Lab+Life SCIENTIST

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FISHING FOR PROTEINS

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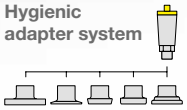

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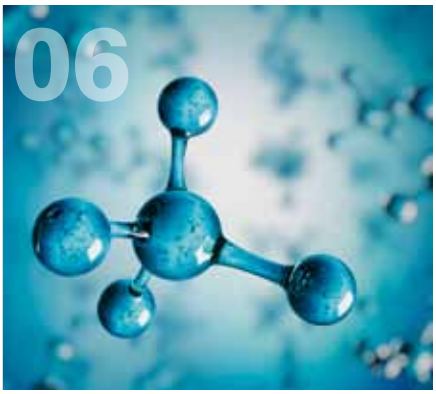

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Is it getting hot in here?

2020 hasn't exactly gotten off to the best start here in Australia, due in part to the ongoing bushfires that have been ravaging the country for several months now. And as the debate continues (mainly outside the scientific community) on whether or not climate change has played any role in this national tragedy, scientists from the University of East Anglia (UEA), Met Office Hadley Centre, University of Exeter, Imperial College London and CSIRO Oceans and Atmosphere have come out with a Rapid Response Review of 57 peer-reviewed papers published since the IPCC's Fifth Assessment Report in 2013.

The literature review was carried out using the new ScienceBrief online platform, set up by UEA's Tyndall Centre for Climate Change Research, which aims to make sense of peer-reviewed publications in a rapid and transparent way. The results? All the studies show links between human-induced climate change and increased frequency or severity of fire weather — periods with a high fire risk due to a combination of high temperatures, low humidity, low rainfall and often high winds — though some note anomalies in a few regions.

The work confirms that rising global temperatures, more frequent heatwaves and associated droughts in some regions increase the likelihood of wildfires by stimulating hot and dry conditions, promoting fire weather, which can be used as an overall measure of the impact of climate change on the risk of fires occurring. Observational data shows that fire weather seasons have lengthened across approximately 25% of the Earth's vegetated surface, resulting in about a 20% increase in global mean length of the fire weather season.

"Overall, the 57 papers reviewed clearly show human-induced warming has already led to a global increase in the frequency and severity of fire weather, increasing the risks of wildfire," said Dr Matthew Jones, Senior Research Associate at the Tyndall Centre. "This has been seen in many regions, including the western US and Canada, southern Europe, Scandinavia and Amazonia. Human-induced warming is also increasing fire risks in other regions, including Siberia and Australia. However, there is also evidence that humans have significant potential to control how this fire risk translates into fire activity, in particular through land management decisions and ignition sources."

So while Australia's science and technology community mobilises to mitigate future bushfire threats, in this issue we're looking at fire prevention on a smaller scale — specifically, in the laboratory. For tips on how to minimise risk of fire and other OHS concerns, check out our articles covering on-site gas generation (page 6) and general lab safety (page 26).

The other issue dominating the news cycle right now is of course the spread of the Wuhan coronavirus, which has at the time of writing killed over 360 people and infected close to 17,000. Scientists from Australia's own CSIRO, University of Queensland and Doherty Institute have already leapt in to help combat the virus — but while I would love to get into the specifics more deeply, I fear that the news would be severely out of date by the time this magazine reaches our readers. So instead we're examining some other recent news from the world of immunology this issue, with articles on dengue-resistant mosquitoes (page 14) and what's going on with whooping cough (page 28).

Yes, the outlook for the rest of the year isn't exactly an optimistic one right now — yet we must press on and, if we have the ability, look to help out however we can. So assuming the world isn't completely ravaged by fire, sickness or World War III (remember that?), I'll see you again next issue.

Regards,
Lauren Davis
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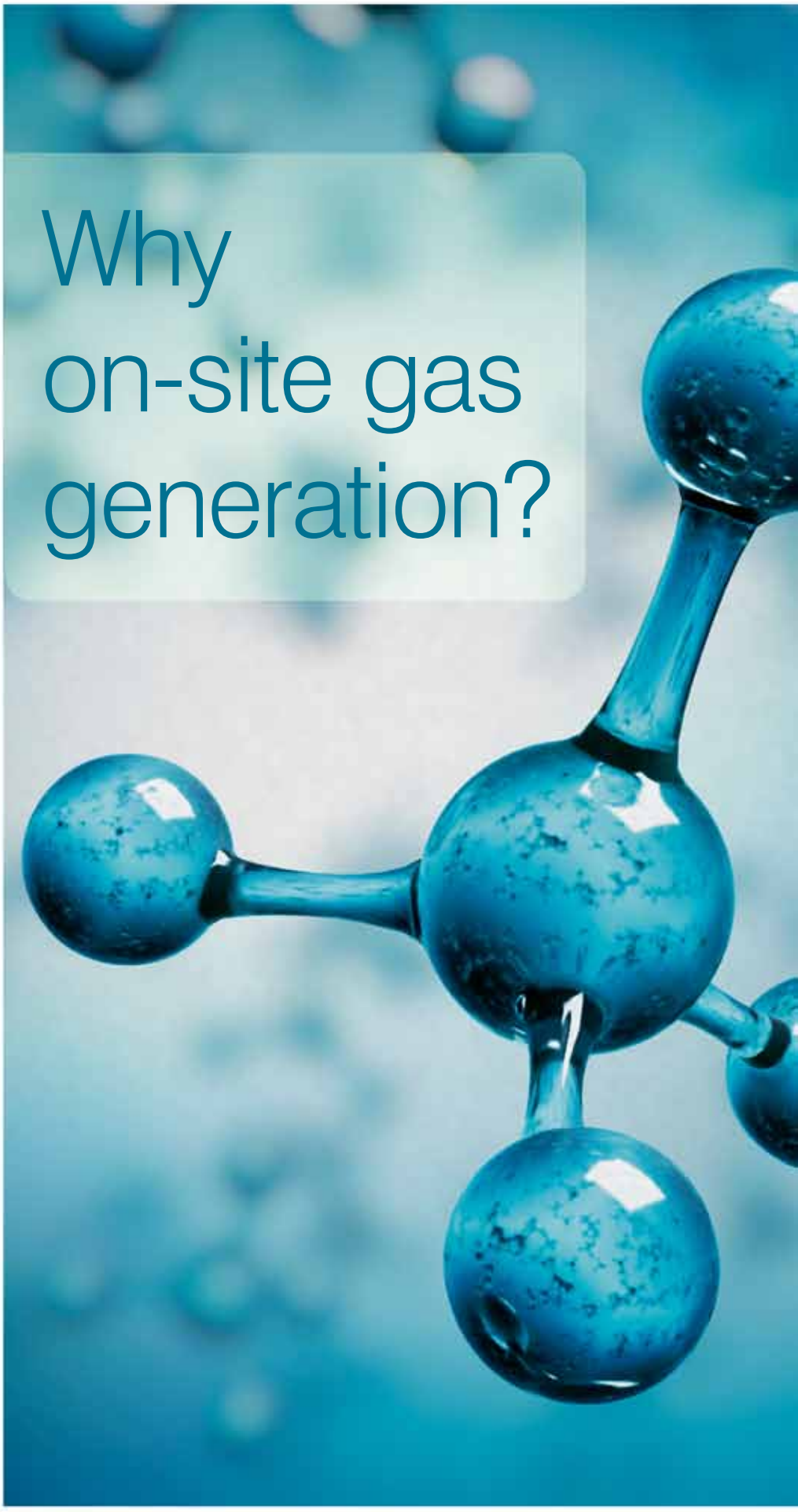
Why on-site gas generation?

Peak Scientific's Dr Nicole R Pendini* reveals how on-site gas generation can help laboratories stay green, increase ROI and decrease OHS concerns.



Nitrogen is the most abundant uncombined element on Earth, comprising 78% of the Earth's atmosphere. It is essential for life as the fourth most abundant element in the human body — primary in amino acids (proteins), RNA, DNA and energy (ATP).

There are several mechanisms by which nitrogen gas can be purified from the air and applications for which it can be used. The classical method of separating the main air gas (N_2, oxygen 20.8% and argon 0.7%) is cryogenic separation (aka distillation or liquification). Ambient air is compressed and filtered to remove impurities. Air is cooled to remove CO_2, trace hydrocarbons and water prior to liquification. In a rectification column of a cryogenic plant, air is further cooled to -190°C, where air gases are separated in the liquid form. N_2 is extracted from the top of the column due to the lower boiling point and O_2 is removed from the bottom of the column.

The major usage for these molecules is in the gaseous form, leading to wastage of pure gas during storage (transportation and evaporation). Boil-off is approximated at 0.2–5% per day (depending on insulation/external temperature), equating to wasted energy from gas–liquid–gas phases and safety risks throughout the process to the required point of use.

Common N_2 cylinders hold the gas at 2200 psi (150 bar) and weigh 70 kg each. Due to the amount of gas required for various equipment and sites, cylinders are grouped in 'man packs' of 12 or 15 cylinders and can require specialist equipment for moving and storage. But on-site nitrogen gas generation has been commercially available for over 30 years in the form of membrane or pressure swing adsorption (PSA) systems.

Cylinders are grouped in 'man packs' of 12 or 15 cylinders and can require specialist equipment for moving and storage. But on-site nitrogen gas generation has been commercially available for over 30 years in the form of membrane or pressure swing adsorption (PSA) systems.

Membrane principle for high-purity nitrogen generation

Each 'membrane' consists of a bundle of hollow fibres in a cylindrical shell. Compressed air supply is filtered and dried prior to entering the membrane. Oxygen, CO_2 and water vapour are separated from nitrogen in the air supply due to the differential pressure created between the air supplied at high pressure and the low-pressure end of a membrane. Due to their efficiency, membrane systems provide gas purities of 95–99.5% (O_2 gas impurity analysis) and typically smaller gas flows (0.5–1000 LPM).

PSA principle for high- to ultrahigh-purity nitrogen generation

PSA technology is used to separate specific gas species from a mixture under pressure. This is achieved by the molecular characteristics of the molecule and affinity for the adsorbent material. This process operates at near-ambient temperatures. The adsorbent material (eg, activated carbon, molecular sieves and zeolites) acts as a 'trap', preferentially adsorbing the target gas species at high pressure. The process will then 'swing' to quickly lower the pressure to desorb the trapped species from the adsorbing material.

A carbon molecular sieve (CMS) is often used in a PSA system because of its shape (cylindrical), consistency in size and high surface-to-mass ratio. A CMS is physically tough, chemically inert and non-crystalline; it is specifically treated activated carbon that forms a pore structure of specific size corresponding to the gas molecule(s) that are to be separated, typically <10 Å. N_2 molecules are 3–4.3 Å and oxygen 2.8–3.9 Å; the molecular sieves used for nitrogen generation are formulated to a 4 Å 'opening'. In practice, PSA systems operate with two columns, banks or towers of CMS, allowing compressed air to enter one CMS bank at high pressure (6–10 bar), before oxygen is adsorbed and nitrogen typically passes to a process or storage tank. PSA systems range in purity — 95–99.99% dependent on the gas flow velocity through the CMS — and can provide flowrates up to 5000 LPM.

Concerns have been raised as the vented gas is enriched with oxygen. The oxygen concentration of the desorption gas averages 30–35% (due to the high partial pressure of nitrogen in air at low pressure at which the regeneration process takes place) and dissipates quickly in a ventilated environment.

Nitrogen generation: the complete system

The entire process of producing nitrogen generation by PSA can be broken down into three core components: compressed air; air drying and purification/filtration; and nitrogen generation (process, supply and storage). Various compressors, from oil-lubricated to oil-free, screw, scroll and piston, are typically used in such systems.

Sufficient filtration (particulate and dust), air drying (refrigerant or desiccant to remove water vapour) and air quality (removal of hydrocarbons) must be considered. The type and overall air quality rating required will be dependent on the type of compressor and the ambient temperature of the system's location. The entire system must be carefully sized and scoped for specific applications, various pressures, location, altitudes, environmental conditions and temperature effects — there is no one size fits all.

>

Energy and the environment

Purity needed at point of use or application can have a huge impact on capital and power costs, hence carbon costs: liquid nitrogen takes approximately 0.7 kW N^{-1} m^{-1} electrical power, whereas this figure is 0.46 kW N^{-1} m^{-3} for 99.9% N_2 gas purity. A full system at 99% purity vs 99.9% will therefore cost approximately half as much to set up and half the electrical usage for the same flow and production rate.

There is also the environmental impact of constant fuel and emissions due to transport of cylinders and tankers to sites. For example, a piece of equipment or application using 35 LPM equates to over 2000 'G' sized cylinders, 135 'man packs' of 15 cylinders on a skid pallet and two deliveries by truck every week. A single gas generator that can fit under a bench can produce 18.4 ML of nitrogen before requiring a service and can continue producing nitrogen gas for 15 years.

Hydrogen gas production

The traditional method of H_2 production is steam reforming or natural gas reforming, which requires high energy consumption. On-site H_2 generation is performed through electrolysis of de-ionised water to oxygen and hydrogen via a proton exchange membrane (PEM). Hydrogen ions diffuse through the PEM membrane, whereas oxygen is retained and is then vented to atmosphere. H_2 gas is then further purified using a desiccant drier/PSA drier before being supplied to the application (ensure no impurities are introduced into the hydrogen gas).

Safety

There are several serious safety concerns when using nitrogen and hydrogen gases, particularly at high pressure and volumes in confined spaces, such as a laboratory. Liquid N_2 has an expansion to gas of 1 L = 696 L of N_2(g). An oxygen-deficient atmosphere (<19.5%) results in asphyxiation, while an oxygen-enriched atmosphere (>21%) can be a fire hazard.

As a working example, a small lab dewar might contain 50 L of liquid N_2, equating to 34,800 L of N_2(g). In a lab measuring 5 x 5 x 3 m (75 m^3) the volume of air might be 75,000 L, with normal O_2 content (21%) of 15,750 L. 11% O_2 content is 8250 L (25% of the small dewar), resulting in serious risk of your staff fainting in minutes.

Similar examples can be observed with hydrogen gas. A laboratory measuring 5 x 4 x 2.5 has a volume of 50 m^3, or 50,000 L. The lower explosive level (LEL) of H_2 is 4.1%. Thus we need 2050 L of H_2 to reach the LEL. But a 50 L gas cylinder contains around 9000 L of hydrogen, so releasing just 25% of the contents would reach the LEL. In contrast, an H_2 generator produces up to 500 cm^3/min and would take 67 h (2.7 days) to reach the LEL, assuming no loss of hydrogen during this time.

The risk associated with cylinders on liquid supply can be decreased by lowering the amount of gas in the room to smaller volumes, moving to a store room and pipe, or looking to alternative gases with lower risk. These options can often be very costly and place more disruptions to the lab and time to personnel to move the gas storage vessel.

On-site gas generation can be a solution as there is a very low stored gas volume of <500 cm^3 for H_2 and <20 L N_2 at 8 bar, compared with 9000 L of gas at 250 bar in a large cylinder. Generators offer automatic shutdown in the case of an external leak, ensuring no more than 10 L of gas leaks into the environment and take 2–3 days to reach lower-explosive or personal harm limits — as opposed to vessels that can reach these hazardous limits in seconds.

Return on investment (ROI)

There are many hidden costs that are driving up gas prices globally, with the cost to operations including energy usage offsite to produce and boost gas pressure; vessel/cylinder manufacture; testing and compliance; logistics/fuel cost; staff training; batch quality variation; PPE; pipework; gauges and regulators; and risk assessment/consultation for explosion and asphyxiation. In addition, there are shortages of non-renewable gas types, so alternative methods must be investigated with renewable gases to continue using certain analytical equipment (eg, helium conversion to H_2 for gas chromatography).

In comparison, costs for an on-site generator include initial installation, power consumption and an annual service for the duration of its life. The savings over a three-year period could be as great as 50%, in addition to greater safety. So what are you waiting for?

**Dr Nicole R Pendini has a PhD in Biochemistry, specialising in structure-based drug design. She has worked with several instrument vendors over the years to understand how various types of equipment operate and their applications for use. For nearly five years Nicole has worked for gas generation company Peak Scientific, specialising in on-site in-laboratory nitrogen, hydrogen and zero air gas generation. She also designs complete reticulated gas systems for laboratories, food and beverage and industry from single rooms to entire building sites, ensuring the right quality, quantity and pressure of gas is supplied in a sustainable, safe and environmentally conscious manner.*

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Blood pressure drug could help treat alcoholism

A drug used to treat high blood pressure may alleviate anxiety induced by long-term heavy alcohol use, and also halt the damage such drinking can cause to the brain's ability to grow new cells.

That's according to new research from the Queensland University of Technology (QUT), conducted in adult mice and published in the journal *Frontiers in Behavioral Neuroscience*.

QUT neuroscientist Professor Selena Bartlett, principal investigator on the study, said repurposing drugs like pindolol serves as a way to fast-track new treatments to manage alcohol dependence, binge-drinking and addiction, which are significant and complex problems both in Australia and globally. Pindolol acts on the receptors for serotonin, the 'feel-good' nerve cell chemical and neurotransmitter, and noradrenaline, which is involved in the body's 'fight or flight' response.

"This is a drug that is inexpensive and already available in the US, Canada, Europe and Australia," Prof Bartlett said. "It's a beta blocker that is prescribed for high blood pressure, angina and heart arrhythmias.

"We have been studying it for a number of years and have already shown in animal models that it reduces alcohol intake when there is long-term consumption.

"In this latest study, we investigated the drug's effect on other alcohol associated issues — anxiety and neurogenesis.

"Long-term and heavy drinking can cause anxiety disorders, and people's anxiety can worsen when alcohol is withdrawn, and alcohol abuse can also reduce neurogenesis, which is the process by which new neurons (cells) are formed in the brain."

The study found that pindolol reduced the anxiety-like behaviour of mice when alcohol was withdrawn after 12 weeks of binge-like consumption. Two weeks of daily pindolol treatment at the end of 18 weeks' alcohol consumption restored damage the alcohol caused to new and immature neurons (cells) in the hippocampus, the primary brain site for new neuron production.

Prof Bartlett said the results add further evidence that pindolol could be beneficial in treating alcohol use disorders, noting, "We showed that pindolol reduced alcohol-associated anxiety-like behaviour in mice and also alleviated the damaging effects of alcohol consumption on newly formed and immature brain cells.

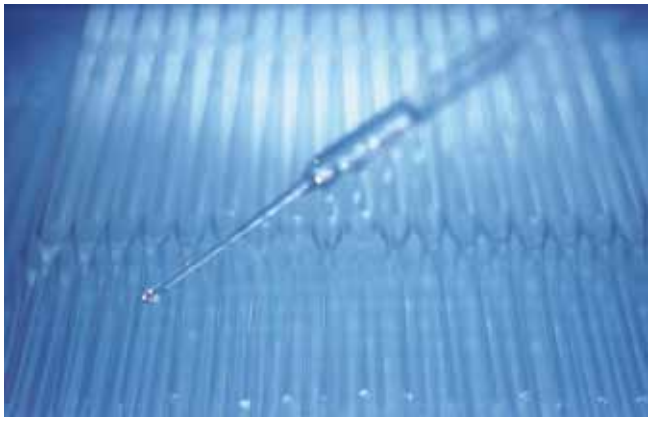
"The next step is to conduct clinical trials with pindolol, and we have started discussions with a medical specialist to progress that."

How to remove air bubbles from your nanopipettes

Researchers at Kanazawa University have reported an efficient method for filling a batch of nanopipettes with a pore opening of no more than 10 nm.

The function of a nanopipette is usually to enable the transport, and their detection, of nanometre-sized objects (in solution) through the pipette pore. Completely filling a nanopipette with a solution is challenging, however; because of the capillary force, an 'air bubble' is nearly always present in the pipette's tip. Removing the air bubble has proven to be especially problematic for nanopipettes with a pore opening of 10 nm or less.

Now, Shinji Watanabe and colleagues have found a simple but efficient way to completely fill a batch of many nanopipettes with a pore opening of 10 nm. Described in the journal *Analytical Chemistry*, their method is based on the application of a temperature gradient to the nanopipette tips so that residual air bubbles are driven out.



The scientists applied their 'thermally driven method' to a batch of 94 pipettes, aligned lengthwise next to each other, all with a pore diameter of around 10 nm. The pipettes were put on a metal plate kept at a temperature of 80°C, with their tips protruding from the plate, resulting in a temperature gradient. Time-lapsed optical microscopy images of the filling process of the nanopipettes showed that after 1200 seconds, the tips were completely filled with solution and the air bubbles were driven out of the pipettes.

In order to double-check that the pipettes were indeed bubble-free, the colleagues performed so-called I–V measurements. Every pipette was filled with a solution of potassium chloride (KCl), which is conducting. Both pipette ends were then contacted with electrodes. If an electrical current runs between the ends — specifically, if the pipette has an electrical conductivity below a few GΩ — then filling with the solution is complete. The researchers observed electrical currents and therefore filling for the whole batch of pipettes.

The scientists also performed transmission electron microscopy (TEM) measurements of pipettes with pore diameters below 10 nm. Although the thermally driven method leads to good electrical contacts, particle-like structures were observed inside the tips of the nanopipettes — demonstrating that, according to the researchers, "TEM observation without inducing pipette deformation is important for accurately determining the characteristics of sub-10-nm nanopipettes."

The colleagues concluded that their method is very practical and easy to introduce in nanopipette fabrication. They said their study "will provide a significant contribution to various fields of nanoscience using nanopipettes".

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A new International Standard has been published to help enable effective risk management of biohazardous materials, which should result in a reduced chance of accidents, less impact on the environment and a more efficient use of time and other resources.

From diagnosing diseases to pharmaceutical and scientific research, the handling of biological materials in laboratories and elsewhere is essential for many industries but doesn't come without its dangers; such materials should therefore be handled in stringent, risk-proof ways. A biorisk management system is a key step towards this as it enables an organisation to effectively identify, control and manage the biosafety or biosecurity risks related to its activities.

ISO 35001, *Biorisk management for laboratories and other related organisations*, is the first International Standard for a biorisk management system. It defines the requirements and guidance for laboratories or any other organisation that works with biological agents to control and reduce any risks associated with their use.

Patty Olinger, convenor of the working group that developed the standard, said that while there are a number of regional or national standards that help organisations manage their risks and meet regulatory requirements, ISO 35001 is the first that harmonises them to deliver international best practice that is recognisable everywhere.

"ISO 35001 provides organisations and individuals with a roadmap of how to organise and systematically manage and structure their biological risk programs," she said.

"This is increasingly important to protect our global public health infrastructure as our world becomes more and more integrated."

ISO 35001 was developed by ISO technical committee ISO/TC 212, *Clinical laboratory testing and in vitro diagnostic test systems*. It is available from Standards Australia or through the ISO Store.

Peanut allergy vaccine rewrites the immune system

Peanut allergies could soon become a thing of the past, thanks to a breakthrough vaccine candidate developed by the University of South Australia's (UniSA) Experimental Therapeutics Laboratory in partnership with biotechnology company Sementis.

Peanut allergies occur when the immune system mistakenly identifies peanuts as an allergen, signalling immune cells to release chemicals and resulting in adverse reactions that can range from mild hives, cramps, nausea and vomiting to life-threatening anaphylactic reactions.

The new peanut allergy vaccine is formulated by packaging bits of peanut proteins into the Sementis Copenhagen Vector (SCV) virus platform, developed by Sementis Chief Scientific Dr Paul Howley and UniSA Professor John Hayball, Head of the Experimental Therapeutics Laboratory. Prof Hayball said the virus platform rewrites the body's natural response to peanut allergens, tricking the immune system so that the body responds normally instead of generating an allergic reaction.

"We're effectively reprogramming the body to see peanuts as an entity that can be cured by a vaccine, rather than an allergen that elicits an allergic reaction," he said.

"Already, the vaccine is showing signs of success, shifting peanut-specific immune responses in mouse models of peanut allergy and in preliminary in vitro vaccination-like studies using human blood samples from clinically confirmed peanut allergic people."

Prof Hayball said the next steps are to gain further human samples and confirm the efficacy of the vaccine, which will demonstrate human translational capacity and increase the chances of success in future clinical trials.

Dr William Smith, Head of the Clinical Immunology and Allergy unit at the Royal Adelaide Hospital and lead clinician involved in the study, said the development of immunomodulatory therapeutics has so far proved extremely challenging for scientists everywhere, with varying degrees of clinical desensitisation of peanut allergy but none that have succeeded in safely and completely eradicating peanut allergy.

"An effective vaccine for use in peanut allergy must be safe to administer with minimal adverse events, have a short immunisation schedule to improve compliance specifically with peanut allergic children and, most importantly, induce lifelong protection," Dr Smith said.

"The preliminary data is encouraging and favours that the vaccine can meet all these criteria. It's very exciting research and we are very positive to take the next step into what we hope will be a cure for peanut allergy."

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Dengue-resistant mosquitoes were given a red-eye gene to distinguish them from regular mosquitoes.

Genetically modified mozzies

completely resistant to dengue

Australian, US and Taiwanese scientists have engineered what is claimed to be the first breed of genetically modified mosquitoes resistant to spreading all four types of the dengue virus (DENV) — a breakthrough that is likely to be crucial for effective disease suppression.

Dengue is a mosquito-borne viral disease that represents a pressing global problem, infecting up to 390 million people every year via *Aedes aegypti* mosquitoes. Typical symptoms include fever, headaches and muscle aches, with severe forms of the disease (around 1% of cases) leading to haemorrhage, shock and even death.

CSIRO Senior Research Scientist Dr Prasad Paradkar said the dengue virus is causing an epidemic in tropical and subtropical regions worldwide, with large outbreaks currently occurring in Bangladesh, Pakistan, Sri Lanka and the Philippines. Indeed, incidences of dengue have increased dramatically in recent years, with more than half of the world's population at risk of infection and global economic losses estimated to be $40 billion a year.

"There is a pressing global demand for effective strategies to control the mosquitoes that spread the dengue virus, as there are currently no known treatments and the vaccine that is available is only partially effective," Dr Paradkar said.

Recent advances in genetic engineering technologies have made it possible to create mosquitoes with reduced vector competence, limiting their ability to acquire and transmit pathogens. Indeed, there have been previous attempts to synthetically engineer dengue-carrying mosquito populations to make them resistant to the virus; however, these approaches had limited success due to their ability to only target one or two of the four major dengue types.

In the latest study, published in the journal *PLOS Pathogens*, the authors describe the development of the first *A. aegypti* mosquitoes synthetically engineered to be resistant to all types of DENV. The mosquitoes were tested in the quarantined insectary at the Australian Animal Health Laboratory — CSIRO's national biocontainment facility, designed to allow scientific research into dangerous infectious agents.

The mosquitoes express a gene encoding an engineered single-chain variable fragment (scFv) derived from a broadly neutralising DENV human monoclonal antibody. Mosquitoes expressing the anti-DENV scFv cannot be infected with or transmit any of the four types of DENV, so they should not be able to transmit the virus to humans.

These results provide a compelling route for developing effective genetic-based DENV control strategies, which could be extended to curtail related viruses. According to the authors, this strategy could be coupled with a gene-drive system to rapidly convert wild mosquito populations into genetically modified mosquitoes that would be completely resistant to DENV transmission.

"The most important aspect of this study is the fact that we engineered mosquitoes to be refractory to all major serotypes of dengue virus," said study

CSIRO Senior Research Scientist Dr Prasad Paradkar observes freshly hatched mosquitoes and larvae.

co-author Associate Professor Omar Akbari, from the University of California, San Diego. "This may serve as a genetic tool to control dengue in the wild in the future.

"This breakthrough work also has the potential to have broader impacts on controlling other mosquito-transmitted viruses," he said. "We are already in the early stages of testing methods to simultaneously neutralise mosquitoes against dengue and a suite of other viruses such as Zika, yellow fever and chikungunya."

The publication of the study comes shortly after another international team of scientists reported their own way to block the transmission of dengue virus, in trials carried out in Malaysia — a country where over 100,000 dengue cases were reported in 2016. Their breakthrough has major implications for countries with hot climates — from island nations in the South Pacific to Saudi Arabia, Africa and South America — all of which experience dengue, Zika, yellow fever and chikungunya.

Using a strain of the bacteria *Wolbachia*, which inhibit mosquitoes from transmitting viruses to humans, researchers at the University of Melbourne, the University of Glasgow and Malaysia's Institute for Medical Research were able to successfully reduce cases of dengue at sites in Kuala Lumpur. Their data, published in the journal *Current Biology*, shows that mosquitoes carrying the *w*AlbB strain of *Wolbachia*, when released into the wild, had the effect of reducing the incidence of dengue cases by 40%.

Previously, scientists have carried out successful mosquito releases using a different strain of the *Wolbachia* bacteria, but while this strain was able to invade wild populations in some conditions, it did not appear to be suitable for use in the very hot conditions experienced in equatorial countries such as Malaysia. Now, the international team has shown that the *w*AlbB strain of *Wolbachia* is stable and effective, even in daily peak temperatures of 36°C and higher, as commonly experienced in areas of Malaysia where dengue is prevalent.

Researchers released batches of *A. aegypti* mosquitoes carrying the wAlbB strain of *Wolbachia* into the wild, in six different sites in greater Kuala Lumpur with high levels of dengue transmission. The *Wolbachia*-carrying mosquitoes — both male and female — then went on to mate with the wild mosquito population, resulting in the spread and establishment of the virus-inhibiting bacteria.

In some sites, *Wolbachia*-carrying mosquitoes were measured at over 90% frequency more than a year after the mosquito releases ended. The success of lowering dengue cases at these sites has led to a cessation of insecticide fogging in these areas, highlighting both the environmental and economic benefits of this method.

"This study provides us with a new *Wolbachia* strain for field release and highlights disease impact within a complex urban setting where dengue incidence rates are high," said Professor Ary Hoffmann, from the University of Melbourne. "The intervention succeeded despite ongoing pesticide applications and other challenges that can make it hard for the *Wolbachia* to become established. The approach holds promise not only in Malaysia but also in other countries."

Professor Steven Sinkins, from the MRC-University of Glasgow Centre for Virus Research, said the breakthrough is promising news for countries that endure mosquito-borne diseases. He noted, "The next step is to deploy this strain in more and larger sites, but we are now confident that this will become an effective way to control dengue on a large scale."

Rapid infection diagnosis in preterm babies

Scientists and clinicians at the Norwich Research Park, UK, have pioneered a new method for profiling the microbiome of preterm babies that can significantly speed up the identification of infections and indicate more effective treatments.

By harnessing next-generation sequencing techniques, the team from the Quadram Institute and the Earlham Institute (EI) showed that they can rapidly and reliably identify the microbes present in a preterm baby's stool sample that may cause life-threatening conditions such as sepsis or necrotising enterocolitis (NEC). The method also uncovers the presence of antimicrobial resistance genes — vital information needed to select the most effective treatment.

Using Oxford Nanopore Technologies' MinION portable sequencing device, coupled with bespoke software to analyse the sequence data in real time, data can be obtained in under five hours. With current methods taking up to 48 hours, developing this platform for routine use in a clinical setting would allow faster and tailored antimicrobial treatments to be used.

"Preterm babies are born with underdeveloped gut physiology [and] immunity, and have an altered gut microbiota, all of which increase risk of life-threatening infections. Time is of the essence in detecting or diagnosing infections," said Dr Lindsay Hall from the Quadram Institute. "Not only could our approach be more effective, it will also reduce the use of antibiotics and help slow the rise of antimicrobial resistance."

Dr Richard Leggett, Group Leader at EI, added, "With the MinION and our own analysis pipeline (NanoOK RT, developed specifically for this work), we can go from faecal sample to pathogen and antimicrobial resistance (AMR) profile in just four to five hours… We can also take advantage of the MinION's long DNA reads to place AMR genes within host bacteria, enabling better understanding of antibiotic resistance."

"Nanopore sequencing is an interesting technology because it provides useful data so quickly," continued Dr Matthew D Clark, former Head of Technology Development at EI. "We were excited to see how well it could perform on clinical samples with our custom software. It hasn't escaped our attention that because it is cheap, small and low powered it could be uniquely useful in lower and middle-income countries."

To test their platform, the researchers used the portable MinION to carry out shotgun metagenomics on mock microbial communities. Shotgun metagenomics analyses the genomic sequence from a mixed collection of organisms — in this case, 20 different microbes. Having confirmed that the MinION approach worked, the researchers progressed to using faecal samples obtained from preterm babies, collected by the Norfolk and Norwich University Hospital's Neonatal Intensive Care Unit (NICU).

The method, published in the journal *Nature Microbiology*, discerned between healthy babies and those diagnosed with NEC or sepsis, with the healthy babies having a strong population of beneficial *Bifidobacterium* and the others harbouring either *E. cloacae* or *Klebsiella pneumoniae*, both of which can cause life-threatening infections.

Professor Paul Clarke, Consultant Neonatologist and Research Lead at the Norfolk and Norwich University Hospital NICU and the University of East Anglia, said, "Preterm babies are a group at high risk of dangerous infection. More than 90% of our preterm babies are presently treated with antibiotics, yet in retrospect most did not need them. This study is important because it raises the hope that we might soon have available the technology that could help us to discern at a much earlier stage which babies really need antibiotics, and which do not need them. This could save many babies from getting antibiotics they did not need and would be an important advance in helping limit AMR."

The system facilitates sampling over a period of time, so that changes in the microbiota profile can be monitored. This is useful for monitoring pathogenic bacteria, but it also lets researchers see how other interventions affect the microbiome over time. For example, it can monitor the effect of antibiotics on the overall microbial profile or measure the effects of probiotic supplementation.

Shotgun metagenomics doesn't just profile the species diversity. In the study, the researchers were particularly interested in profiling the genes that confer antibiotic resistance in the microbiome — known as the 'resistome'. Klebsiella, in particular, is of concern as it is becoming increasingly resistant to multiple antimicrobials. An expansion of shotgun metagenomics could therefore help in surveillance for AMR in these clinical settings.

The development of the platform for rapid, portable microbiota profiling brings its use in a clinical setting closer, though more trials at different locations are required before it can be adopted as a routine diagnostic tool. However, there is clear potential for its deployment to save lives in the clinical setting.

Oxford Nanopore Technologies
nanoporetech.com

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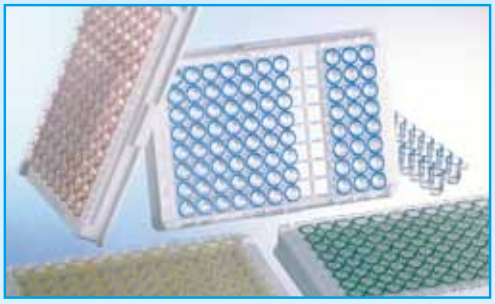

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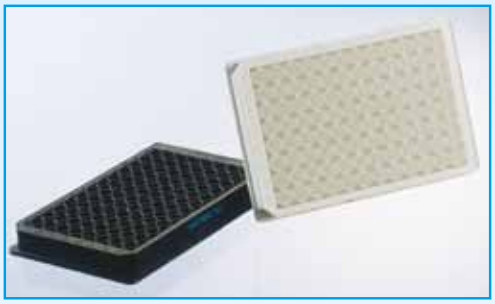

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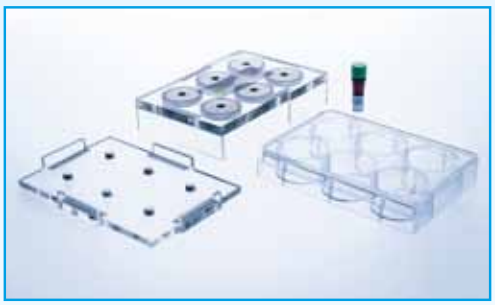
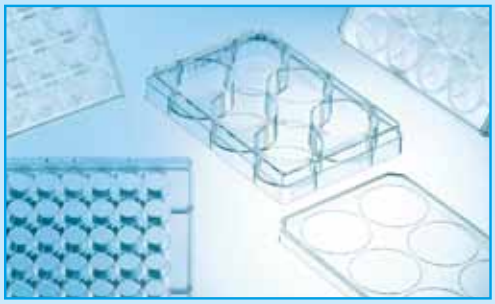
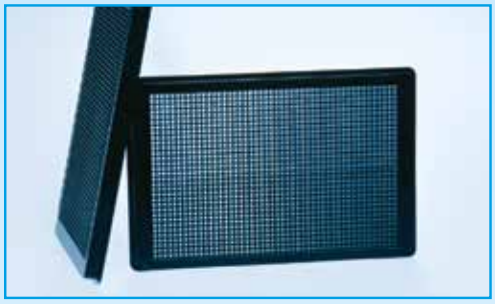


3D Cell Culture



Cell Culture



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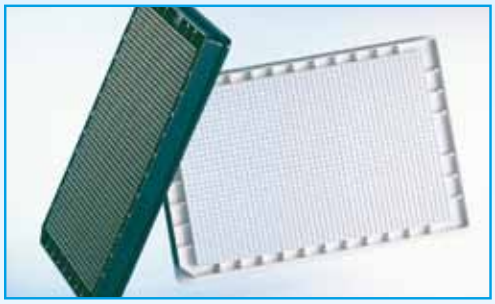

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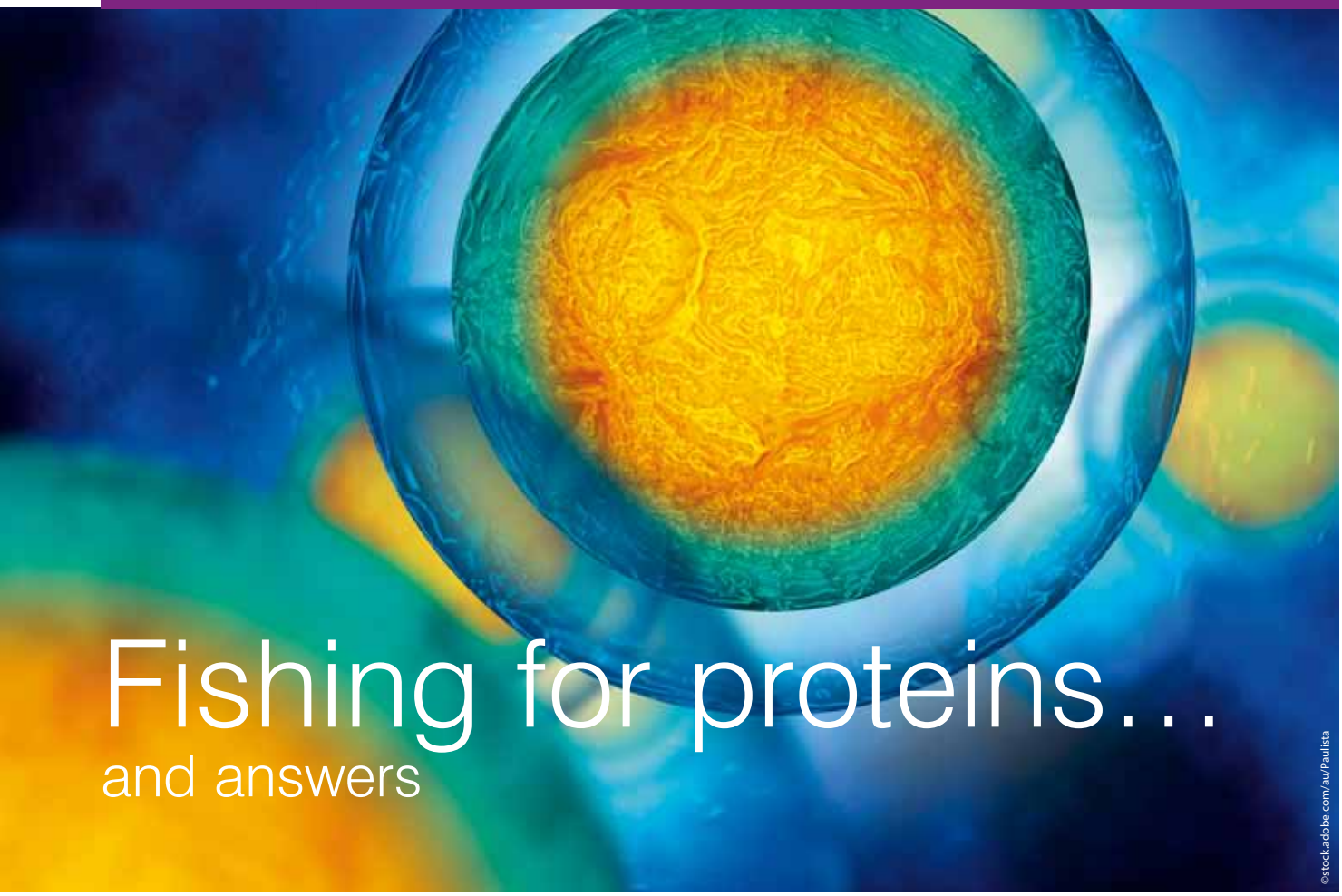

Fishing for proteins…
and answers

Using a microscopic 'fishing' technique, Canadian scientists have successfully cast lines into human cells to snag proteins — solving a 20-year-old mystery of cell biology in the process.

The researchers, from the Montreal Clinical Research Institute (IRCM) and Université de Montréal (UdeM), threw 56 'baits' into human cells they were incubating in their laboratory. The goal was to catch and identify the proteins that attach to those of the Rho family, famous in the cell biology world since the discovery in the early 1990s that they dictate how pieces of the cell skeleton — the 'cytoskeleton' — are assembled.

In humans, the 20 members of the Rho family are scattered on the inner surface of cell membranes and act like small switches. When a signal from outside or inside the cell activates them, they stimulate other proteins to force the cytoskeleton to add to or remove parts from its framework.

Out of all these proteins, only three, to date, have been thoroughly studied by researchers: Cdc42, Rac1 and RhoA. Cdc42 acts as the lead protein: it indicates the path that white blood cells must take to find a site of infection. Rac1 activates the engines that drive a non-muscular cell forward. RhoA stimulates the formation of fibres that allow cells to contract or form resistant tissues as they come together to produce, for example, the wall of a blood vessel.

But what are the other proteins doing? And what other proteins do they interact with? To find out, UdeM cell biologist Jean-François Côté and his team went fishing for answers, with the results published in the journal *Nature Cell Biology*.

Into human cells growing in incubators in their lab, they cast their baited lines, forcing these cells to produce proteins with two heads: one containing a single side of a protein in the Rho family, the other a 'biotin ligase' enzyme. The latter acts like an elite sniper in the cell, luring and labelling every passing protein with the help of its partner, a member of the Rho family. Every protein that approached the bait was thus labelled with biotin. Next, Côté and his team had to shred the cells to identify, one by one, each labelled protein.

Using 28 two-headed proteins and presenting the GTPases — a superfamily of enzymes that function as 'molecular switches' and are involved in regulating many cellular processes — in both active and inactive configurations, the team caught a total of 9939 proteins. Some were already known to the scientists, including the GTPases' activators and deactivators. But the researchers also discovered hundreds of individual proteins with yet-to-be-defined roles.

These discoveries include the missing link of the cytoskeleton Rho process identified in the early 1990s. Back then, researchers noticed that the RhoA protein indirectly activates another protein, ERM, causing it to stabilise the cytoskeleton — but they didn't know the precise mechanism behind this process. Côté and his team have now found the answer: what forges the link between RhoA and ERM is a protein called SLK.

The IRCM team also looked at other proteins that, until now, were virtually unknown to biologists, namely GARRE and PLEKHG3. The scientists demonstrated that these proteins naturally attach to the active forms of Rac1 and RhoG, respectively. What's left to understand is the exact function of these associations. To accelerate the process, the team revealed characteristics of other molecules they caught in their experiments — enough to give raw material to dozens of laboratories worldwide.

Through their research, Côté and his team have not only cleared up a whole area of cell biology, but have also demonstrated the effectiveness of their unique 'fishing' method. Côté now plans to use it to better understand how other molecular switches work, especially those in the Ras family — proteins that lie at the centre of many types of cancer.

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The epMotion 5070 is a compact automated liquid handling workstation for normalisation, PCR or qPCR set-up of 96 samples.

The device's flexible four-position worktable can be configured to suit user needs and increased to hold extra PCR or sample plates using space saving accessories to store reagents, consumables and tips on deck.

The product is compatible with a wide range of predefined tubes (0.2 to 50 mL) and microplates, which allows established manual procedures to be automated with ease. An onboard optical sensor verifies set-up prior to each run checking liquid volume and tips, as well as labware type and position for safe operation.

The epMotion 5070 comes with a single- and 8-channel pipetting tool, both of which are based on Eppendorf's classic and proven air-cushion pipetting technology to give users maximum pipetting accuracy and precision in the range of 0.2 to 1000 µL. It can be easily programmed using the epBlue software PCR assistant on the user's choice of the EasyCon, touch screen tablet or Multicon touch PC.

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Differential scanning calorimeter

The Nano DSC is a powerful thermal scanning instrument that utilises a 300 µL capillary cell design and solid-state thermoelectric temperature control.

The product is a powerful tool for measuring the biologic thermal stability of protein and other biological systems of clinical importance. Applications range from drug formulation optimisation to monitoring biomolecular stability and basic understanding of protein folding/unfolding. Nano DSC experiments are label-free direct measurements of biomolecular unfolding under native condition, and do not rely on fluorescence detection (intrinsic or extrinsic).

The device is designed for ultrasensitive measure of heat absorbed or released by dilute in-solution biomolecules as they are heated or cooled. The 300 µL capillary cell design, solid-state thermoelectric temperature control and easy cleaning ensure high sensitivity and data reproducibility for a wide variety of applications.

TA Instruments
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Temperature- and CO_2-controlled live cell transport

Transporting living complex cells while retaining their full viability and functionality can be challenging, as traditionally cells and other biological material have been stored and transported at low to cryogenic temperatures. During this process, cells often suffer from exposure to suboptimal life-sustaining conditions (eg, temperature, pH, etc) as well as damage due to shear stress. Not only does cell viability need to be considered, but inadequate cryopreservation may introduce variations between different batches or could even cause genetic and epigenetic modifications.

CellBox is said to be the first portable CO_2 incubator that enables safe shipping of intact cell/tissue constructs from one facility to another that overcomes these obstacles. Suitable for air and ground transport, CellBox provides a regulated CO_2 environment and can maintain temperatures between 28 and 37°C while also monitoring the health of cells via the CellBox app.

Specially developed for the transport of sensitive cells and cell cultures, the product is suitable for iPSCs and iPSC-derived cells, such as sensory neurons, microglia and cardiomyocytes. Cells can be transported under laboratory conditions in the CellBox while avoiding unwanted changes in metabolism, gene expression and protein profiles.

Long-term cell storage and biobanks can benefit from receiving fresh material and performing the cryopreservation in-house. Recipients can benefit by receiving thawed and recovered cells from a biobank, ready to use. Lab-on-a-chip or tissue-on-a-chip products can meanwhile be seeded with living cells before shipping under laboratory conditions in the CellBox.

Cells are shipped ready to use, so users can simply unpack and go.

ATA Scientific Pty Ltd
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*Claudio Bui**

Liquid Handling 4.0

What to consider when selecting OEM robotic components

Lab automation and liquid handling solutions are evolving rapidly, shaped by many of the same forces and disruptive technologies that define the Fourth Industrial Revolution. Alongside Industry 4.0, you could say that the era of Liquid Handling 4.0 has arrived.

In today's fast-paced environment where engineers need to develop and adapt analytical platforms rapidly to address new markets and ever-changing applications, the choice of core robotics architecture and components can be crucial for success. Here are some important questions to ask when selecting OEM components and robotic platforms for automated liquid handling.

1. Do OEM liquid handling pump choices support your intended applications?

Liquid handling pump requirements can differ greatly from application to application. Source vessel, fluid viscosity, solvent choice and dispense volumes are some of the many variables to consider when selecting a liquid handling pump.

Integrated pump sensors are also a critical consideration, especially when including liquid level detection (LLD), for accurate and robust aspirating and dispensing — even in the presence of foam and bubbles.

Finally, consider pump quality and reliability: your requirements may vary depending on the application, target market and expected system lifetime. For example, devices designed for the clinical environment are often expected to meet more exacting standards than those designed for research.

2. Are the available OEM components scalable?

As development projects, applications and target markets evolve, laboratory automation platforms need to be quickly adaptable to meet changing demands and scope. For example, a system may need to process more samples or run multiple processes in parallel to enable higher throughput. On the other hand, you might want to scale down system capabilities to narrow the application range and cater to specific niche markets.

To maintain maximum flexibility and avoid future design constraints, look for OEM product lines that include modular solutions and a range of customisation options, such as a selection of different work-deck sizes and the ability to readily scale the number of channels, independently, as needed.

3. Is there enough flexibility to accommodate current and future labware form factors?

Labware requirements and preferences can change unexpectedly as analytical technologies, protocols, regulatory requirements and customer preferences evolve. Futureproofing is easiest when you start with OEM components and product ranges that have been designed with flexibility in mind. Features to look for include an easily configurable chassis, interchangeable carriers to accommodate different types of labware and multifunctional pipetting arms that can accommodate gripper accessories.

4. How adaptable is the software development kit (SDK)?

A good SDK with rich command libraries and code repositories makes programming much easier and puts more power in the hands of your developers. As a result, the software development process can be accelerated while improving cost-efficiency at the same time. Look for a development platform that includes an SDK with preconfigured and easily manipulated layouts. 'Drag and drop' capability is another empowering feature that enables experimentation with different work deck layouts and configurations in a virtual environment. The included 3D simulator enables you to do so without having to wait for hardware design and delivery.

5. How does your OEM partner help you to accelerate the development process?

One of the easiest and most efficient ways to speed up development is to allow and encourage processes to occur in parallel, instead of sequentially, through a robust SDK. The access to an SDK that includes 3D simulation for application development regardless of the availability of a hardware prototype can be a huge factor in reducing risk in development. Prototyping in a virtual environment can reduce time spent in the development phase and cost too.

A well-designed SDK enables multiple engineers to work in parallel, decreasing testing time and increasing collaboration. Easy access to a virtual work deck and simulated test sequences provides a quick and cost-effective evaluation of the work deck layout, making it easier to make minor adjustments, and saves development costs by removing the risk of hardware damage.

Intelligent OEM solutions improve performance

Advances in robotic components, sensor technologies and machine learning mean that liquid handling modules are getting smarter and more sophisticated. As a result, engineers have more options and more power to integrate diverse lab devices and to automate more of the application workflow.

When looking for pre-developed liquid handling modules, consider features that will help maximise flexibility and efficiency. For example, robotic arms that can be used for both pipetting and gripping; these lend versatility, help reduce your system footprint and lower costs. Channel synchronisation and collision avoidance, auto-alignment capabilities and readily available accessories can all save development and test time as well as avoid potential headaches downstream.

When it comes to the successful development of liquid handling automation solutions and the implementation of robotic components, hardware alone is not enough. Hardware components need to be integrated into a flexible architecture that can adapt and scale according to your application needs.

The right mix of product features, compatibilities and support, combined with your OEM partner's know-how of intelligent solutions, will ensure you reach your desired goal. Tecan's core robotic architecture is designed to evolve into a complete automation solution for your specific application.

**Claudio Bui is the Head of Product Concepts for the Partnering Business in Tecan's Components Marketing Team. The primary function of his team is to work closely with customers to develop new concepts and proposals based on a thorough analysis of their specific requirements. Claudio started at Tecan in 1990 in R&D developing components and has been involved in the development of a number of small laboratory instruments. In 2005, he joined the marketing team.*

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Human nerve cells
transplanted into a mouse brain

Understanding the mechanisms underlying brain circuit formation is important, for example, if we want to treat brain disease. Now, Belgian researchers have developed a novel strategy to transplant human neurons as individual cells into a mouse brain and to follow their development over time.

As explained by Professor Pierre Vanderhaeghen, from the VIB-KU Leuven Center for Brain & Disease Research and Université libre de Bruxelles, "One remarkable feature of human neurons is their unusually long development. Neural circuits take years to reach full maturity in humans, but only a few weeks in mice or some months in monkeys.

"This long period of maturation allows much more time for the modulation of brain cells and circuits, which allows us to learn efficiently for an extended period up until late adolescence. It's a very important and unique feature for our species, but what lies at its origin remains a mystery."

Dr Daniele Linaro, also from VIB-KU Leuven and Université libre de Bruxelles, revealed, "We differentiated human embryonic stem cells into neurons and injected them into the brains of young mouse pups. This allows us to investigate human neurons in a living brain over many months. We can also apply a whole range of biological tools in these cells to study human neural circuit formation and human brain diseases."

The researchers discovered that the transplanted human cells follow the same developmental plan as they would in a human brain, with a months-long period of maturation typical for human neurons. This means that our nerve cells may follow an 'internal clock' of development that is surprisingly independent of the surrounding environment. Moreover, the human cells were able to function in the mouse neural circuits.

"After months of maturation, the human neurons began to process information, for example, responding to visual inputs from the environment," said Dr Ben Vermaercke, from VIB-KU Leuven and NeuroElectronics Research Flanders (NERF). "The human cells even showed different responses depending on the type of stimulus, indicating a surprisingly high degree of precision in the connections between the transplanted cells and the host mouse's brain circuits."

Published in the journal *Neuron*, the study is said to constitute the first demonstration of genuine circuit integration of neurons derived from human pluripotent stem cells. According to NERF's Professor Vincent Bonin, "It's a technological milestone that opens up exciting possibilities to study how genetic information, environmental cues and behaviour together shape how the brain wires itself up."

On the one hand, this model could be applied to study a whole range of diseases that are thought to impact the development of human neurons into neural circuits. The researchers plan to use neurons with genetic mutations linked to diseases such as intellectual disability to try and understand what goes wrong during maturation and circuit formation.

"Disturbances of circuit development have been linked to intellectual disability, for example, and to psychiatric diseases such as schizophrenia," Prof Bonin said. "However, it has remained impossible to study human neural circuits in action in great detail — until now."

"Our findings also imply that nerve cells retain their 'juvenile' properties even in an adult (mouse) brain," Prof Vanderhaeghen added. "This could have potentially important implications for neural repair. The fact that transplanted young human neurons can integrate into adult circuits is promising news in terms of treatment development for neurodegeneration or stroke, where lost neurons could potentially be replaced by transplanting new neurons."

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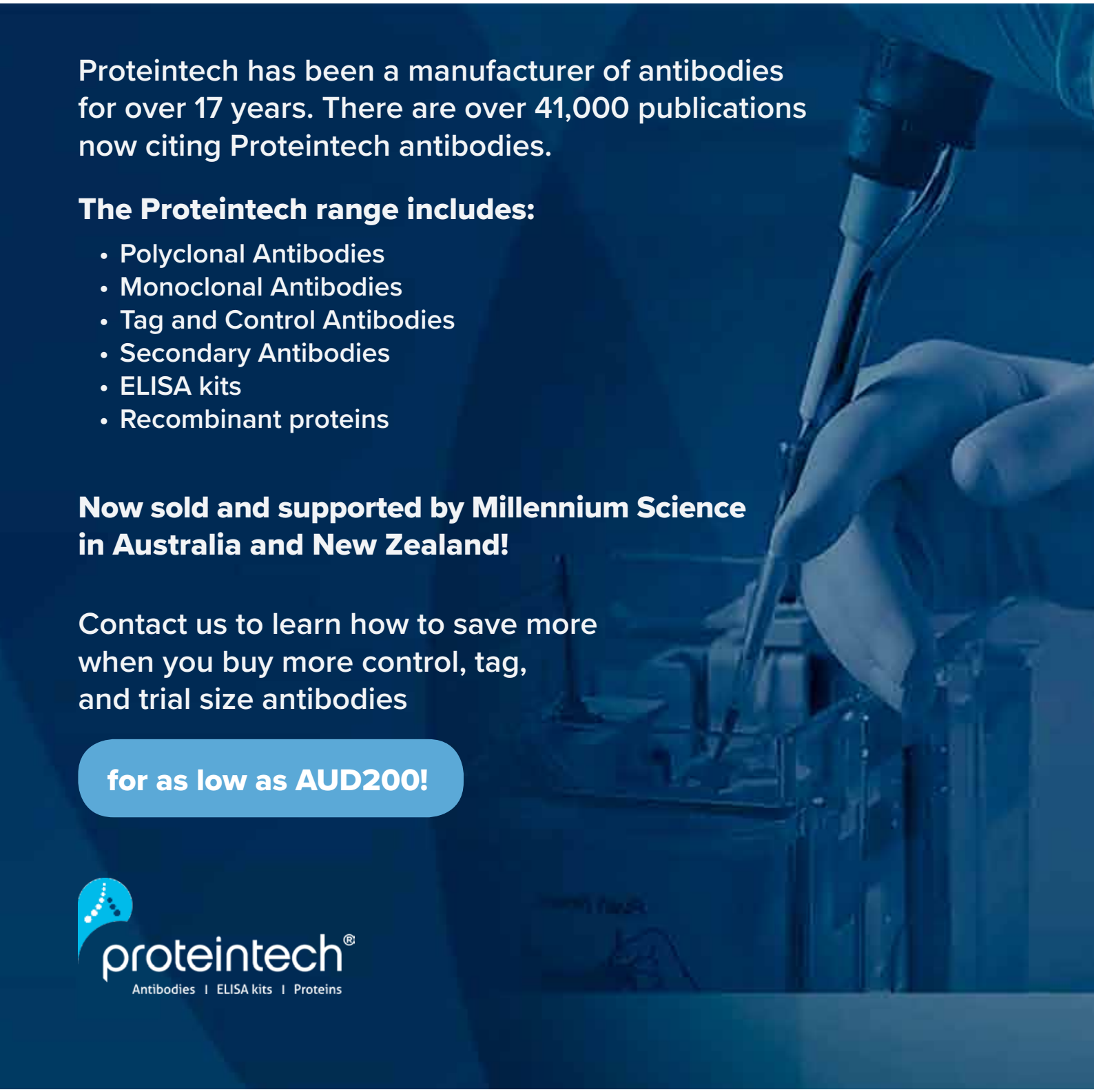

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The challenges of working in a lab

Accidents in the lab are often unavoidable, but if you exercise attention to detail and thoroughness, you contribute to the excellent reputation of your lab and your research integrity. Lab managers should exercise standard procedures for cleaning, clothing and personal protective equipment (PPE) and should comply with all regulations and legislations.

Cross-contamination is normally the outcome of trivial incidents of carelessness or oversight, or conversely, unavoidable mishaps. Nevertheless, without careful attention to the task, it is surprisingly easy to unintentionally combine an alien substance/s with a specimen or accidentally soil an otherwise sterile substance. Oversight can result in the loss of thousands of dollars' worth of research and alteration of results, and can overall change lives for the worse. Yes, it's serious business. Avoid these common mistakes to avoid cross-contamination:

- Using unsterile water.
- Poor air quality or ventilation.
- Letting in air pollutants like smoke or exhaust — this can cause the result to be compromised.
- Not using a new set of gloves for the task at hand — a tiny sample falling off your used glove into a testing substance will not work out for you.

Quality assurance can prove tedious and taxing, but can be approached in every situation with the famous PDCA cycle (plan, do, check, act) — an excellent methodical approach to achieving quality.

However, the lab is a setting wherein there is a complex system which presents obstacles in terms of simplicity in the QC and QA processes. For example, if a client requests a simple percentage and is given a PPM (parts-per-million) measurement, they may receive unanticipated and unwanted costs, or an irrelevant answer. Conversely, if a customer needs a PPB (parts-per-billion) measurement and is given a PPM measurement, it can waste time and require higher costs to the lab. The lab should therefore conduct research into quality systems and invest in systems and roles that can assist in keeping the reliability and effectiveness of the lab.

Expensive lab equipment is also a complaint of many laboratory workers. Indeed, equipment will always ultimately be expensive, especially for specialist labs and clinical laboratories. Equipment can cost hundreds of thousands of dollars, and require thousands of dollars of maintenance, upkeep and running.

Lab safety is heavily regulated. Here are a few fundamentals you must have:

- An eyewash station
- Appropriate signage
- Fire provisions (extinguisher, blanket, smoke alarms, etc)
- Dangerous goods/hazardous materials labelling
- Dangerous goods cabinets
- Appropriate hardware (tap handles, gas connections, ventilation, sink specifications, etc)
- PPE (personal protective equipment)

That said, there is a lot to go through and it is essential that regulations — and conformity to said regulations — are documented and clearly rehearsed. There are three clear classes to the safety requirements that should be borne in mind: physical, biological and chemical safety. Probably the most important safety aspect is covered, however, by common sense. The world of WHS practices is a huge one, and only intensified in the laboratory. It should not be considered a challenge, however, but an opportunity that makes the laboratory an effective workplace. It is a protocol that not only protects you from hazard and harm, but also ensures high quality standards.

Avoid lab bloopers!

- Eyewash stations should be flushed weekly, tagged and documented — just like a fire extinguisher. This makes sure you have the assurance you are not going to further hurt your eyes if you do need to use the eyewash station and makes sure it actually works. It might save your eyesight and, indeed, your career.
- Clearly label chemicals/containers and maintain the labels. Replace old, deteriorated labels. You don't want to muddle up your research with something as trivial as this.
- Indeed, clearly label chemical waste. Make sure this also is maintained, and that the waste tag remains on the container at all times.
- Segregate chemicals properly according to classification. Use chemical cabinets with the appropriate labelling to store whichever dangerous goods you possess.
- Keep your chemical waste containers closed.
- Wear appropriate PPE in the lab: no open-toed shoes or shorts when in the presence of hazardous materials.
- Have appropriate spill supplies ready for any incidents.

Conclusion

Working in the lab is very challenging, as you can see. What is important is to embrace the challenges, see them as opportunities and make every effort to make the lab the best place to work. You will love every minute of it.

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Lauren Davis

Whooping cough vaccine

may prevent food allergies … but will it protect against superbugs?

Australian researchers have discovered that a dose of the whooping cough vaccine might reduce cases of childhood food allergies — but their celebrations may be short-lived, as whooping cough bacteria appear to be evolving to better adapt and survive.

A retrospective study led by the Wesfarmers Centre of Vaccines & Infectious Diseases, based at the Telethon Kids Institute, recently found that using two different types of the whooping cough vaccine could have the added benefit of boosting protection against life-threatening allergies to foods like eggs, milk, soy, peanuts, tree nuts, wheat, fish and shellfish. Their work, published in *The Journal of Allergy and Clinical Immunology: In Practice*, thus advocates for a return to a whooping cough vaccine that has actually been phased out in Australia.

Serving as corresponding author on the study was Professor Tom Snelling, a paediatrician and vaccine researcher at the Wesfarmers Centre. He explained that in Australia doctors these days administer an 'acellular' whooping cough vaccine that targets three antigens in the bacteria of the highly contagious respiratory disease, which can be fatal to infants. All babies need to receive a dose from six weeks old, and then again at four and six months.

"Many countries around the world use an older 'whole-cell' whooping cough vaccine; however, this was replaced by the updated acellular vaccine across Australia in the late 1990s," Prof Snelling said. "Since use of the whole-cell vaccine was phased out, researchers noticed an increase in both the number of cases of food allergies and their severity."

Researchers reviewed the cases of 500 children diagnosed with food allergy by specialist allergists over the past 20 years, discovering that children who had received one or more doses of whole-cell vaccine in the late 1990s were 23% less likely to be diagnosed with a food allergy than those who didn't.

"There are currently 250,000 young Australians living with severe food allergy, and up to three in every 10 babies born each year will develop either a food-related allergy or eczema," Prof Snelling said.

"These allergies occur when the immune system reacts to everyday substances such as different types of food. We believe that by harmlessly mimicking infections, some vaccines such as the whole-cell whooping cough vaccine have the potential to help steer the immune system away from developing allergic reactions."

Professor Katie Flanagan from Launceston General Hospital and the University of Tasmania, who was not part of the study, said such non-targeted effects of vaccines have been well described in the literature in recent years. She explained that they occur "because vaccines can modify the immune profile and thereby alter susceptibility to allergy and infections that are not targeted by the vaccine".

The research team has since been awarded a $3.9 million grant from the National Health and Medical Research Council (NHMRC) to further investigate these findings and is conducting a carefully controlled study involving 3000 Australian babies throughout 2020.

"Babies participating in the study will be randomly assigned to receive either one dose of whole-cell whooping cough vaccine followed by two doses of acellular vaccine, or to just have the usual schedule of three doses of the acellular whooping cough vaccine," Prof Snelling said.

"Participants will be followed until they are 12 months old to confirm whether the whole-cell vaccine truly helps to protect against food allergies in infancy and, if successful, a new vaccine schedule could form part of an effective strategy to combat the rise in food allergies."

There's just one problem with the plan to bring back the whole-cell vaccine — whooping cough bacteria appear to be becoming smarter, and that could mean the need for an entirely new vaccine.

Australia's whooping cough epidemic from 2008 to 2012 saw more than 140,000 cases — with a peak of almost 40,000 in 2011 — and revealed the rise of evolving strains able to evade vaccine-generated immunity. In a series of studies

> Whooping cough bacteria appear to be becoming smarter, and that could mean the need for an entirely new vaccine.

led by UNSW, the latest published in the journal *Vaccine*, researchers took this knowledge further and showed that the evolving strains made additional changes to better survive in their host, regardless of that person's vaccination status. They also identified new antigens as potential vaccine targets.

Microbiologist Dr Laurence Luu, co-leader and first author on the study, said whooping cough's ability to adapt to vaccines and survival in humans might be the answer to its surprise resurgence despite Australia's high vaccination rates.

"We found the whooping cough strains were evolving to improve their survival, regardless of whether a person was vaccinated or not, by producing more nutrient-binding and transport proteins, and fewer immunogenic proteins which are not targeted by the vaccine," Dr Luu said.

"This allows whooping cough bacteria to more efficiently scavenge nutrients from the host during infection, as well as to evade the body's natural immune system because the bacteria are making fewer proteins that our body recognises.

"Put simply, the bacteria that cause whooping cough are becoming better at hiding and better at feeding — they're morphing into a superbug."

Dr Luu said it was therefore possible for a vaccinated person to contract whooping cough bacteria without symptoms materialising, claiming, "The bacteria might still colonise you and survive without causing the disease — you probably wouldn't know you've been infected with the whooping cough bacteria because you don't get the symptoms.

"Another issue with the vaccine is that immunity wanes quickly — so we do need a new vaccine that can better protect against the evolving strains, stop the transmission of the disease and provide longer lasting immunity."

Study co-leader Professor Ruiting Lan said while he would like to see a new vaccine developed and introduced in the next 5–10 years, the research team's discovery did not render Australia's whooping cough vaccine redundant; indeed, he said it is critical that people are vaccinated to prevent the spread of whooping cough.

"We [also] need more research to better understand the biology of the whooping cough bacteria, how they cause disease and what proteins are essential for the bacteria to cause infection, so that we can target these proteins in a new and improved vaccine," he said.

"This will all help to futureproof new vaccines against the evolving whooping cough strains."

Dr Luu agreed that it is crucial for Australia to maintain its high vaccination coverage for whooping cough, with case numbers still well below what they were before the introduction of the vaccine.

"Vaccination is especially important for children, people who are in contact with children and pregnant women who need the vaccine to produce antibodies to protect their newborns from developing whooping cough in the first few weeks of life," he said.

Sensitive back-illuminated sCMOS camera

Andor Technology has announced the launch of Sona 4.2B-6 — the latest model in the ultrasensitive back-illuminated Sona microscopy camera series. The Sona 4.2B-6 provides a balanced combination of sensitivity, speed and resolution, making it suited to the needs of challenging microscopy applications.

The camera features a 4.2 MP sensor format with a 6.5 μm pixel size. This format is suitable for obtaining maximum resolution from the commonly used 60x and 40x objective lens magnifications. It also complements the existing Sona 4.2B-11 model, with a larger, 32 mm field of view for imaging large sample area.

The Sona 4.2B-6 shares many of the key features that have made the existing Sona models effective, including high-sensitivity sensors with 95% quantum efficiency and permanent vacuum-sealed sensor chambers with cooling down to -45°C. The Sona series offers high sCMOS sensitivity, meaning signal to noise can be optimised under reduced illumination conditions, thus preserving the biology of living cells during extended measurement periods.

Andor Technology is an Oxford Instruments company and supplier of scientific imaging and spectroscopy solutions.

Coherent Scientific Pty Ltd
www.coherent.com.au

Phospholipid removal SPE products

Laboratory professionals can simultaneously remove phospholipids and proteins in a single, simple procedure with Resprep PLR (phospholipid removal) SPE products.

Whole blood, serum and plasma all contain proteins and phospholipids that can interfere with target analytes and hasten the need for instrument maintenance. It is important to remove them from samples prior to analysis to avoid signal suppression, and Resprep PLR SPE cartridges or 96-well plates make this an easy task by combining protein precipitation and phospholipid removal in one sample preparation process.

No analyte-specific method development is required because the same procedure can be used for samples containing acids, bases or neutral compounds. In addition, effective removal of phospholipids and proteins from sample extracts reduces contamination, minimising the frequency of instrument maintenance.

Leco Australia Pty Ltd
www.leco.com.au

Automated liquid handler

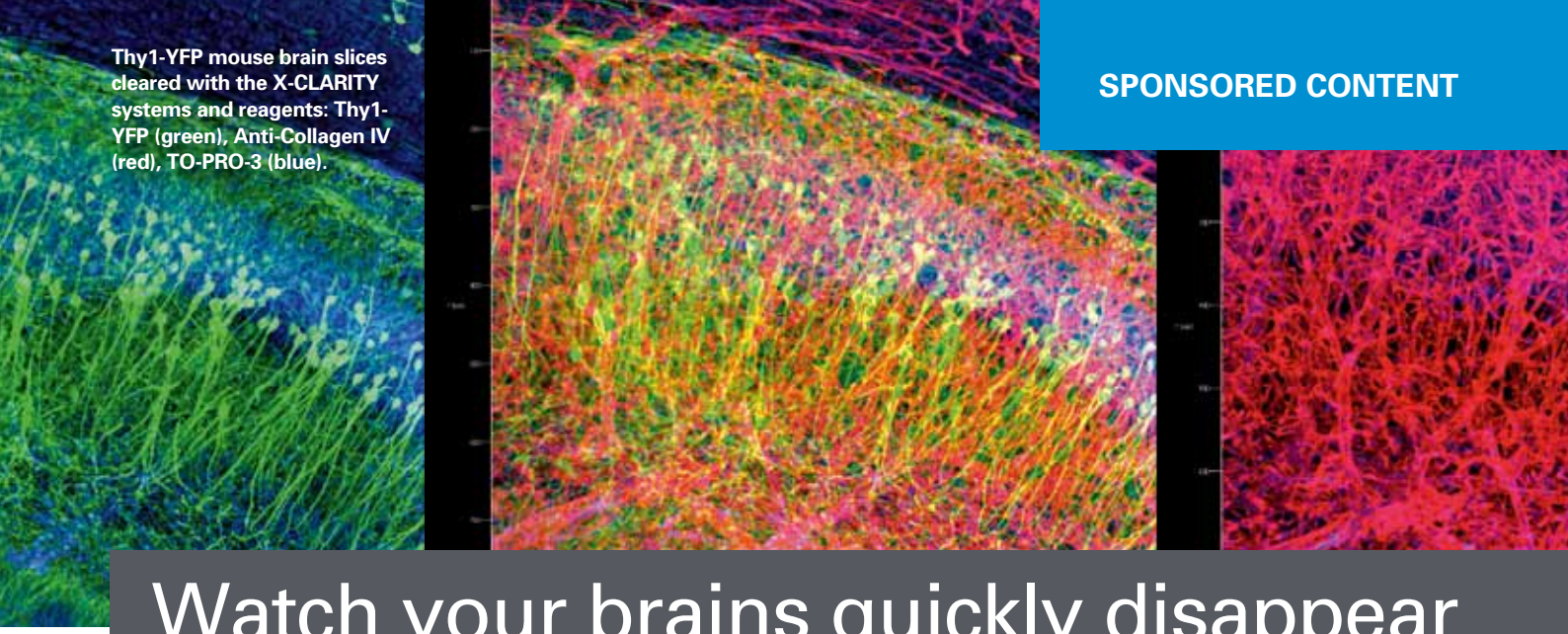
Bio-Strategy and Hamilton introduce the compact Microlab Prep automated liquid handler — a suitable entry-level solution for those transitioning away from manual pipetting in 96- and 384-well microplates and other sample vessels. Standard configuration consists of two independent pipetting channels. The product is also available with a high-speed multiprobe head (MPH) and a configuration containing both single channels and eight channels. It easily fits on a lab bench or in many biological safety cabinets.

Microlab Prep uses air displacement pipetting technology, designed to eliminate the risk of liquid-induced contamination and reduce maintenance frequency compared to liquid displacement pipettors. High pipetting precision and consistency are offered throughout the dynamic pipetting range of 0.5–1000 μL.

Hamilton's wide range of pipette tips offer patented Compressed O-Ring Expansion (CO-RE) technology, creating a tight seal for measurement precision without tip distortion or aerosol generation during tip pick-up and ejection. Optional CO-RE paddles provide automatic sample vessel transport around the Microlab Prep deck to optional peripherals, such as the Hamilton Heater Shaker. A mounted camera detects and identifies labware to facilitate protocol programming and verify labware type and placement.

A touchscreen interface facilitates rapid recall of pre-programmed protocols and enables users to create, simulate and save custom liquid handling protocols. The interface also displays pertinent information during protocol runs, including time remaining, current actions and remaining steps.

Bio-Strategy Pty Ltd
www.bio-strategy.com

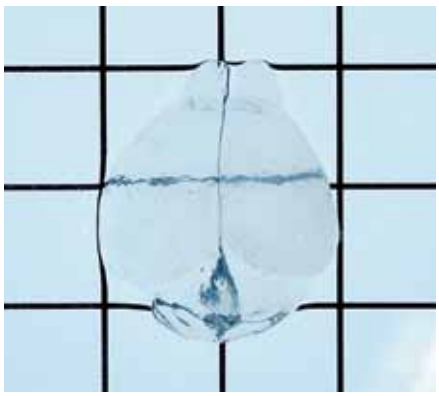


Thy1-YFP mouse brain slices cleared with the X-CLARITY systems and reagents: Thy1-YFP (green), Anti-Collagen IV (red), TO-PRO-3 (blue).

Watch your brains quickly disappear — accelerate your research with X-CLARITY

Techniques that can render tissues clearer than glass allow scientists to reveal the inner workings of biological systems. Clearing tissue helps to drive deeper explorations of structures to expand our understanding of internal functions buried within cells and how these are associated with disease.

Traditional analysis of large-scale tissues has mostly depended on microtomes to cut thin sections, but this process can lead to loss of information. Reconstructing 3D images from thin tissue slices by aligning hundreds or even thousands of snapshots to map long-range projections of cells is laborious and error-prone, and can render fine-grain analysis of whole tissue practically impossible. Recent innovations have led to new tissue-clearing techniques that can be used to acquire high-resolution 3D images without the need to reduce samples to thin serial sections.



Whole Thy1-YFP mouse brain.
The Thy1-YFP signal is preserved and vibrant after tissue clearing with the X-CLARITY™ systems and reagents.

The X-CLARITY (Logos Biosystems) is an all-in-one, easy-to-use solution for electrophoretic tissue clearing. Based on the pioneering work of the Deisseroth lab in Stanford, it enables biological tissue to be transformed into a transparent state for single-cell resolution imaging. Its unique design accelerates the efficient removal of lipids, the main component of light scattering in biological tissues from the tissue hydrogel hybrid. The cleared tissue can then be labelled with appropriate probes such as fluorescent-labelled antibodies and mounted in a refractive index (RI) matching medium to enhance optical clarity for 3D imaging. This provides an optimal environment for 3D imaging with fluorescent microscopy and for prolonged preservation of fluorescence signals in the labelled tissue.

The X-CLARITY tissue clearing system is capable of clearing tissue in half the time of the original method and has become the system of choice for leading research institutes and pharma globally. Using easy-to-follow workflows, efficient control of temperature and a uniform electric current, even the most challenging samples such as bone, spinal cord and plants can be cleared rapidly and reproducibly. By simply pushing a few buttons and applying ready-to-use reagents, a whole mouse brain can be cleared in just six hours.

Optical clarity for 3D imaging is enhanced using specifically designed consumables that help make the process even more convenient. Transparent samples can be labelled with antibodies using the DeepLabel™ Antibody Staining Kit, which can rapidly and efficiently penetrate thick, protein-dense tissues for site-specific binding at lower antibody concentrations. DeepLabel facilitates homogenous antibody staining with 2.6x greater signal-to-background than conventional staining methods. It allows for vibrant fluorescence imaging at subcellular resolution and is compatible with virtually all antibodies and all cleared tissues.

Finally, the labelled tissue is infused and mounted in a refractive index (RI) matching medium to enhance optical clarity for 3D imaging. X-CLARITY Mounting Solution is a newly developed optical clearing agent specifically formulated to overcome known challenges of similar products, mainly lack of availability and high cost. X-CLARITY Mounting Solution is a high-quality refractive index matching solution that minimises photobleaching and preserves fluorescence signals for vibrant fluorescence imaging, making it an ideal solution for clarified and labelled tissue samples.

For more information, please contact Peter Davis at pdavis@atascientific.com.au.

ATA SCIENTIFIC instruments

ATA Scientific Pty Ltd
www.atascientific.com.au

IoT laboratory temperature monitoring solution

Now laboratory professionals can view critical environmental information concerning their laboratory refrigerators, freezers, incubators and ovens from the convenience of their own web browser, be it on desktop, tablet or phone.

MySirius is a cloud-based service from JRI that coordinates the collection of sensor data to the cloud and enables users to receive alarms via SMS and email, no matter where they are. The product requires no software and users view information online, in the cloud. Automatic backup and archiving functions are included.

Data is recorded into small sensors called Nano Spy recorders placed inside or outside thermal equipment and transmitted to MySirius using Nano Links, which are small locally connected gateways. These can be LAN, Wi-Fi, 3G/4G or Bluetooth enabled. Data is always secure and accessible, even during network failure.

Parameters such as temperature, relative humidity, CO_2, O_2, pressure and particle counts can all be recorded and monitored using the Nano Spy and MySirius solution. SMS and email alarms can be sent to any user and are priority managed, so every alarm should always be received and dealt with.

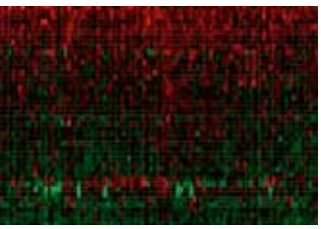
Butler Techsense
www.butlertechsense.com.au

Protein microarrays

GeneCopoeia's OmicsArray protein microarrays are powerful tools for many applications, including autoantibody detection, biomarker profiling and characterisation of protein–molecule interactions. Protein microarrays enable parallel detection of antibodies or other biomarkers present in patient samples for diseases including rheumatoid arthritis, muscular dystrophy, systemic lupus erythematosus and type 1 diabetes.

Each array contains high-quality purified proteins spotted onto nitrocellulose filters, which are adhered to glass slides. Proteins known to be associated with specific diseases are chosen based on a thorough review of peer-reviewed publications. In addition to predesigned arrays, arrays containing customised sets of proteins are available, as well as array profiling services and data analysis.

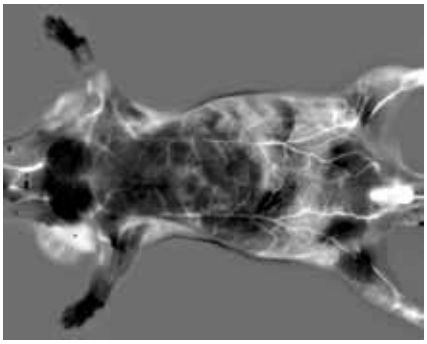
The protein microarrays contain up to 120 purified proteins, compared with one protein at a time for ELISA. In addition, eight spots are included for normalisation.



Each slide carries 16 identical arrays, and so can be used to process up to 15 samples simultaneously as well as a negative control.

Each array can detect as little as 1 pg/mL of antibody, which is 100-fold more sensitive than ELISA. As little as 1 uL of serum or 50 uL of other bio fluids is needed for detection, and the time from sample to data can be as little as two weeks.

United Bioresearch Products Pty Ltd
www.unitedbioresearch.com.au



Small animal imaging system

The IR VIVO system from Photon etc. is a turnkey hyperspectral preclinical imager optimised for imaging in the second biological window of the near-infrared (NIR-II)/short-wave infrared (SWIR) range from 900–1620 nm. Applications include in vivo studies on small animals or living organisms.

Measurement of heart rate, respiratory rate, hepatic function, hepatobiliary and intestinal function, blood flow and angiography in small animals is possible. The increased penetration depth and contrast of NIR-II imaging, combined with its fast acquisition speed and micron-scale spatial resolution, enables users to visualise simultaneously microvasculature and blood flow through an intact cranial bone. Other biological applications include pharmacokinetics of chemotherapy drugs, lipid quantification in liver and blood circulation, monitoring of deep-seated tumours and monitoring cell environment (pH, lipid, mRNA).

The IR VIVO system combines micron-scale spatial resolution, real-time imaging and full spectral coverage throughout small animals. Emission of several fluorophores can be isolated with a high-efficiency tuneable filter and ultralow-noise, scientific-grade InGaAs camera.

Incorporating near- and short-wave infrared, the product is said to benefit from reduced scattering as well as minimal tissue absorption and auto-fluorescence, allowing deeper, clearer imaging than standard optical imaging. It also takes advantage of the most recent developments in SWIR imaging, combining Photon etc.'s ultralow-noise InGaAs camera (ZephIR 1.7) with novel illumination and powerful analytical software to provide fast, high-resolution and deep imaging.

SciTech Pty Ltd
www.scitech.com.au

Sequencing systems

To support demand for clinical-grade genomic information, Illumina has announced the NextSeq 1000 and NextSeq 2000 Sequencing Systems — offering clever system design, chemistry innovations and on-instrument integrated informatics for rapid secondary analysis in as little as 2 h.

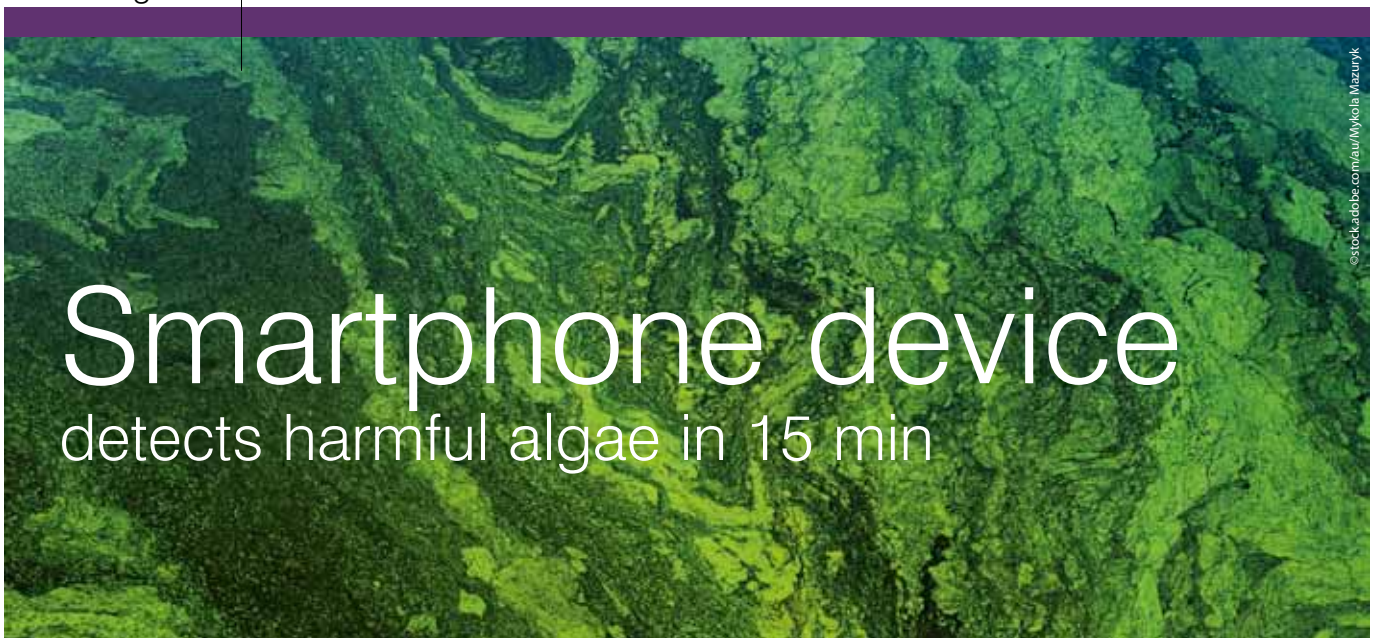
The benchtop sequencers were designed with the aim of simplifying workflows and overcoming challenges faced by users of mid-throughput sequencers today. The company's sequencing by synthesis (SBS) chemistry, coupled with super-resolution optics, an ultrahigh-density flow cell and versatile informatics solutions, enables NGS discovery in a flexible sequencer format. This should enable labs of any size to run tests and experiments more frequently, sequencing at depth and volume with a high level of flexibility and efficiency.

The sequencers incorporate more than 75 innovations — including the combination of super resolution and blue chemistry — that are said to enable an increase in density and throughput as well as a reduction in operating costs. They are designed to enable core labs, small-to-medium research labs and clinical facilities to access high-intensity sequencing applications using SBS technology.

Designed to create a user-friendly, end-to-end experience, the systems integrate DRAGEN on board, powering a flexible informatics suite and featuring both local and cloud-based options for run set-up, management and analysis. The combination of robust instrument performance and run economics delivers the ability to take on applications like single-cell RNA-seq, ctDNA and a variety of oncology panels.

The systems support emerging and current mid-throughput sequencing applications as well as a broad range of methods such as exome sequencing, target enrichment, single-cell profiling, transcriptome sequencing and more. They offer an intuitive workflow with load-and-go ease and visual cues about run status.

Illumina Australia Pty Ltd
www.illumina.com



Smartphone device
detects harmful algae in 15 min

Engineers at the National University of Singapore (NUS) have developed a highly sensitive system that uses a smartphone to rapidly detect the presence of toxin-producing algae in water within 15 minutes — a technological breakthrough that could play a big role in preventing the spread of harmful microorganisms in aquatic environments.

A sudden surge in the volume of algae and their associated toxins in lakes, ponds, rivers and coastal waters can adversely affect water quality, and in turn may have unfavourable effects on human health, aquatic ecosystems and water supply. For instance, in 2015 an algae bloom wiped out more than 500 tonnes of fish in Singapore and caused some fish farmers to lose millions of dollars.

Conventional methods of algae detection and analysis are time-consuming and require specialised and costly equipment, as well as skilled operators to conduct water sampling and testing. One approach is to test for the presence of chlorophyll using complex instruments that cost more than $3000. Another common method is to carry out cytometric and image analysis to detect algal cells — this method involves equipment that costs more than $100,000.

"Currently, it can take a day or more to collect water samples from a site, bring them back to the laboratory for testing and analyse the results," said Assistant Professor Bae Sung Woo, who led the NUS study. "This long lead time is impractical for monitoring of algae blooms, as the management of contamination sources and affected waters could be slowed down."

To address the current challenges in water quality monitoring, Asst Prof Bae and his team took a year to develop the novel device that monitors microbial water quality rapidly and with high reliability. Described in the journal *Harmful Algae*, their invention can generate test results onsite, and findings can be reported in real time using the smartphone's wireless communications capabilities.

The device comprises three sections — a microfluidic chip, a smartphone and a customisable 3D-printed platform that houses optical and electrical components such as a portable power source and an LED light. The chip is first coated with titanium oxide phthalocyanine, a type of photoconductive polymer-based material. The photoconductive layer plays the important role of guiding water droplets to move along the chip during the analysis process.

The coated chip is then placed on top of the screen of a smartphone, which projects a pattern of light and dark regions onto the chip. When droplets of the water sample are deposited on the surface of the chip, a voltage drop difference, created by the light and dark areas illuminated on the photoconductive layer, modifies the surface tension of the water droplets. This causes the water droplets to move towards the dark illuminated areas. At the same time, this movement induces the water droplets to mix with a chemical that stains algae cells present in the water sample. The mixture is guided by the light patterns towards the camera of the smartphone.

Next, an LED light source and a green filter embedded in the 3D-printed platform, near the camera of the smartphone, create the conditions suitable for the camera to capture fluorescent images of the stained algae cells. The images can be sent to an app on the smartphone to count the number of algae cells present in the sample. The images can also be sent wirelessly to another location via the smartphone to quantify the number of algae cells. The entire analysis process can be completed within 15 minutes.

The portable and easy-to-use device costs around $300 — excluding the smartphone — and weighs less than 600 g. The test kit is also highly sensitive, hence only a small amount of water sample is needed to generate reliable results.

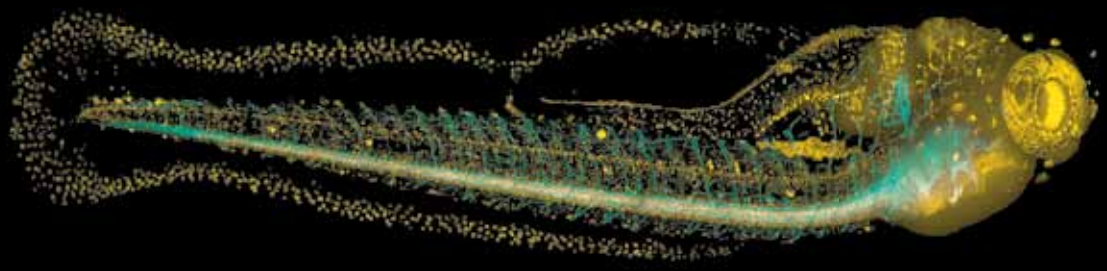
The NUS research team tested their system using water samples collected from the sea and reservoirs. The water samples were filtrated and spiked with specific amounts of four different types of toxin-producing algae — freshwater algae *C. reinhardtii* and *M. aeruginosa*, and marine water algae *Amphiprora sp* and *C. closterium*.

Experiments using the new device and a hemocytometer, a standard cell-counting technique commonly used for water quality monitoring, were conducted to test for the presence of algae. The new smartphone system was able to detect the four types of algae with an accuracy of 90% — comparable with the results generated by the hemocytometer.

"The combination of on-chip sample preparation, data capture and analysis makes our system unique," Asst Prof Bae said. "With this tool, water quality tests can be conducted anytime and anywhere. This new method is also very cost-efficient as the microfluidic chip can be washed and re-used. This device will be particularly useful for fish farmers who need to monitor the water quality of their fish ponds on a daily basis."

The research team is currently in discussion with industry partners to commercialise their technology. The researchers are also developing a new microfluidic chip that can be integrated with a modified version of the current 3D-printed smartphone platform to detect the presence of foodborne pathogens such as *Salmonella* and other infectious pathogens.

Innovative Imaging and Microscopy Solutions



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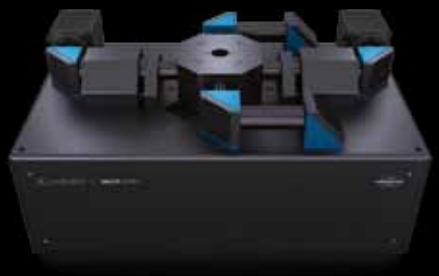

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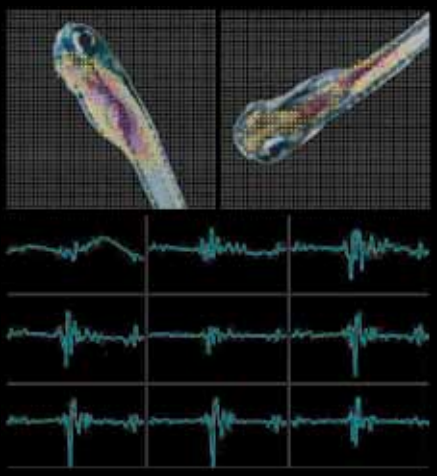
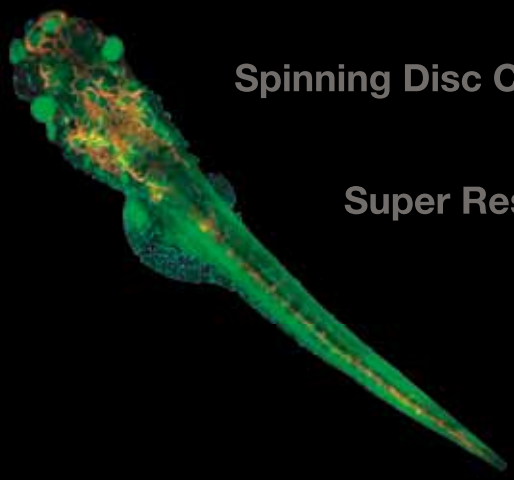


3·Brain

High Performance Microscopy for Life Sciences



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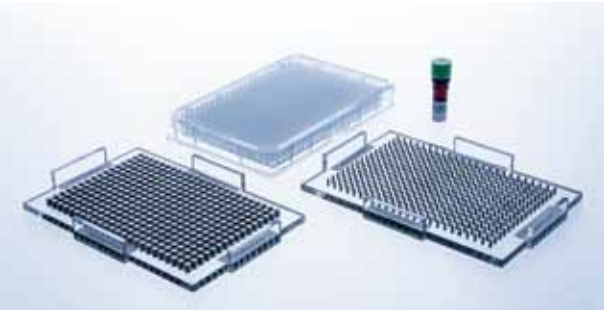
Magnetic 3D cell culture

The core technology of Greiner Bio-One's magnetic 3D cell culture is the magnetisation of cells with NanoShuttle-PL. The cells can be aggregated with magnetic forces, either by levitation or printing, to form structurally and biologically representative 3D models in vitro.

Magnetic levitation is an easy tool to create native tissue environments in vitro. Cells are magnetised through overnight incubation and dispensed into a cell-repellent dish or multiwell plate, where they are levitated off the bottom by a magnet above the cell-repellent vessel. In contrast to magnetic levitation, with magnetic 3D bioprinting, cells incubated with NanoShuttle-PL overnight are printed into spheroids by placing a microplate containing magnetised cells atop a drive of magnets.

NanoShuttle-PL consists of gold, iron oxide and poly-L-Lysine. These nanoparticles (~50 nm) magnetise cells by electrostatically attaching to cell membranes during an overnight static incubation. Magnetised cells will appear peppered with dark nanoparticles after incubation.



The product is biocompatible, having no effect on metabolism, proliferation and inflammatory stress. Additionally, it does not interfere with experimental techniques, such as fluorescence or Western blotting. With magnetised spheroids, solution addition and removal is made easy by using magnetic force to hold them in a stationary position during aspiration, thereby limiting spheroid loss. Spheroids can also be picked up and transferred between vessels using magnetic tools such as the MagPen.

Advantages of magnetic cell culture include mimicking native tissue environment; rapid 3D model formation within hours; no specialised media; easy handling; no sample loss; and co-culture allowed.

Interpath Services Pty Ltd
www.interpath.com.au

Ultralight pipette

The Eppendorf Research plus is a safe and ergonomic pipette, designed to protect the health of users during their daily work. It incorporates the PhysioCare Concept, which should reduce the strain on the hand and arm during pipetting.

The product is an air-displacement pipette for use with aqueous solutions. The user can adjust the pipette in seconds to improve accuracy when pipetting various difficult liquids. They can also choose among single-channel pipettes in fixed or variable volumes as well as 8-, 12-, 16- and 24-channel pipettes.

The Research plus is the pipette family with the lowest weight and lowest operation forces in the Eppendorf product families. The spring-loaded tip cone (not available for 2.5, 5 and 10 mL pipettes) ensures low tip attachment and ejection forces, helping to reduce stress. The device has the ability to be autoclaved without the need to be disassembled.

Bio-Strategy Pty Ltd
www.bio-strategy.com

Pressure sensors and level switches

VEGA's measurement portfolio for pharmaceuticals production now includes the VEGABAR pressure switches/sensors and VEGAPOINT level switches. Robust, versatile and easy to use, even under extreme conditions or strict regulations, the compact series are designed to show that automation can be simple and efficient at the same time, without compromising on hygiene or quality.

The measuring instruments are tailored to standard applications that nevertheless require high quality. Their standardised hygienic adapter system provides the flexibility needed to keep installation effort and parts inventory to the minimum. The process fittings can be interchanged and adapted to local requirements.

Due to the all-round status display, all sensor states can be easily seen from any direction. This illuminated ring, which can be customised from a choice of 256 different colours, remains clearly visible, even in daylight. At a glance, the user can see if the measuring process is running, if the sensor is switching or if any sensor management is required.

Sensor intelligence is built into the measuring instrument series: the standard IO-Link protocol ensures both universal and simple communication. Via the standardised communication platform, this enables seamless data transfer and simple system integration. VEGA has also integrated wireless communication into the series, with the sensors able to connect via smartphone or tablet. This makes set-up and operation easy in environments such as clean rooms, where physical access involves a lot of effort.

Designed for pharmaceutical processes, the products offer users a range of level and pressure measurement technology — all in the form of hygiene-optimised instrument designs that are easy to install and use.

VEGA Australia Pty Ltd
www.vega.com/au

CD spectrophotometers

Circular dichroism (CD) measurements can be used to determine the secondary structure content of a biomolecule to elucidate the relationship between structure and function or verify protein stability.

The J-1500 CD spectrometer allows measurements with high signal-to-noise (S/N) ratio in the vacuum-UV region down to 163 nm. It incorporates several of the latest technologies, such as digital lock-in detection (up to four data channels), high-throughput optics (minimises risk for sample degradation), double prism design (provides low stray light) and an effective nitrogen gas purging system. These features ensure that CD spectra can be obtained from both strongly absorbing and high S/N samples across the spectrum and into the vacuum-UV region and as a result should enable more accurate protein secondary structure analysis.

The J-1500 CD spectrometer has been designed as a multipurpose, flexible system with a wide dynamic range to meet demanding CD applications with high sensitivity. The high-throughput (HTCD) system offers automated protein secondary structure estimation.

The Jasco CD series also includes the J-1100 CD spectrometer, designed for routine, conventional CD applications in a compact package; and the J-1700 CD spectrometer, designed for more demanding near-infrared CD applications such as magnetic CD and covering the wavelength range from UV, visible and NIR up to 2500 nm.

ATA Scientific Pty Ltd
www.atascientific.com.au

Laboratory freezers

The 597-litre Laboratory Upright Freezer with electronic controller (LGPv 6520) is designed to offer safe cold storage for critical samples and reagents in PC2 facilities.

Critical samples and reagents can be optimally stored between -10°C to -30°C with temperature set to 1/10°C accuracy using the flush-mounted keypad on the high-tech electronic controller. The keypad can be locked to prevent temperature setting changes, and a physical lock protects samples and reagents against unauthorised access.

Refrigeration components are top mounted to comply with PC2 requirements, and functional parts like fans and evaporators are located outside the unit for servicing and to increase the net capacity of the freezer.

The 1361-litre Laboratory Freezer with electronic controller uses a forced-air cooling system for maximum temperature uniformity and fast temperature recovery after door openings. Manual defrosting is reduced by the automatic 12 min hot gas defrost cycle which removes ice-build without compromising temperature and integrity of contents.

Castors allow the 1361-litre freezer to be moved easily for cleaning purposes or to reposition in the lab. Eight height-adjustable plastic-coated grid shelves help users maximise their storage capacity.

Visual and audible alarms warn users of temperature breaches and when the door is ajar for more than 1 min, and a 72 h battery backup monitors temperature in the event of a power outage. The freezer is equipped with an access port for independent temperature sensors to be connected and has a volt-free alarm contact and RS 485 interface for communicating temperature data and alarms to remote monitoring or building management systems.

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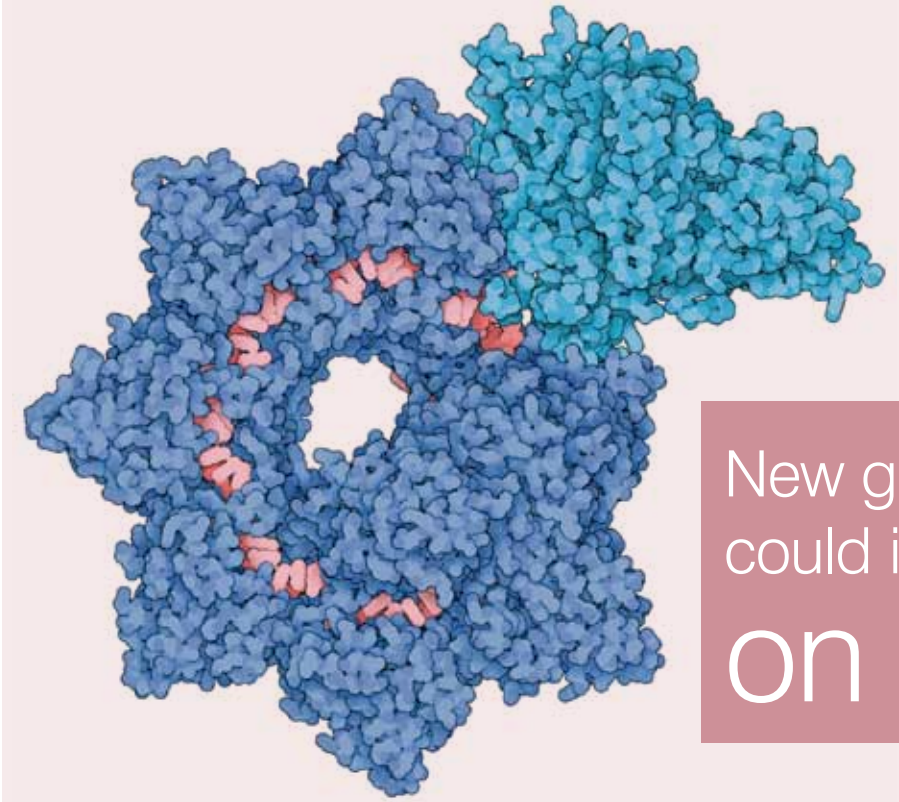

Structure of the INTEGRATE complex showing Cascade (dark blue), TniQ units (light blue) and guide RNA (red).

Image credit: Sternberg and Fernández Labs/Columbia University Irving Medical Center.

New gene editing tool could improve on CRISPR

Scientists from Columbia University Irving Medical Center have captured the first images of a new gene editing tool that could improve on existing CRISPR-based tools. Their work has been published in the journal ***Nature***.

Many researchers around the world use CRISPR-Cas9 to quickly and cheaply make precise modifications to the genome of a cell. However, most uses of CRISPR involve cutting both strands of the target DNA, and the DNA break must then be repaired by the host cell's own machinery.

Controlling this repair process is still a major challenge in the field, and undesired gene edits are often introduced inadvertently in the genome. Additionally, existing tools often perform poorly at inserting large genetic payloads in a precise fashion. Improving the accuracy of gene editing is thus a priority for researchers and is critical for ensuring the safety of therapies developed with this technique.

The newly developed 'INTEGRATE' system, on the other hand, can accurately insert large DNA sequences without relying on the cell's machinery to repair the strands. As a result, INTEGRATE could prove to be a more accurate and efficient way of making certain gene modifications than the original CRISPR-Cas system. The new tool could also help scientists perform gene editing in cell types with limited DNA repair activity such as neurons, where attempts to use CRISPR have been comparatively less successful.

INTEGRATE was made possible after Columbia researchers, led by Assistant Professors Sam Sternberg and Israel Fernandez, discovered a 'jumping gene' in *Vibrio cholerae* bacteria that could insert large genetic payloads in the genome without introducing DNA breaks. The researchers harnessed cryo-electron microscopy to flash freeze a sample of the gene editing complex in liquid nitrogen, before bombarding it with electrons. They then used the images they captured with the electron microscope to generate atomic resolution models of the INTEGRATE system.

Their structural model reveals that the complex is made up of two main sections that are arranged in a helical filament. The larger portion, called Cascade, winds around and carries a guide RNA that it uses to scan the cell for a matching sequence in DNA. Once it locates and binds the target sequence, it threads the DNA strand through the TniQ 'transposition' proteins that sit on the end of the complex and recruit other enzymes that help modify the DNA.

The scanning mechanism of INTEGRATE appears to work in a similar way to other CRISPR systems, some of which also contain a Cascade complex with guide RNA. However, unlike other CRISPR systems that use Cascade to target DNA for cutting, the function of Cascade within INTEGRATE is to target DNA for highly accurate insertion of genetic payloads.

In a previous study, Asst Prof Sternberg and colleagues used genetics and biochemistry to propose how the CRISPR machinery would functionally link to the transposition machinery — the molecules responsible for gene 'jumping' — and the study proved their hypotheses were correct. As noted by Asst Prof Sternberg, "We showed in our first study how to leverage INTEGRATE for targeted DNA insertions in bacterial cells. These new images, a wonderful collaboration with Israel Fernández's lab, explain the biology with incredible molecular detail and will help us improve the system by guiding protein engineering efforts."

"Visualising biology on this scale is truly amazing and can easily excite even those unfamiliar with the topic," added Columbia PhD student Tyler Halpin-Healy, first author of the study. "The quality of this work, and the speed at which it was accomplished, is emblematic of the collaborative environment afforded by great mentors like Sam and Israel."

In addition to informing future engineering efforts, the structures highlight a possible proofreading checkpoint. Existing CRISPR technologies often suffer from so-called 'off-target effects', in which unintended sequences are promiscuously modified. The new structures reveal how Cascade and TniQ work together to ensure that only the correct 'on-target' sequences are marked for DNA insertion. The researchers plan to further explore this checkpoint while developing the tool for new therapeutic approaches to disease.

Safety glasses and goggles

DEWALT safety glasses and goggles are designed to ensure safe, efficient and comfortable vision in the occupational situation, protecting against such common occupational hazards as flying particles and fragments, dusts, splashing materials and molten metals, as well as invisible dangers including harmful gases, vapours and aerosols, glare and harsh optical radiation in the natural environment. Featuring three key products, the range has been certified to meet Australian and New Zealand safety standards.

Rotex Safety Glasses are available in Clear and Smoke colours, making them suitable for indoor and outdoor use. With an ultralightweight frame, the glasses feature a moulded nosepiece and flexible temples with rubber grips for a comfortable fit. They have impact-resistant polycarbonate lenses with 99.9% UV protection.

Excavator Safety Glasses come in a lightweight, full frame in Smoke colour. They feature a self-adjusting rubber nosepiece and dual mould rubber temple grips to provide a comfortable, secure fit. The lens is made from a tough, polycarbonate material, providing impact resistance and 99.9% UV protection.

Concealer Safety Goggles can be worn when there is a high dust element or risk of splash, or over prescription glasses. They feature a ToughCoat hard coated lens, providing tough protection against scratches, or XtraClear anti-fog lens coating, which provides tough protection against fogging. Made of a soft, dual-injected rubber that conforms to the face to provide high-level protection from dust and debris, the goggles are fitted with an adjustable, elastic cloth head strap that provides a comfortable fit, with ventilation channels that allow breathability and added protection against fogging. The low-profile design provides full field of vision, with polycarbonate lens offering 99.9% UVA/UVB protection.

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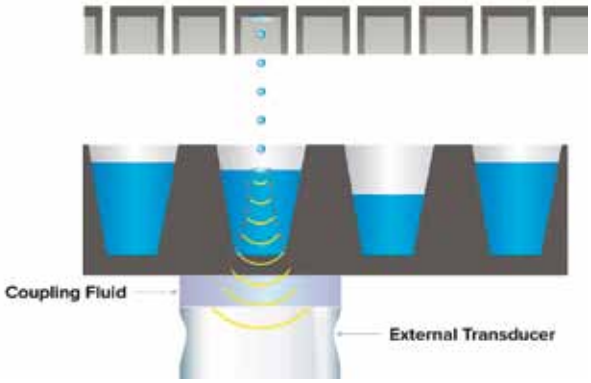
Liquid handlers

Labcyte (now Beckman Coulter) has produced an innovative non-contact liquid handling technology that is claimed to produce faster and more accurate results than traditional pipetting methods. Utilising sound energy, Echo acoustic droplet ejection (ADE) technology will be useful to scientists involved in drug discovery, compound management, genomics research, synthetic biology, proteomics, functional screening and other research applications.

Echo systems are said to provide improved data quality with lower risk of cross-contamination, carryover or leachates when compared to use of pipette tips. They also offer precise, low-volume liquid transfers that should help to miniaturise assays, reduce reagent costs and conserve precious samples. High-throughput 'any well to any well' transfers meanwhile enable the rapid execution of highly complex, multicomponent assays and experiments.

Beckman Coulter Australia
www.beckman.com.au



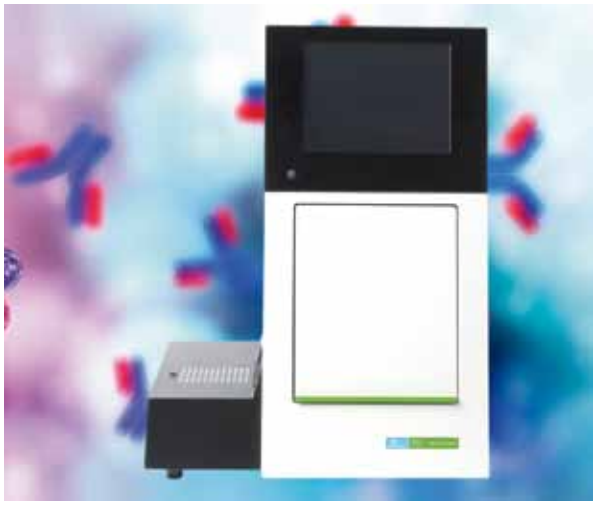
Ribosomal RNA depletion pools

Ribosomal RNA depletion pools (riboPOOLs) by siTOOLs Biotech provide a flexible solution for rRNA depletion. With a diverse selection of ready-made riboPOOLs and the ability to create custom riboPOOLs, the products are suitable for sequencing experts with custom demands and scientists working on rare species.

Composed of high-complexity pools of optimally designed biotinylated DNA probes, riboPOOLs are efficient and specific. Additionally, they do not depend on polyA enrichment, enabling detection of non-polydenylated RNA.

For microbiologists, the Pan-Prokaryote riboPOOL provides universal rRNA depletion for a wide spectrum of microbes and is suitable for metagenomic or microbiome samples. Combination riboPOOLs are also available to deplete rRNAs from samples containing multiple species.

Sapphire Bioscience
www.sapphirebioscience.com



N-linked glycan assay

The LabChip Extended Range N-Linked Glycan Assay enables the high-throughput sizing and quantification of both neutral and charged N-linked glycans on the LabChip GXII Touch protein characterisation system for the assessment of protein-based biotherapeutics.

The assay includes pre-plated reagents in a 96-well format, enabling high-throughput sample preparation that should reduce hands-on time and total preparation time for sample preparation. Samples are transferred between three SBS compliant 96-well plates to support automation-friendly sample preparation on liquid handlers equipped with thermal elements to support lid transfer and incubation steps.

Automated peak detection and N-glycan relative abundance analysis is preformed in under 45 s/sample, enabling the profiling of 96 samples in under 90 min. The LabChip GXII Touch protein characterisation system delivers the data in three digital formats: gel-like image, electropherogram and tabular formats with automated sample alignment, overlay, scaling and zooming features. This data can be conveniently shared, stored and archived.

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AusMedtech 2020

May 20–21, Melbourne

With the theme 'Medtech made to measure', AusMedtech 2020 is set to present an engaging and innovative line-up of keynote speakers and expert panellists who will share their expertise, insight and commentary on a range of topics both practical and inspirational. The event will focus on the increasing personalisation in medical technology, from customised prosthetics and surgical advances to personalised implants and connected devices. It offers an opportunity to connect with like-minded leaders, growing the Australian and global medtech industry to further advance the sector and ultimately benefit people around the world.
https://www.ausmedtech.com.au/

International Youth Nuclear Congress
March 8–13, Sydney
https://iync2020.org/

FOODCON 2020
March 23–25, Melbourne
https://www.foodconferencesaustralia.com/

TSANZSRS 2020
March 27–31, Melbourne
https://www.tsanzsrs2020.com/

Human Genome Meeting 2020
April 5–8, Perth
http://hugo-hgm2020.org/

AXAA-2020
April 29–May 1, Gold Coast
http://www.axaa.org/

Global Academic Programs (GAP) Conference
May 11–13, Melbourne
https://www.gap2020.com.au/

Science at the Shine Dome 2020
May 26–28, Canberra
https://aas.eventsair.com/2020-science-at-the-shine-dome/

ASID Annual Scientific Meeting 2020
June 3–5, Melbourne
https://www.asid.net.au/meetings/ASM2020

International Statistical Ecology Conference
June 22–26, Sydney
http://www.isec2020.org/

AMSA/NZMSS 2020 Conference
July 5–9, Sydney
https://amsa2020.amsa.asn.au/

14th Asia-Pacific Regional IAU Meeting (APRIM)
July 6–10, Perth
https://aprim2020.org/

15th International Symposium on Macrocyclic and Supramolecular Chemistry
July 12–16, Sydney
https://www.ismsc2020.org/

6th International Archean Symposium
July 14–16, Perth
https://6ias.org/

HGSA 44th Annual Scientific Meeting
August 1–4, Adelaide
https://aacb.eventsair.com/hgsa-44th-annual-scientific-meeting/

International Conference on the Physics of Semiconductors 2020
August 9–14, Sydney
https://www.icps2020.org/

Agriculture Summit 2020
August 14–15, Melbourne
https://agrisummit.net/

43rd COSPAR Scientific Assembly
August 15–22, Sydney
http://www.cospar2020.org/

ACS 43rd Annual Scientific Meeting 2020
August 26–28, Queenstown
https://acs2020.org.au/

Energy Oceania 2020
September 7–9, Melbourne
https://www.energyconferenceaustralia.com/

IAFS 2020
September 21–25, Sydney
https://iafs2020.com.au/

ComBio2020
September 29–October 2, Melbourne
http://www.combio.org.au/combio2020/

Linking the Galactic and Extragalactic
November 30–December 4, Wollongong
http://extragalactic-milkyways.org/

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