role in the renin-angiotensin system (RAS). GeneCopoeia carries a HEK293T cell line expressing ACE2, the receptor needed for SARS-CoV-2 infection in humans.

In addition to the ACE2 stable cell line, the company also offers lung cancer cell lines, which contain both firefly luciferase and GFP or GFP alone, integrated into the genome. These are valuable for COVID-19 coronavirus research since the SARS-CoV-2 virus enters the body via lung epithelial cells, and can be used for drug target identification and compound screening either in vitro or in vivo.

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## NATA accredited cleanroom certification

Airepure NATA certified technicians are accredited to perform various compliance tests to validate cleanrooms to meet Australian Standard specifications, ISO

cleanroom classifications and relevant state or industry requirements.

The company's experienced technicians are familiar with various positive pressure (or in some instances negative pressure) cleanroom environments, and can assist with their customers' specific validation requirements — including hospital, pharmacy, manufacturing and PC4/PC4 rated exhaust filtration containment installations.

The company can also test and validate cleanroom equipment, including clean workstations/laminar flow cabinets, Class 1 and Class 2 biological safety cabinets, fume hoods (both recirculating and non-recirculating), pharmaceutical isolators and cytotoxic cabinets.

Airepure Australia is a national air filtration company providing professional, on-site NATA accredited testing and certification services to help organisations meet and maintain Australian standards for controlled environments, and to help ensure the conformance, ongoing safety and operating efficiency of contamination control equipment.

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## Automated liquid handling system

Whether it is for nucleic acid purification, PCR set-up or general liquid handling, the epMotion 5075t liquid handling system fully automates routine pipetting tasks in the lab to increase productivity and throughput.

The epMotion 5075t has 14.5 deck positions, 14 SLAS/ANSI plus small position for special reagent reservoir racks to accommodate complex applications and labware, and an integrated Eppendorf ThermoMixer module with <sup>20</sup>Mix-Control technology can mix, heat or cool samples and reagents on the deck. The module is software controlled, enabling pipetting onto other worktable positions while the mixer is in operation.

Compatible with a wide range of tubes (0.2 to 50 mL) and microplates (96 and 384 wells), the epMotion 5075t has a gripper tool to transport labware and stack up to five plates on one deck position. The worktable can hold four pipetting tools to dispense volumes in the range of 0.2 to 1000 µL into tubes and plates using Eppendorf's classic and proven air-cushion technology.

The epMotion 5075t is equipped with a contact-free optical sensor to detect liquids, labware and tips before each run, and an optional CleanCap with UV lamp and HEPA filter minimises cross contamination and provides clean air conditions for PCR set-up. Protocols can be easily programmed by the experienced user or beginner using the epBlue software on either the EasyCon touch screen tablet or MultiCon touch PC.

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# Liveocyte — not another microscope!

Reveal complex individual cell behaviours and unlock unique insights in every assay.

Live-cell time-lapse microscopy is an established and powerful technique for the study of mammalian cell biology in vitro. Multiple microscopy technologies exist each presenting their own set of benefits and limitations.

Individual cell segmentation and tracking using traditional label-free methods such as brightfield or phase contrast is challenging due to lack of inherent imaging contrast. Fluorescent labels enhance cell contrast but also have the potential to alter normal cell function and induce toxicity. The high-intensity light required to excite fluorophores can also alter cell behaviour and induce cell death largely due to photodamage. A consequence of this is the subtle changes in cell morphology, motility and proliferation that may have unforeseeable effects on experimental outcomes that are often overlooked.

## Why aren't conventional systems delivering?

The loss of true data is increasingly normalised; subtle phenotypical changes are lost due to deficient modalities forcing constant compromises to gain contrast. Throughput often trumps detail! In an attempt to create a stable environment of temperature and humidity, some microscopes are subjected to a life in an incubator, leaving them prone to mould and degradation of electronic componentry leading to unanticipated repair costs. Microscopy seems to have moved from an investigatory tool to a mass screening machine. Remember — the devil is in the detail!

## So how do we do this better?

Ideally, live-cell imaging needs to identify and track individual cells for prolonged periods without the need for perturbing labels and provide high-contrast images under low levels of light intensity, to preserve natural behaviours and allow recovery of cells for subsequent experimentation or downstream analysis.

The ability to segment and track individual cells and their generational lineages is paramount

for accurate quantification of cell behaviour. A continuous, large field of view with no loss of resolution or focus that permits even highly motile cells to be tracked during time-lapse imaging can prevent potentially important cells from being lost or overlooked.

Information-rich reliable data is key where each experiment automatically yields a plethora of phenotypic parameters such as cell thickness, volume, dry mass in addition to kinetic behaviour characterised by cell speed, displacement and confinement ratio. Imaging systems should be easy to use, require no calibration and no dedicated consumables, and have no hidden costs.

## Phasefocus Liveocyte delivers all of this!

Phasefocus Liveocyte generates high-contrast, fluorescent-like images, using low-powered illumination ( $4\text{--}7\text{ }\mu\text{W}/\text{mm}^2$ ) in which cells appear as bright objects on a dark background. The enhanced contrast in combination with phase retrieval data increases the robustness of single-cell segmentation and tracking algorithms without the need for dyes or probes. This form of quantitative phase imaging (QPI), ptychography, is an emerging imaging technique that retrieves phase-delay of light passing through a cell. Liveocyte can provide you with data not available with any other instrument.

## How can you extract more knowledge from your assays?

Liveocyte can extract the changes in morphology, motion and dry mass of each cell over time. This leads to a more complete characterisation of cell phenotypic properties. Tracking and analysis of individual cells, along with population metrics, to monitor cell speed and directionality of migration together with cell proliferation can allow greater insights into biological processes. Liveocyte offers the versatility to measure and monitor sensitive cell types such as primary cells, patient-derived cells and stem cells. These types of cells are

much closer to their natural origins compared with immortalised cell lines, providing a more realistic account of cell behaviour in response to treatment conditions. Liveocyte can also perform correlative fluorescence and brightfield imaging.

## Dry mass — a class above confluence

You know from your cultures that cells spread out, ball up and grow without dividing, and their division is not always symmetrical. Given confluence simply measures the change in plate coverage by cells; relying on this rudimentary metric alone clearly results in unacceptable misleading outcomes. Dry mass is the summed mass of all cellular components excluding water. As such, the dry mass measurement is an accurate measure of cell size, accounting for the extent of biosynthetic and degradative processes in addition to uptake and expulsion material by the cell.

## Achieve more from one experiment

Liveocyte enables a vast array of metrics to be calculated and combined to perform a number of applications such as **true proliferation, advanced scratch wound, cell motility, mitotic time** and **morphology**. Within each dashboard application there are a wealth of outputs. Imagine this kind of depth of analysis for every dashboard, for every well, for every cell, for every experiment.

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## National Science Week 2020

August 15–23, online

National Science Week is switching to being a digital and at-home festival this year. The 2020 edition is a special chance to recognise the lifesaving work being done by medical researchers and health professionals, as well as the meteorologists and modellers who supported fighting the bushfires. Virtual tours, online events, DIY science and more will be on offer for homes across Australia.

<https://www.scienceweek.net.au/>

### ISLH 2020

June 22–September 25, online

<https://www.islh.org/2020-virtual/index.php>

### Agriculture Summit 2020

August 14–15, Melbourne

<https://agrisummit.net/>

### FOODCONF 2020

September 21–23, Melbourne

<https://www.foodconferencesaustralia.com/>

### AusBiotech 2020

October 28–30, Melbourne

<https://www.ausbiotechnc.org/>

### Global Academic Programs (GAP) Conference

November 16–19, online

<https://www.gap2020.com.au/>

### Linking the Galactic and Extragalactic

November 30–December 4, Wollongong

<http://extragalactic-milkyways.org/>

### Eradicate Cancer 2020

December 14–16, Melbourne

<https://www.eradicatecancer2020.org/>

### 43rd COSPAR Scientific Assembly

January 28–February 4, Sydney

<http://www.cospar2020.org/>

### Lorne Proteins 2021

February 7–11, Lorne

<https://www.lorneproteins.org/>

### Science Meets Parliament 2021

March 15–17, Canberra

<https://scienceandtechnologyaustralia.org.au/what-we-do/>

### ASID Annual Scientific Meeting 2021

March 24–26, Melbourne

<https://www.asid.net.au/meetings/ASM2020>

### TSANZSRS 2021

April 30–May 4, Melbourne

<https://www.tsanzsrs2021.com/>

### IAFS 2020

May 17–21, Sydney

<https://iafs2020.com.au/>

### 2021 ISFPX and ASP Annual Conference

July 5–8, Cairns

<https://www.isfpx.org/>

### 20th International Conference on Biological Inorganic Chemistry

July 18–22, Adelaide

<https://www.icbic2021.org/>

### 6th International Archean Symposium

July 21–23, Perth

<https://6ias.org/>

### HGSA 44th Annual Scientific Meeting

August 14–17, Adelaide

<https://aacb.eventsair.com/hgsa-44th-annual-scientific-meeting/>

### ACS 43rd Annual Scientific Meeting 2021

August 24–28, Queenstown

<https://acs2020.org.au/>

### ASCIA 2021 Conference

September 1–3, Melbourne

<https://www.ascia2021.com/>

### AACB 58th Annual Scientific Conference

September 28–30, Brisbane

<https://aacb.eventsair.com/aacb-58th-annual-scientific-conference/>

### Materials Oceania 2021

October 11–14, Brisbane

<https://www.materialsconferenceaustralia.com/>

### 16th Congress of the FAOBMB

November 22–25, Christchurch

<https://www.faobmb2021.org/>

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