Lab+Life SCIENTIST

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FROM AN ANCIENT SPECIES

MAPPING THE EPIGENOME

INSTANT CHEMICAL IDENTIFICATION

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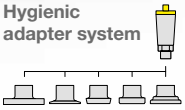

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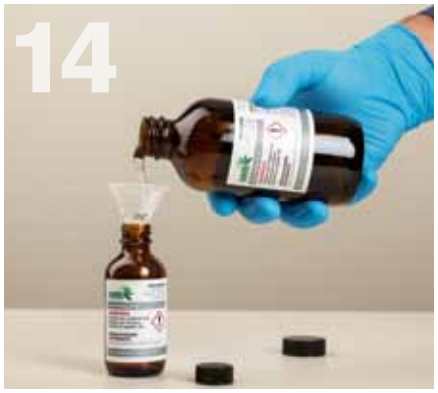

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Optimisation, innovation and remuneration

I recently attended the 2019 Australasian Laboratory Management Conference, hosted by the Australasian Laboratory Managers Association and Science Industry Australia. With the theme of 'Change Management in an Agile World', the conference was focused on how scientists can utilise new methods and technologies in order to better optimise their time in the lab, resulting in a more efficient, innovative way of working.

Indeed, efficiency is probably top of mind for many laboratory managers right now, if the results of the 2019 Professional Scientists Employment & Remuneration Report from Professional Scientists Australia and Science & Technology Australia are to be believed. For while average salaries for members of Australia's science, technology, engineering and mathematics (STEM) sectors have grown in the past year, concerns remain about working conditions.

While base salaries paid to professional scientists increased by an average 2% over the past 12 months — slightly outpacing inflation — this is lower than the average 2.3% increase in earnings across the Australian economy as measured by the ABS Wage Price Index. Almost two-thirds of respondents said cost-cutting is occurring at the expense of their organisation's scientific capability, with large numbers also reporting a decline in the number of scientists in decision-making roles over the past year and a loss in science-driven innovation.

The survey found 71.4% of respondents agree that attracting, developing and retaining the next generation of scientists is one of the most important priorities for developing a sustainable STEM workforce in Australia, but many voiced fears that the lack of value placed on their skills, experience and qualifications is driving talented scientists overseas. Indeed, the latest figures show that Australia invests 1.88% of GDP in research and development — well below the OECD average of 2.38% — and it is perhaps as a result of this that 72.3% of those surveyed believe Australia is not well prepared to meet emerging challenges.

Clearly, then, greater investment in the Australian STEM sector is important. But until that happens, scientists may wish to consider how they can make use of scientific and technological advances, as detailed in this issue, to streamline their work — from LIMS taking over tedious manual tasks, to a more efficient way of mapping the epigenome. We also reveal how the NSW Active MedTech Community is helping to get promising new devices out of the lab and into the world — arguably the most difficult part of the product development process — by teaching medtech entrepreneurs the expertise they need to succeed in commercialisation.

Finally, it should be acknowledged that Australia's scientists have made some impressive breakthroughs over the past 12 months, even working under less-than-ideal conditions. Just imagine what they could achieve in the next 12 months with a little more funding and support — and let's see what we can do to make that happen.

Regards,
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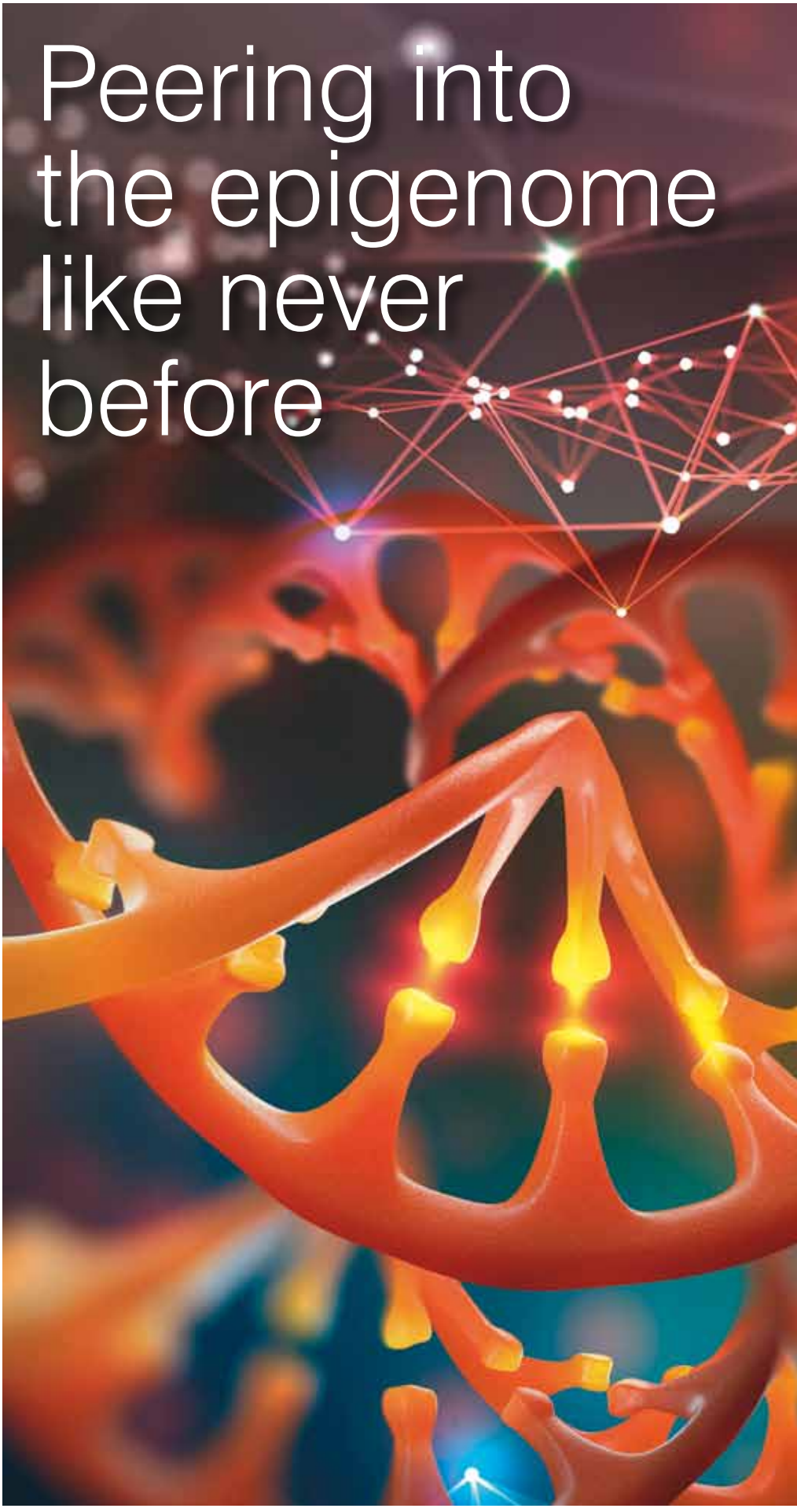

scATAC-seq technology provides unprecedented opportunity to study the impact of epigenetic changes on development and disease.

Our genetic sequence is generally the same in all cells in our body. However, throughout our lifetime, epigenetic modifications can change the way genes are expressed, without altering the gene itself, affecting how a single cell or small groups of cells (cell types) function. Due to their significant effects on cellular function and their dynamic nature, epigenetic changes play critical roles in development and disease.

Mapping the epigenome greatly facilitates our understanding of the epigenetic mechanisms underlying cellular differentiation and disease. The epigenome includes multiple types of modifications that can be different in each cell and can change over time, such as methylation, histone modifications, nucleosome positioning, higher order chromatin structure, nuclear location and proximity to other co-regulated regions of the genome. Until recently, the tools to study these complex, dynamic epigenetic changes consisted largely of bulk assays and assays that focused on specific fragments of DNA. Now technological advances, centred around the single-cell assay for transposase accessible chromatin (scATAC-seq), have allowed scientists to map the epigenome at the level of a single cell across entire tissues and organs. Using this technology, researchers are

scATAC-seq is helping researchers achieve the goal of creating a 'cell atlas' that maps out all the features that define different cell types throughout development and catalogues pathogenic epigenetic modifications associated with specific diseases.

discovering new cell types and gaining insight into how different cell types work together to form functioning organs. This article will explore how epigenetic changes work and how scATAC-seq is poised to transform how they are studied.

Epigenetic changes and cell function

A cell's entire genome, containing both coding and non-coding DNA, is stored carefully within its nucleus. Inactive regions of the genome are packed tightly away, wrapped around proteins called nucleosomes in the form of chromatin that is inaccessible to proteins that transcribe DNA. On the other hand, biologically active regions can be modified to transition from closed to open chromatin that is accessible to transcription machinery. Epigenetics add a layer of regulation to this process, controlling how genes are expressed by changing DNA accessibility. Epigenetic mechanisms, such as chromatin remodelling, DNA methylation and nucleosome positioning, can make DNA more or less accessible.

Sometimes, epigenetic factors can ramp up a gene's expression so that a cell is producing many times more of the gene product as neighbouring cells are. Other times, epigenetic modifications can block transcriptional machinery, decreasing how much the gene is expressed. The full gambit of epigenetic modifications present in a cell together fine-tune how much of each gene gets transcribed into RNA, and subsequently how much of an RNA transcript gets translated into the protein or goes on to perform a structural or enzymatic function within the cell itself.

Creating a 'cell atlas' by mapping the epigenome at scale using scATAC-seq

So, what is scATAC-seq and how does it help scientists map the epigenome? scATAC-seq is a single-cell adaptation of a parent method, the ATAC-seq.

There are enormous cell-to-cell epigenetic differences that evolve over time. Single-cell tools enable us to study this heterogeneity and understand how cell populations are different and how they fit into an entire organism. scATAC-seq technology is ideally suited to address this challenge as it is designed to allow researchers to study vast cell populations simultaneously. scATAC-seq is helping researchers achieve the goal of creating a 'cell atlas' that maps out all the features that define different cell types throughout development and catalogues pathogenic epigenetic modifications associated with specific diseases.

ATAC-seq is a method to survey the epigenetic landscape of hundreds to thousands of cells. Jason Buenrostro and colleagues at Stanford University pioneered the work behind ATAC-seq and published their research in 2013 in *Nature Methods*. ATAC-seq requires relatively few cells as a starting material compared to other methods of studying epigenetic changes, such as MNase-seq, ChIP-seq and DNase-seq, and can collect the desired information in a single assay in a single day. In ATAC-seq, Tn5, a hyperactive transposase mutant, binds to open regions of the genome, cutting the bound DNA and ligating NGS adapters. After end polishing and PCR, these prepped fragments are sequenced to discern those regions of the

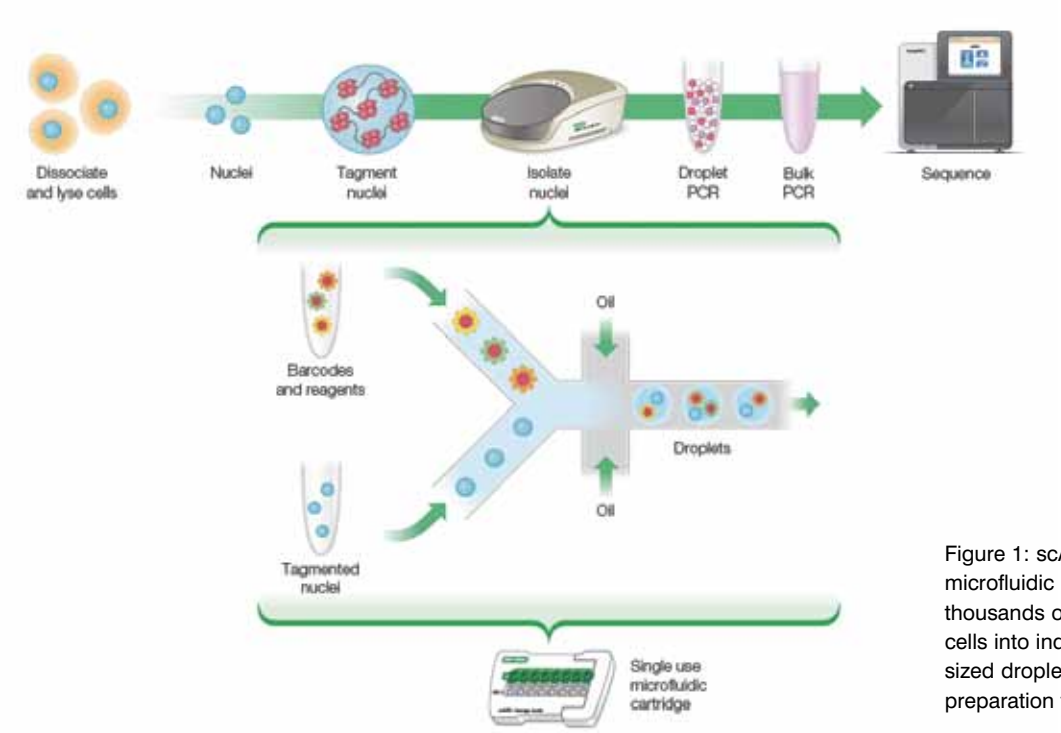

Figure 1: scATAC-seq uses a microfluidic platform to partition thousands of nuclei or whole cells into individual nanolitre-sized droplets to facilitate library preparation for ATAC sequencing.

chromatin that were open. Thus ATAC-seq can give information about the average epigenetic state of the population of cells in a sample, and map where in the genome nucleosomes are positioned and transcription factors can bind.

While ATAC-seq is very useful, it still does not give information at the single-cell level, which is essential to create an epigenetic cell atlas. Working out of Harvard, Buenrostro used microfluidic chip technology to segregate individual cells before employing ATAC-seq, creating scATAC-seq. The technique, published in the journal *Nature* in 2015, uses a microfluidic platform to isolate hundreds of individual cell nuclei, after which the Tn5 transposase tags open chromatin regions with sequencing adapters. The open chromatin library is then amplified with cell-identifying barcoded primers. Once amplified, libraries each representing different cells are pooled and sequenced to reveal open regions in the genomes of individual cells. One scATAC-seq experiment can generate profiles of open chromatin regions for thousands of cells, offering a snapshot of epigenetic similarities and differences. This single-cell approach provides classification of different cell types within a sample, for example, a cell type's relative frequency within a tissue, and also identifies distinct epigenomic changes that occur within a given cell type.

Classic scATAC-seq has given researchers across numerous disciplines key insights into the etiology of some of the most complex and far-reaching human diseases including various cancers, autoimmune disorders and neurological disorders like Huntington's, Alzheimer's, Parkinson's and schizophrenia. However, the assay was originally designed to sample hundreds to thousands of cells per experiment. More recently, the scATAC-seq method has been further refined into methods that can process even more cells in a single experiment. Ron Lebofsky at Bio-Rad Laboratories and Caleb Lareau at Harvard University collaborated with Buenrostro to further scale up scATAC-seq using Bio-Rad's droplet-based technology to partition cells (Figure 1).

First, they developed a droplet-based version of scATAC-seq (dscATAC-seq) that harnesses the power of the ddSEQ Single-Cell Isolator and Bio-Rad's Droplet Digital technology to partition thousands of nuclei or whole cells into individual nanolitre-sized droplets to facilitate library preparation for ATAC sequencing. Use of a droplet-based solution instead of the original microfluidic technology leverages an industry-leading workflow that is scalable, easy to use and saves time. The new workflow also significantly improved library complexity due to a custom hyperactive transposase that cuts the strands between the nucleosomes into very short fragments for greater resolution. Together these improvements enable researchers to gain greater biological insight with less sequencing, more robust detection of cell-to-cell differences, in less time spent in the lab. Researchers have used dscATAC-seq to perform an unbiased study of different cell types and regulatory elements within a mouse brain.

To further augment the capabilities of dscATAC-seq, they added a feature called combinatorial indexing to create single-cell combinatorial indexing for the ATAC-seq (dsciATAC-seq) assay. In this approach, a hyperactive mutant the transposases are loaded with indexed sequencing adapters or a first set of barcodes that are integrated into regions of accessible chromatin. Then, instead of a single cell or nucleus being encapsulated into a single droplet, the requirement for one cell per droplet is no longer needed. Cells can be loaded at much higher density because when droplets have more than one cell, the cells' ATAC fragments can be distinguished by their initial barcode. This combinatorial indexing approach of barcoding cells in two different ways allowed the researchers to process many more cells at once, generating high-quality chromatin accessibility profiles of as many as 50,000 cells for each sample. In practice, researchers have used dsciATAC-seq to discover how different stimulation conditions affect the chromatin accessibility landscape in immune cell clusters from human bone marrow derive cells, to reveal changes across cell types and upon stimulation conditions at single-cell resolution.

Overall, these methods represent the massive scalability of the scATAC-seq-type methods and their potential ability to create a high-resolution cell atlas of the estimated 37.2 trillion cells that make up the human body. Such an atlas will give researchers an unprecedented look at the human body, allowing them to discover new clues about how biological processes work and apply their insights towards developing better treatments for a range of diseases.

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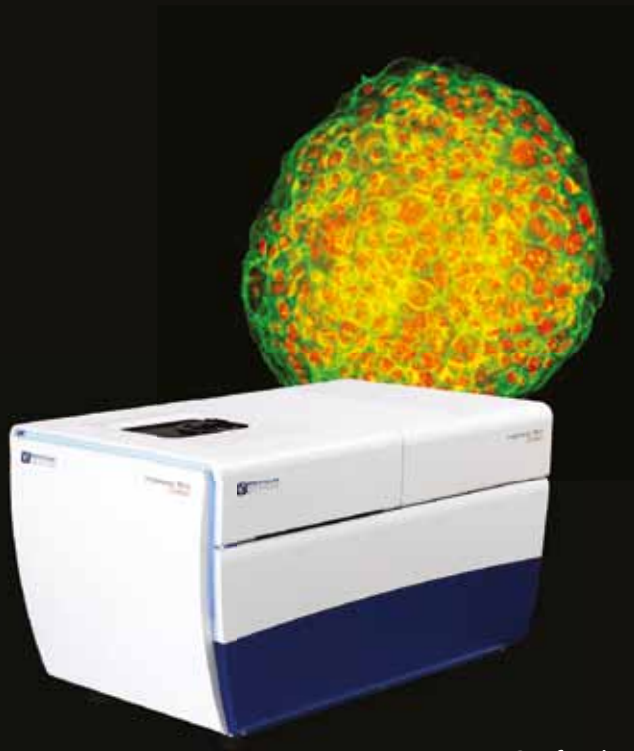

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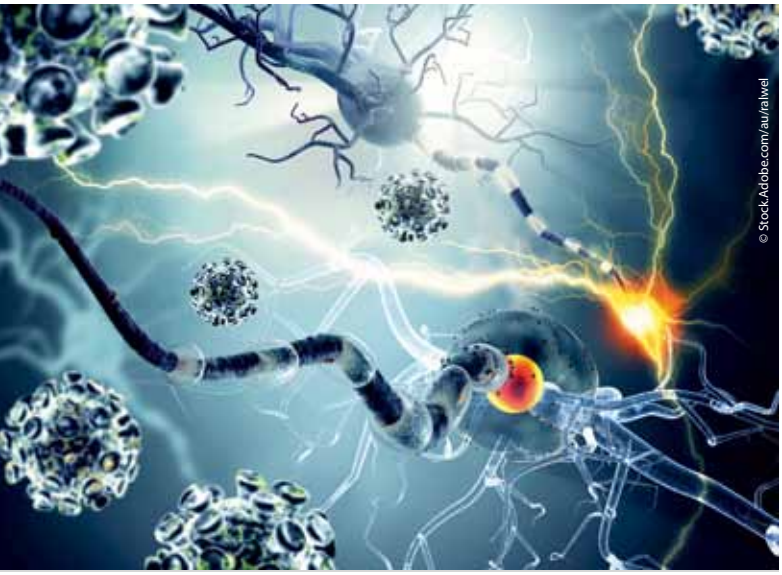

Molecule could be targeted to slow MS progression

By identifying a molecule that plays a role in multiple sclerosis, Canadian researchers have paved the way for new therapies to treat this autoimmune disease.

Multiple sclerosis (MS) can cause symptoms such as extreme fatigue, lack of coordination, vision problems, cognitive impairment and mood changes. 60% of adults with MS are between the ages of 20 and 49 and women are three times more likely than men to be diagnosed with the disease. The cause remains unknown and there is presently no cure.

The good news is that researchers at the University of Montreal Hospital Research Centre (CRCHUM) have identified a molecule named ALCAM, which, once blocked, delays the progression of the disease. Their results, obtained from in vitro human and in vivo mouse studies and published in the journal *Science Translational Medicine*, could lead to the development of a new generation of therapies.

Under normal conditions, the blood–brain barrier protects our brain from exposure to harmful elements; for example, it prevents cells of the immune system such as lymphocytes from invading our central nervous system. However, in people with MS this barrier is permeable; thus, a large number of lymphocytes (white blood cells) manage to migrate into the brain and deteriorate its tissues via destruction of the myelin sheath that protects the neurons and enables the transmission of nerve impulses.

Lymphocytes known as B cells have already been shown to contribute to the progressive phase of MS; certain medications, commonly known as anti-B-cell drugs, reduce its progression and the resulting disability. Now, the CRCHUM researchers have shown that the molecule ALCAM (Activated Leukocyte Cell Adhesion Molecule), expressed by B cells, controls their entry into the brain via blood vessels.

"It allows them to migrate to the other side of the blood–brain barrier in mice and humans," said CRCHUM researcher Dr Alexandre Prat. "By blocking this molecule in mice, we were able to reduce the flow of B cells into their brains and, as a result, slow the progression of the disease.

"The molecule ALCAM is expressed at higher levels on the B cells of people with multiple sclerosis," Dr Prat continued. "By specifically targeting this molecule, we will now be able to explore other therapeutic avenues for the treatment of this disease."

Portable brain scanner used to identify stroke

The ability to perform a brain scan on stroke patients at almost any location could soon become a reality, thanks to the development of a portable, lightweight clinical prototype by EMVision Medical Devices and The University of Queensland.

The portable brain scanner technology, which has been close to a decade in development, is the size of an ultrasound unit and easy to use. It has the potential to enable clinicians to make critical decisions earlier — shortening time to treatment, classifying stroke subtypes and improving patient outcomes as a result.

Currently, there is no point-of-care imaging solution allowing the assessment and monitoring of stroke patients without having to transport them to fixed CT or MRI scanners. Not all patients have access to these imaging devices, nor are they accessible at rural medical clinics. Furthermore, they cannot be carried by first response paramedic teams or moved around the hospital wards.

"One of the most powerful global trends in healthcare accessibility and delivery is the rise of point-of-care imaging," said EMVision CEO Dr Ron Weinberger. "Point-of-care ultrasound, as an example, has revolutionised the practice of medicine, influencing how care is provided in nearly every medical and surgical specialty. Whilst ultrasound is great for a wide range of applications, it is very poor for use in stroke care due to its inability to image the brain. We aim to fill this void for stroke."

To create quality images of the brain, a lightweight headset containing an antenna array transmits safe low-power electromagnetic signals into the brain, relying on the differing electrical properties and contrast of healthy and unhealthy tissue. These interactions are then picked up by proprietary AI software, which reconstructs and displays an image on the screen to guide diagnosis.

A commercial generation of EMVision's brain scanner will now be developed to scan stroke patients at their bedside while recovering, providing the capability for hospitals to monitor for recurrent strokes and track response to treatments. A future handheld version is also expected to provide rapid stroke decision support and triage in ambulances. This could allow patients to be identified and transported directly to specialist hospitals for earlier intervention or even provide the opportunity to treat patients pre-hospital.

The device will be based at Brisbane's Princess Alexandra Hospital for an upcoming clinical trial, which will collect data from patients with diagnosed ischaemic and haemorrhagic stroke, with confirmatory CT or MRI images. Dr Weinberger said, "Our ICU and neurology clinical collaborators are excited to start the trial very soon."

Device co-inventor Dr Konstanty Bialkowski (left) and EMVision CEO Dr Ron Weinberger (right) stand alongside the EMVision clinical unit.

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The S-Monovette is an innovative enclosed blood collection system that allows the user to draw blood from the patient using the syringe or vacuum method, uniting the advantages of both techniques in a single product.

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

The S-Monovette can also be used as an evacuated tube by drawing the plunger fully down and snapping it off immediately prior to blood collection. This creates a fresh vacuum and ensures a precise filling volume, ensuring a correct dilution ratio.

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

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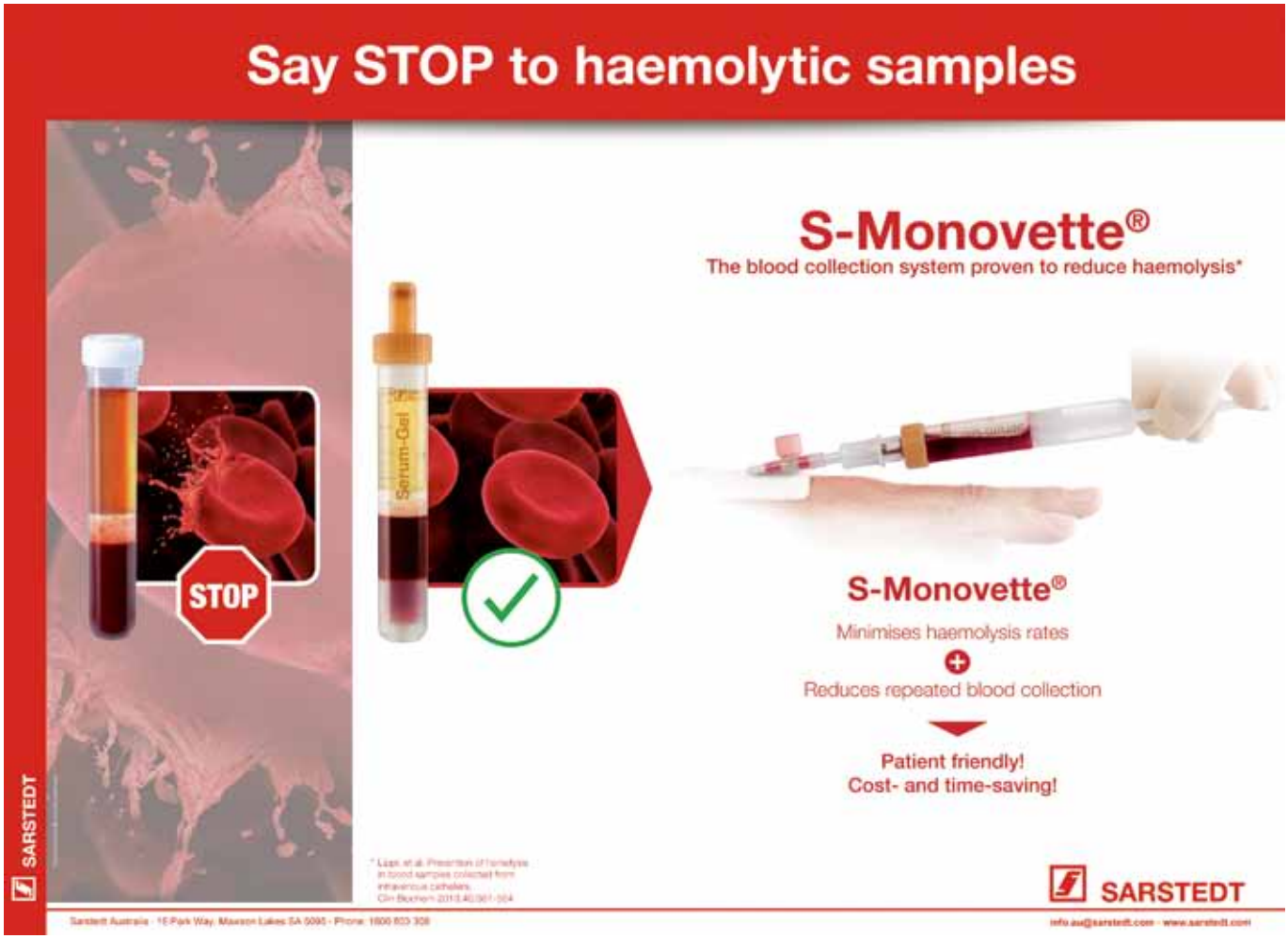

Blood test to detect multiple types of cancer

US researchers are developing a blood test that has shown the ability to screen for numerous types of cancer with a high degree of accuracy, with the results presented at the European Society for Medical Oncology (ESMO) 2019 Congress in Barcelona.

The test, developed by California biotech company GRAIL, looks for DNA, which cancer cells shed into the bloodstream when they die. In contrast to liquid biopsies, which detect genetic mutations or other cancer-related alterations in DNA, the technology focuses on modifications to DNA known as methyl groups. Methyl groups are chemical units that can be attached to DNA, in a process called methylation, to control which genes are 'on' and which are 'off'. Abnormal patterns of methylation turn out to be, in many cases, more indicative of cancer — and cancer type — than mutations are. The test zeroes in on portions of the genome where abnormal methylation patterns are found in cancer cells.

The study saw investigators analyse cell-free DNA (DNA that had once been confined to cells but had entered the bloodstream upon the cells' death) in 3583 blood samples, including 1530 from patients diagnosed with cancer and 2053 from people without cancer. The patient samples comprised more than 20 types of cancer, including hormone receptor-negative breast, colorectal, oesophageal, gallbladder, gastric, head and neck, lung, lymphoid leukaemia, multiple myeloma, ovarian and pancreatic cancer.

The test successfully picked up a cancer signal from the cancer patient samples, with an overall specificity of 99.4% meaning only 0.6% of the results incorrectly indicated that cancer was present. The sensitivity of the assay for detecting pre-specified high-mortality cancers (the percentage of blood samples from these patients that tested positive for cancer) was 76%. Within this group, the sensitivity was 32% for patients with stage I cancer; 76% for those with stage II; 85% for stage III; and 93% for stage IV. Sensitivity across all cancer types was 55%, with similar increases in detection by stage. For the 97% of samples that returned a tissue of origin result, the test correctly identified the organ or tissue of origin in 89% of cases.

"Our previous work indicated that methylation-based assays outperform traditional DNA-sequencing approaches to detecting multiple forms of cancer in blood samples," said study lead author Dr Geoffrey Oxnard, from the Dana-Farber Cancer Institute.

"The results of the new study demonstrate that such assays are a feasible way of screening people for cancer," he added, noting that detecting even a modest percentage of common cancers early could translate into many patients who may be able to receive more effective treatment if the test were in wide use.


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How can tomatoes improve sperm quality?

Scientists from The University of Sheffield have discovered that sperm quality can be improved with a simple diet supplement containing a compound found in cooked tomatoes — a breakthrough that could transform the outlook for men with fertility problems.

Writing in the *European Journal of Nutrition*, the researchers noted that poor sperm quality is a major contributor to infertility in heterosexual couples, but at present there are few empirical therapies.

"Several studies have examined the role of dietary factors and data from randomized controlled trials suggest that oral antioxidant therapy can improve some sperm parameters," the study authors wrote. One such antioxidant is lycopene, which has previously been proposed as a supplement to treat a number of health conditions.

Lycopene can be found in some fruits and vegetables, but the main source in the diet is from tomatoes. Dietary lycopene is poorly absorbed by the human body, so the researchers decided to trial the use of a commercially available formulation called LactoLycopene, designed by FutureYou Cambridge to improve bioavailability.

Led by Professor Allan Pacey and Dr Liz Williams, the double-blind trial involved 60 healthy volunteers aged 19 to 30. Half took LactoLycopene supplements and the other half took placebos every day for 12 weeks; sperm and blood samples were collected at the beginning and end of the trial.

As expected, the level of plasma lycopene was increased in the men randomised to receive lycopene supplementation. The researchers found there was no significant change in motile sperm concentration in response to LactoLycopene intervention; however, the proportion of fast progressive sperm and sperm with normal morphology did improve significantly — by up to 40%.

"We didn't really expect that at the end of the study there would be any difference in the sperm from men who took the tablet versus those who took the placebo," said Prof Pacey, a world expert in male reproduction. "When we decoded the results, I nearly fell off my chair.

"The improvement in morphology — the size and shape of the sperm — was dramatic. We used a computer system to make these measurements, which takes a lot of the human error out of the results. Also, the person using the computer didn't know who had taken LactoLycopene and who had taken the dummy pills either."

Prof Pacey said the work so far has not investigated the mechanism for lycopene's beneficial action but suggested it is potentially inhibiting the damage caused by oxidation of sperm, which is a known cause of male fertility problems. He believes this antioxidant effect is key in producing the improvements in sperm quality seen in the trial, and is hoping to investigate this more.

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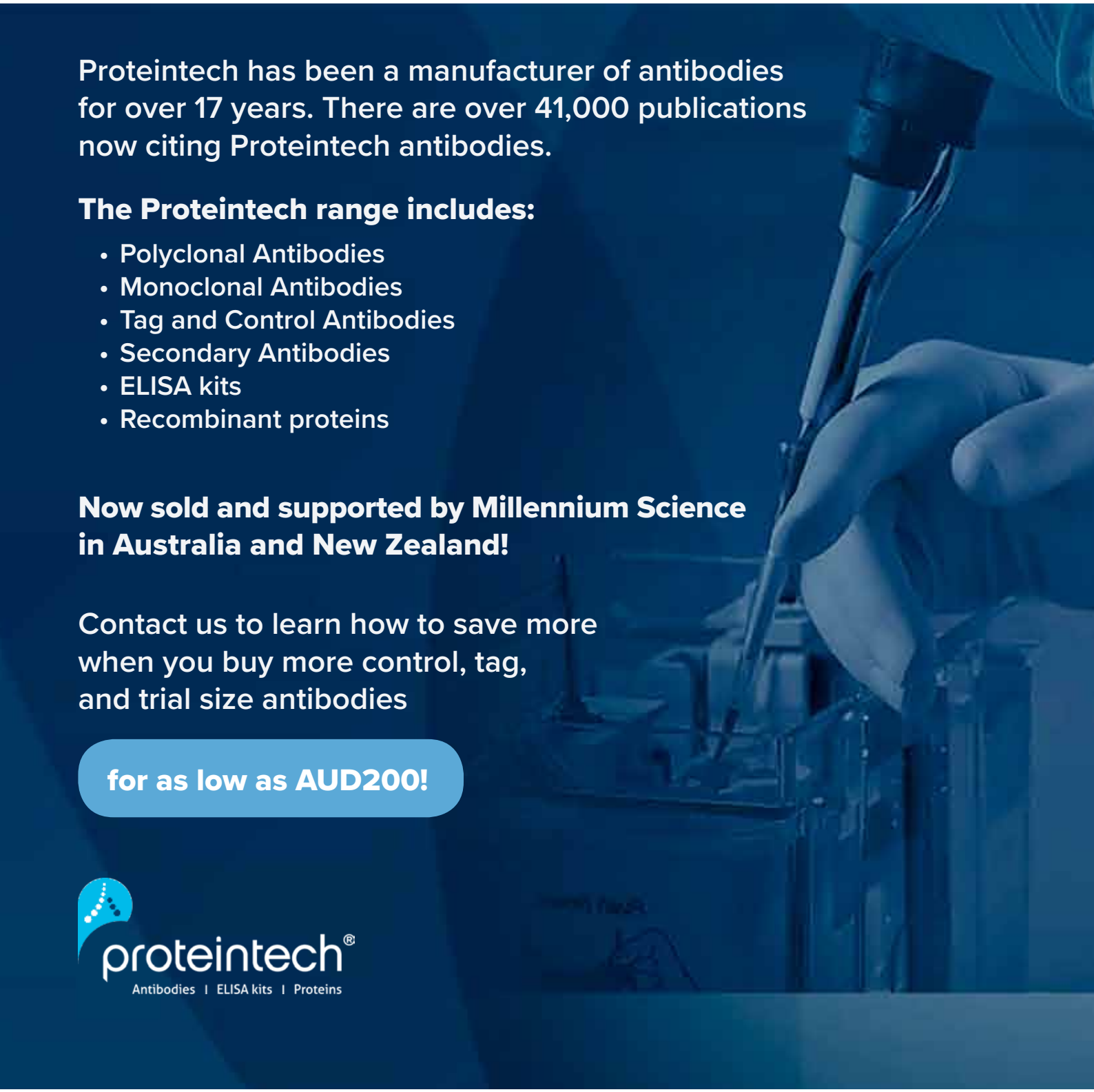

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Safe and practical sign usage in laboratory settings

Due to the varied and critical nature of the research conducted within them, labs can be high-risk environments for accidents. Risk factors that can become potentially fatal hazards include chemicals, sharp instruments, breakable glass and flammable materials.

In a laboratory, the safety of researchers, scientists, staff and visitors depends on adequate communication and training. They must be able to identify the potential for accidents within the lab setting and be aware of procedures and policies to minimise risks and ensure the safety of all involved.

Safety signage is an effective way to regularly remind all employees, contractors and visitors of their safety responsibilities and it can assist with everything from chemical and biological hazards to infection control alerts, personal protective equipment (PPE) education and streamlining the organisation's processes. The correct signage helps important research to continue efficiently without interruption or accident.

During an emergency or crisis, employees without appropriate signage may lack the necessary knowledge required to handle the situation, and under pressure be unable to remember important procedures. A sign is a powerful visual reminder that often has universal iconography that is instantly recognisable to people from all around the world, allowing them to act fast in an emergency. Having these extra measures and reminders can help employees and employers feel more secure in hazardous situations.

While organisations may understand the practical value in having signage, the quality of the signage used can have a significant impact on ensuring accidents and incidents are successfully avoided.

Labs and research facilities across the country often use regular office supplies, which are not fit for industrial purposes, to create makeshift signs. Not only do the DIY signs not stay up or last, they have the potential to cause real danger. Improper signage may fall, cause someone to slip or prevent staff from access to vital information in an emergency. If genuine industrial-grade products are not used, in time the signs will crumble, fade and fall down, and have a huge potential to result in injury, miscommunication and avoidable incidents.

Employees creating their own signage quickly and independently is and should be a vital part of the safety process, allowing staff to instantly respond to risks and communicate important information such as spills, wet floors or even timetable changes. However, this need for quick signage has led facilities to use materials inappropriate for the purpose. Paper signs are held up with sticky tape or put in plastic sleeves and tacked to the wall. If labs want quality signs, the inconvenience of ordering them can be costly and they may take days or weeks to arrive. Avery Design and Print Online provides a solution that allows labs to instantly print industrial, laboratory-grade labels in the office, enabling organisations to rapidly respond to incidents. As a result, facilities can be safer for longer with customised signs on quality industrial-grade materials able to withstand extreme temperatures, rough handling and chemical spills.

Chemicals are not the only risk apparent in labs — with the space consisting of many pieces of equipment and implements, improper management can lead to injury or death. All electrical equipment should be tested regularly, with maintenance signs used as soon as repairs are needed and power is cut off. If a safety sign is made out of paper and sticky-taped to a machine, it's likely to blow off or tear — if this happens it could have potentially fatal consequences for someone using a faulty machine without knowledge or an electrician conducting tests while power is restored.

Labs are notoriously controlled environments in relation to their experiments and research; however, there are often many different departments who are stakeholders in this process, and this can lead to different strategies and expectations, as well as many interruptions. It can mean a huge difference in the way each division handles its safety procedures, including the creation of safety labels and signs. Inconsistencies in an organisation not only look messy, they also leave room for error as there is not a cohesive expectation set for each employee. This is where safety standards slacken and home-made signs and memos appear and become hard to oversee. One master policy across an organisation allows management to strategically review and identify quickly where improvements need to be made and uniformity will follow.

In many cases lab workers may be choosing time and convenience over quality and are not aware of the effect this may have on safety in the workplace. Prioritising industry-specific products will lead to safer, professional environments where staff understand their responsibilities. It is possible for labels and signs to be created once and withstand the rigorous conditions of a laboratory, so investing in quality products will help to ensure lasting safety benefits for both employers and employees.

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New strain of HIV discovered

Scientists from healthcare company Abbott have identified a new subtype of the human immunodeficiency virus (HIV), called HIV-1 group M subtype L.

But it's not all bad news, as the results of their study — published in the ***Journal of Acquired Immune Deficiency Syndromes (JAIDS)*** — show how next-generation genome sequencing is helping researchers stay one step ahead of mutating viruses and avoiding new pandemics.

Since the beginning of the global AIDS pandemic, 75 million people have been infected with HIV and 37.9 million people today are living with the virus. Thanks to the work done by the global health community over the past few decades, the goal of ending the HIV pandemic is becoming feasible. Yet researchers must remain vigilant to monitor for new strains to make sure testing and treatments continue to work.

As a leader in blood screening and infectious disease testing, Abbott created its Global Viral Surveillance Program 25 years ago to monitor HIV and hepatitis viruses and identify mutations to ensure the company's diagnostic tests remain up to date. In partnership with blood centres, hospitals and academic institutions around the world, Abbott has collected more than 78,000 samples containing HIV and hepatitis viruses from 45 countries, identified and characterised more than 5000 strains, and published 125 research papers to date to help the scientific community learn more about these viruses.

Abbott scientists have now confirmed that its core and molecular laboratory diagnostic tests can detect this new HIV strain — the first new subtype of 'group M' HIV virus to be identified since guidelines for classifying new strains of HIV were established in 2000. Group M viruses are responsible for the global pandemic, which can be traced back to the Democratic Republic of Congo (DRC) in Sub-Saharan Africa.

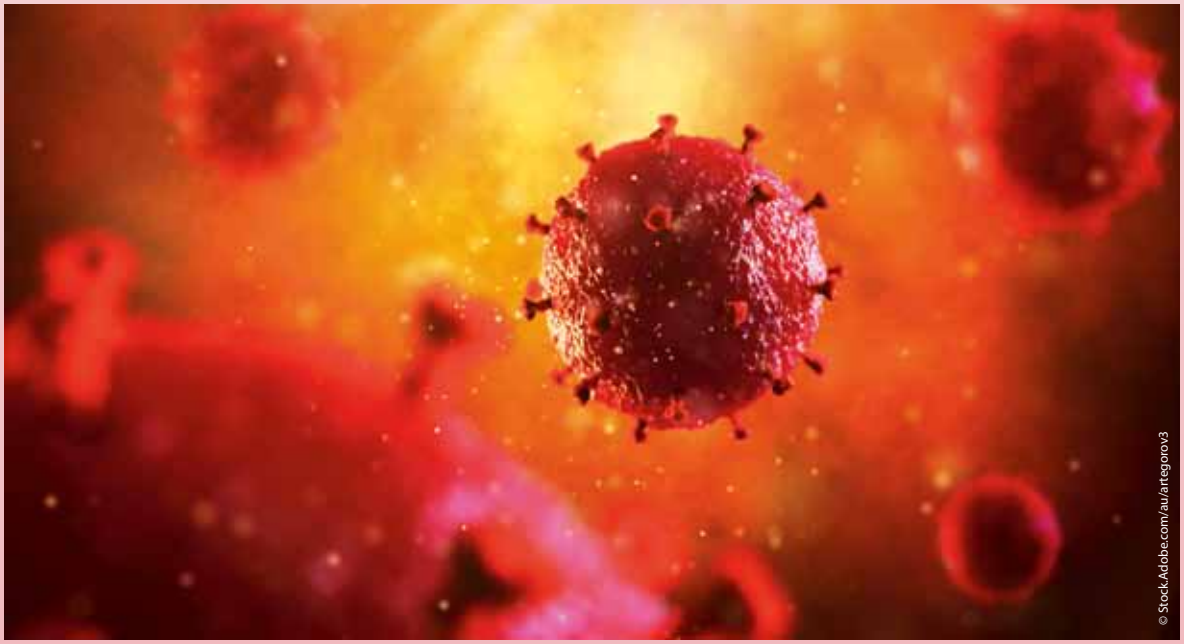
To determine whether an unusual virus is in fact a new HIV subtype, three cases must be discovered independently. The first two samples of this subtype were discovered in DRC in the 1980s and the 1990s. The third, collected in 2001, was difficult to sequence at that time because of the amount of virus in the sample and the existing technology.

Today, next-generation sequencing technology allows researchers to build an entire genome at higher speeds and lower costs. In order to utilise this technology, Abbott scientists had to develop and apply new techniques to help narrow in on the virus portion of the sample to fully sequence and complete the genome.

"Identifying new viruses such as this one is like searching for a needle in a haystack," said Mary Rodgers, a principal scientist and head of the Global Viral Surveillance Program, Diagnostics, Abbott, and one of the authors of the latest study. "By advancing our techniques and using next-generation sequencing technology, we are pulling the needle out with a magnet. This scientific discovery can help us ensure we are stopping new pandemics in their tracks."

"In an increasingly connected world, we can no longer think of viruses being contained to one location," said Professor Carole McArthur from the University of Missouri-Kansas City, one of the authors on the new study. "This discovery reminds us that to end the HIV pandemic, we must continue to out-think this continuously changing virus and use the latest advancements in technology and resources to monitor its evolution."

Abbott Australasia Pty Ltd
www.AbbottLabs.com.au



Nanomedicine development

Conventional nanoparticle manufacturing methods can be sensitive to reaction conditions, difficult to reproduce, labour intensive and challenging to scale. NanoAssemblr Ignite solves these significant issues and allows scientists to create transformative medicines at the bench scale. It paves the way for new nanomedicine-based gene and cell therapies, as well as small molecule- and protein-based drugs to treat cancer, rare disease and infectious disease.

NanoAssemblr Ignite is designed to make preclinical laboratory-scale nanoparticle production efficient, reproducible and tuneable. Validated by over 100 peer-reviewed publications, the system is fast, simple and intuitive to operate. Nanomedicines are prepared in less than a minute, allowing rapid optimisation of particle properties.

NanoAssemblr technology takes advantage of the physics of fluids confined to channels about the width of a human hair and containing specially engineered microscopic features that control the conditions of nanoparticle formation. By controlling fluid flow in the microchannels, users can reproducibly control particle properties and manufacture high-quality drug products through a single mixer across scales.

NanoAssemblr Ignite enables rapid benchtop-scale development of nanoparticle-based RNA, DNA, CRISPR, small molecule and protein therapeutics. Optimised drug products are predictably scaled to advanced preclinical and clinical scale with the NxGen technology on the NanoAssemblr Blaze and GMP Systems.

ATA Scientific Pty Ltd
www.atascientific.com.au

High-content imaging systems

The ImageXpress Micro Confocal High-Content Imaging System, from Molecular Devices, is a scalable, high-performance, high-content screening solution that is designed to allow users to capture more data at greater depths for 3D and thick tissue samples. The imaging system can include customised software and hardware, as well as integration of other lab components such as incubators, liquid handlers and robotics for a fully automated work-cell.

Users can scale up automation in order to increase throughput, eliminate human errors, maintain sterility and achieve consistent sample handling. Components can be added in modules and are upgradeable.

Customised optics and light sources can be used to improve image quality, system sensitivity and the ability to image at depth using water immersion objectives. Speed and image quality can be improved with multiple laser upgrade options.

Offering real-time dose response, an automatic pipettor enables compound addition while simultaneously live streaming at >100 fps.

With turnkey high-throughput long-term kinetics, users can schedule and image multiple plates over long periods of time while keeping consistent temperature, O_2 (hypoxia), CO_2 and humidity conditions. Live cell walk-away capacity can be expanded to 200+ plates; add media exchange for a turnkey high-throughput organoid screening solution.

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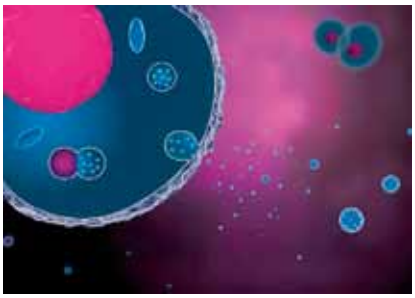
www.bio-strategy.com



Exosome miRNA qPCR arrays

GeneCopoeia's miProfile exosome miRNA qPCR arrays profile the expression of exosome-related miRNAs, which are carefully chosen for their close exosome correlation based on a thorough literature search of peer-reviewed publications. Arrays are available for expression profiling of specific types of exosome-related miRNAs or overall exosome-related miRNAs.

Exosomes have important roles in the spread of protein, mRNA, miRNA and DNA, and they are the contributing factors in the development of several diseases. Exosomes essentially deliver many of their functions as an intercellular shuttle with a cargo of proteins and RNAs for the target cell regulation. The miProfile exosome arrays allow researchers to profile the differential expression of miRNAs in exosomes from different samples (urine, blood or milk) and various cancers to gain understanding of the role of miRNA in the intercommunication occurring between different cells.

Exosomal miRNAs in the tumour microenvironment may impact tumour proliferation, vascularisation, metastasis and other biological characteristics. Exosomal miRNAs are likely to be applied as promising non-invasive biomarkers and potential targetable factors in cancer diagnosis and treatment.

The arrays are sensitive, with the ability to detect miRNA from as little as 10 pg of small RNA or 20 pg of total RNA. They are also specific enough to distinguish miRNAs with single nucleotide mismatches; each primer set has been experimentally validated for specific amplification.

Featuring broad linearity, the arrays allow miRNA at variable expression levels to be detected simultaneously and offer high reproducibility (R2>0.99) for inter-array and intra-array replicates. Each miRNA primer is designed using a proprietary algorithm and experimentally validated.

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

Foetal bovine serum

Bovogen Biologicals' foetal bovine serum (NZ origin) is manufactured in a fully validated sterile filtration facility, following strict GMP process, and is fully traceable. The FBS manufacturing process follows a strict quality controlled protocol.

All batches of FBS are triple 0.1 μm sterile filtered in a validated aseptic sterile filtration suite using a fully disposable closed loop filtration train. The closed-loop filtration system is fully disposable to ensure that all product contact parts are only used once, minimising any risk of contamination or human error.

The company's latest product release is the Bovogen Ultra Low IgG FBS. Using a proprietary chromatographic process, IgG has been removed from the FBS with the ultimate goal of retaining the serum's cellular viability and biological growth promoting activity. The IgG level in the UL IgG FBs is <0.5 ug/mL. Specific applications include monoclonal antibody research and production or where extremely low levels of IgG are required for cell culture and protein purification applications.

The product is manufactured by Bovogen Biologicals in 100 and 500 mL bottles, and distributed exclusively in Australia by Scientifix and Scientific Partners (WA).

Scientifix Pty Ltd
www.scientifix.com.au

ADC production services

Merck has introduced its ADC Express services for the rapid production of ADCs, designed to reduce the time needed to produce development-grade constructs for target molecule identification. Merck's established platform technology can efficiently turn an antibody, linker and payload into an ADC. The company offers a platform approach to ADC constructs and bioconjugation, which is said to result in increased flexibility and speed.

The company's ADC Express services include mini-prep scale (10–20 mg ADC construct ± column purification); medium-prep scale (~100 mg ADC ± column purification); and a certificate of testing with key quality attributes, including ADC concentration, payload density/DAR (drug antibody ratio) and monomer/aggregate content and free residual payload.

For companies that have a rich pipeline of monoclonal antibodies (mAbs) and want to enter the ADC space, Merck's services allow them to obtain ADCs without having to invest in potent handling capabilities. Companies can either bring their own linker technology or procure a linker payload from Merck.

Traditionally, several CDMOs across the globe were involved in the development and production of ADC programs. Merck's comprehensive ADC service portfolio combines the crucial steps of drug development and production — mAb solutions, linker, payload and the final conjugation — all from a single source.

Merck Pty Ltd
www.merckmillipore.com

Instrument bench

The LabBench 1278GCMS is a strong, durable and aesthetically pleasing scientific research instrument bench suitable for underpinning a gas chromatography mass spectrometry instrument.

The mobile instrument bench is used as an ergonomic instrument stand in the laboratory. Its handmade stainless steel construction with infill cabinetry has numerous practicalities designed to improve researchers' workspace.

Other features include: incorporated pump housing with antivibration, noise reduction and cooling features; power distribution with earth and overdraw protection; and storage and personal computer hardware options.

The 1278GCMS is only one product in the modular LabBench instrument bench range.

Lab Bench
www.labbench.com.au

Lauren Davis

Driving laboratory efficiency with LIMS

In an ever-changing world, how can researchers use modern technology to their advantage without compromising the scientific method? Speaking at the 2019 Australasian Laboratory Management Conference, held in Rosehill Gardens in November, Daren Cumberbatch* revealed how laboratory information management systems (LIMS) can be used to streamline scientific processes and drive operational efficiency.

Cumberbatch explained that we are in the midst of the Fourth Industrial Revolution — a digital age characterised by trends including cloud computing, the Internet of Things (IoT), big data, social media, mobility and autonomy. Many of these trends are willingly followed by young people, who according to Cumberbatch "don't understand the concept of waiting", because everything they need is on their smartphones — an attitude that is now starting to leak into the business world. But rather than chastising the younger generation for their impatience, Cumberbatch argued that this mindset could be valuable if taken into the lab, where tradition still reigns supreme — in many cases at the cost of efficiency.

Cumberbatch explained that scientists are currently undergoing a "reproducibility crisis" in which different research groups are unnecessarily producing the same data, either because they do not know of this data's prior existence or they cannot easily track it down — researchers thus need a more robust way of storing and sharing data with their peers. Data sharing is also essential for collaboration, Cumberbatch said, which is itself key to innovation — but collaboration and innovation take time, which a lot of scientists simply do not have at their disposal.

So how can scientists improve their operations to better enable sharing of data and free up time for collaboration and innovation? The answer, said Cumberbatch, is to assess your workflow and ask two key questions: "How can I automate any of these steps?" and "What's preventing me from doing this in real time?" Then, use whatever technology you have at your disposal to make your dreams of an automated workflow into a reality. Such technology is in many cases readily available, and may include the camera in a tablet, which Cumberbatch claims to work as well as any scanner; Wi-Fi, to prevent the need for physically connecting various laboratory instruments; and, of course, LIMS.

LIMS can be used for a wide variety of tasks, according to Cumberbatch — all of which are vital to smooth laboratory operations but some of which may be considered more mundane than others. For example, inventory management functions mean that a LIMS can monitor all equipment in the lab and reorder when stock is low, ensuring scientists are never caught short. The system can also automate quality assurance/quality control workflows, ensuring experiments are being carried out correctly.

The largest bottleneck in any experiment, said Cumberbatch, occurs right at the end — with the manual entry of the results, as every single piece of data is painstakingly typed out. This is where LIMS can speed things up significantly, importing all results automatically. Advanced analytics functions are meanwhile designed to make it easier for scientists to assess these results, and the system should be easily searchable, thus improving traceability.

According to Cumberbatch, the future will see businesses increasingly divided into the haves and have nots of advanced technologies — and when it comes to laboratory environments, that could mean a substantial difference in the amount of work that is carried out on a day-to-day basis. With LIMS now available to take care of all those tedious manual tasks that were until recently a necessary evil, scientists have an opportunity to spend their time and their energy on longer-term, larger-scale assignments that have the potential to truly make a difference to the world.

**Daren Cumberbatch is National Sales Manager ANZ, Digital Science, Thermo Fisher Scientific.*

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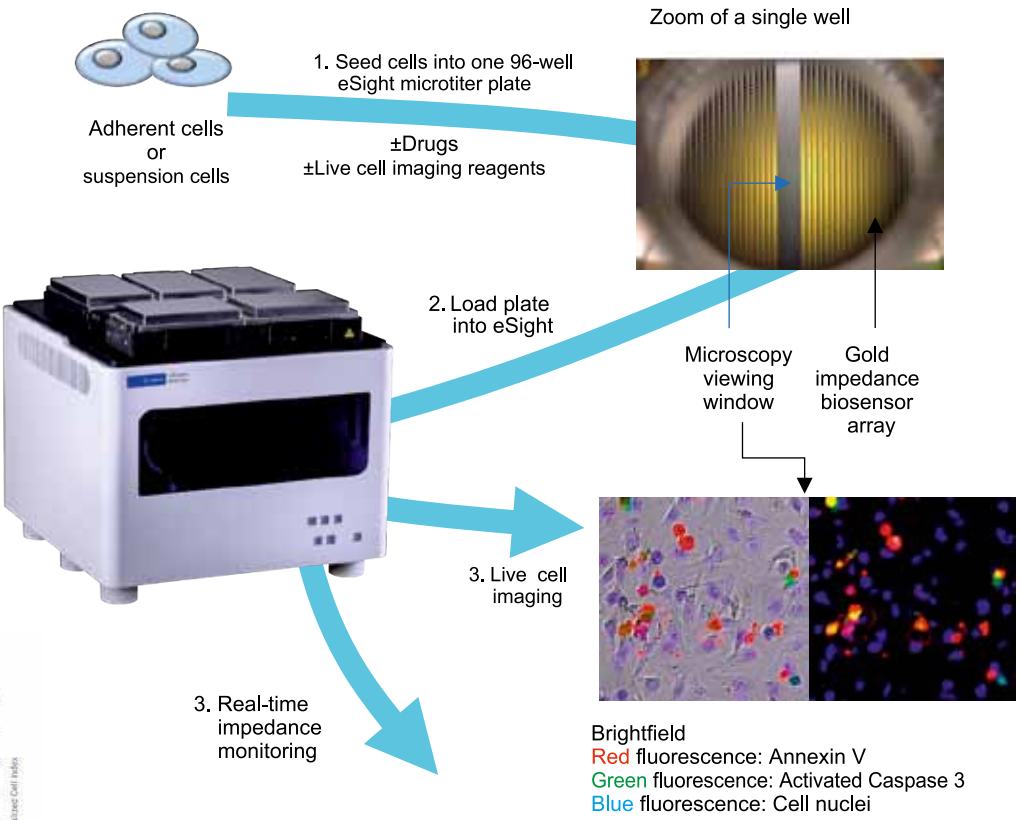
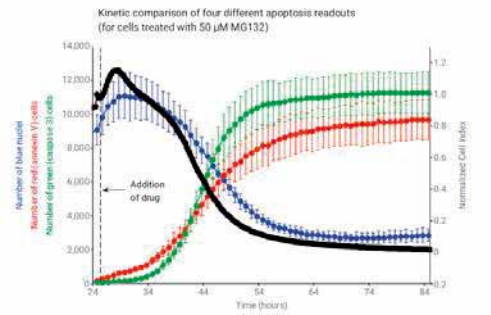
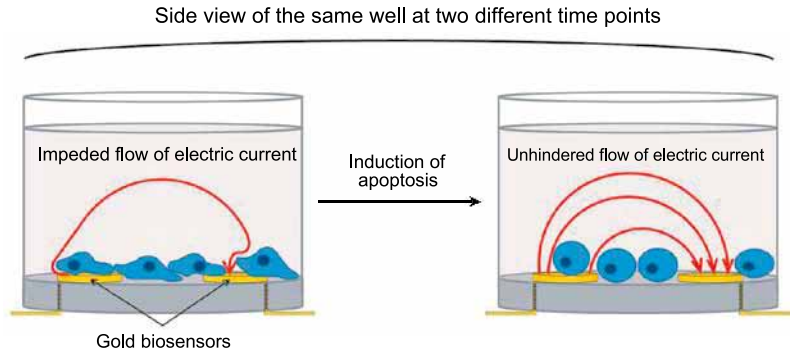




Overlay multiple real-time plots for impedance and imaging for the same sample.



Pre-apoptosis
- Large biosensor surface area covered by cells
- Strong interactions between cells and biosensors
- Large impedance of electric current

During apoptosis
- Small biosensor surface area covered by cells
- Weak interactions between cells and biosensors
- Small impedance of electric current

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Engineered knockout cell lysates

Abcam's engineered knockout cell lysates enable proteomic studies by providing researchers with 'true negative' controls.

Acquiring off-the-shelf knockout mouse models or cell lines that match specific experimental requirements can be challenging, and so the products often need to be sourced directly from individual researchers or labs. Abcam's latest collection addresses this issue by providing access to over 2800 diploid KO cell lysates.

The lysates are useful for studies requiring loss-of-function phenotypes at the proteomic level as well as routine applications such as Western blotting and mass spectroscopy. They also can be used to support antibody and target validation. The use of diploid cells makes the lysates well suited to the more complex studies often carried out in cancer research.

Derived from commonly used immortalised cell lines, KO lysates have been engineered using CRISPR-Cas9 and are accompanied by Sanger sequencing and Western blotting validation data. Corresponding wild-type controls are also provided so that the biological impact of each KO lysate can easily be assessed within a consistent cellular background.

Abcam offers access to thousands of CRISPR-Cas9-engineered KO cell lysates of interest, without needing to generate or purchase a KO cell line, saving on average 4–12 weeks' work in the lab. Diploid KO lysates are derived from commonly used cell lines including HeLa, HEK293T, A549, HCT116, Hep G2 and MCF. There is minimal preparation required.

Abcam Australia Pty Ltd
www.abcam.com

Hygiene monitoring and management system

The 3M Clean-Trace ATP-based Hygiene Monitoring and Management System features a Luminometer LM1 unit, ATP Tests and Hygiene Management Software. The reinvented system is designed to give users peace of mind, allowing them to quickly prepare for and pass audits.

The redesigned 3M Clean-Trace Luminometer is said to feature improved ease of use, faster time to result and simple, one-handed operation due to an easy-to-use user interface featuring intuitive navigate and screen menus. Its ergonomic design makes testing simple, minimising training time. It has a higher degree of repeatability and lower variability.

Robust hardware allows the Luminometer to stand up to harsh manufacturing environments and the capless design allows for easy access. Combined with the 3M Clean-Trace ATP Tests, its intuitive design makes it easy to use and implement with a long, flexible shape allowing users to swab difficult-to-reach areas. These sleek, portable swabs are easy to activate with one hand.

The Hygiene Management Software meanwhile simplifies and streamlines data to present it as information that helps users make educated decisions. For example, users can quickly pinpoint exactly where a sanitation problem has occurred and address it.

3M Food Safety
www.3m.com.au

Tissue clearing system

Conventional tissue imaging techniques require thin tissue sectioning; however, this process can be labour-intensive and is usually prone to errors. Recent advances in tissue clearing technology can now allow visualisation of cellular structures and neural networks inside of unsectioned whole tissues or even the entire body.

The X-CLARITY is an all-in-one system with ready-to-use reagents for simple, rapid and reproducible tissue clearing. The system has been developed to standardise, simplify and accelerate each step of the tissue clearing process, with a design that accelerates the removal of lipids from tissues in an efficient manner. Challenging samples such as bone, spinal cord and plants can be cleared using easy-to-follow workflows. A whole mouse brain takes just 6 h to clear.

With the CLARITY method, preserved tissues are embedded in a hydrogel matrix and lipids are actively extracted through electrophoresis to create a stable and optically transparent tissue-hydrogel hybrid that is chemically accessible for multiple rounds of antibody labelling and imaging. Native cytoarchitecture remains intact and even endogenous fluorescence proteins are preserved for robust fluorescence imaging downstream. Once cleared, tissues can be imaged using confocal, multiphoton or lightsheet microscopes.

Based on the work of the Deisseroth lab in Stanford, the X-CLARITY is suitable for leading research institutes and pharma globally.

ATA Scientific Pty Ltd
www.atascientific.com.au

Medtech community shares the secrets of commercialisation

Saving and improving lives by making it easier to develop medical devices with electronics and software is the mission of the newly launched NSW Active MedTech Community.

There is a perception that developing medical devices is hard — so hard that it scares off a lot of people with otherwise great ideas. Indeed, it is reported that 90% of innovations fail — a figure that is likely to be higher in the active medtech space, given that the regulatory requirements for medical devices involving electricity are more onerous than for inert products.

Of course there are always exceptions, and one device that is currently experiencing some success is MOSkin — a sensing technology for measuring the effective depth and intensity of radiation doses in real time during radiotherapy treatments. The technology was created by the Centre for Medical Radiation Physics at the University of Wollongong and is being commercialised by Electrogenics Laboratories, with the next stage of commercialisation being to develop a single-use, disposable sensing system customised for use during a variety of cancer treatments, as well as angiogram, diagnostic and interventional scans.

So what would it take to make technologies like MOSkin the rule rather than the exception, and to turn that 90% failure rate into a 90% success rate? That is a key question the NSW Active MedTech Community aims to address.

The community is the brainchild of Genesys Electronics Design and Circuitwise Electronics Manufacturing, contract developers of active medtech products. The two companies focus on the electronics and software aspects of a medtech device but work with a wide range of other service providers to help the client bring their product to life.

Genesys CEO Geoff Sizer and Circuitwise GM Serena Ross observed that a key challenge medtech entrepreneurs face is the number of steep learning curves in multiple disciplines required to develop a product. Indeed, Genesys has mapped up to 40 distinct skillsets required for successful commercialisation of medical devices, and claims that NSW has world-class service providers in every category of expertise required — including industrial design, regulatory strategy, quality systems, intellectual property, financing, software, electronics and more.

"An entrepreneur can hire expert service providers in all these areas, but they must still be an informed buyer," Ross said. "In addition, expert service providers can be very siloed, with little knowledge of the critical success factors underpinning the skillsets of other service providers. This puts the onus back on the entrepreneur to get a multitude of stars to align. Unfortunately, this can be too much to handle for inexperienced medtech developers."

In order to help reduce the learning curve for entrepreneurs, Sizer suggested running a series of thought leadership webinars from experts in each of the 40 skill areas identified in his company's medtech industry mapping exercise. These presentations, to be run by the NSW Active MedTech Community, will highlight the critical success factors required for successful medtech commercialisation.

"Efforts to date encouraging innovation in the medtech industry have largely focused on connecting 'industry' to our research institutions," Sizer said. "While research plays an important role in innovation, it is only one of the 40 categories we identified. We need to have a greater focus on the important role other service providers play in bringing innovation to life."

The first of the webinars, serving as an introduction to active medtech, will be held on 5 February 2020 and hosted at the community website — www.nswactivemedtech.com.au — with further webinars to follow. Membership of the community is free and open to all, not just those in NSW.

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Airborne chemicals can now be instantly identified

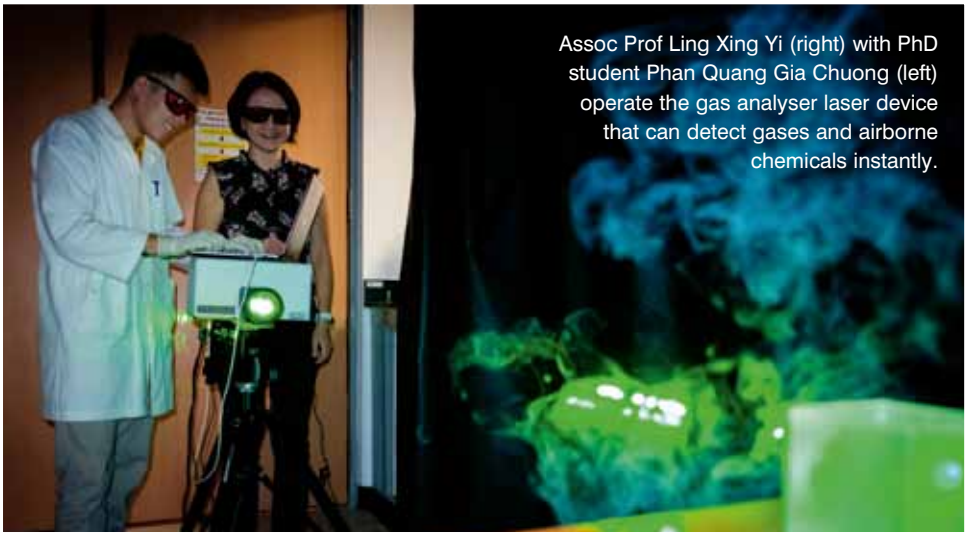
Scientists at Nanyang Technological University, Singapore (NTU Singapore) have developed a device that can identify a wide range of airborne gases and chemicals instantly.

Described in the journal *ACS Nano*, the prototype device is portable and suitable for rapid deployment by agencies to identify airborne hazards, such as from tiny gas molecules like sulfur dioxide. It can also identify larger compound molecules such as benzene, known to be harmful to human health. It could thus provide real-time monitoring of air quality such as during haze outbreaks, and assist in the detection of gas leaks and industrial air pollution.

Emergency scenarios require a fast and ongoing analysis of potential air contamination, such as following a natural disaster, chemical spill or illegal dumping of toxic waste, so that emergency responders can take appropriate action. Current methods of identifying gases in the air use a laboratory technique called gas chromatography–mass spectrometry (GC-MS), which is reliable but requires tedious sample collection and takes between a few hours and a few days to obtain results.

By contrast, the new device utilises Raman spectroscopy — a long-established technique for identifying chemical substances. Typically, this has been used only on solid and liquid samples, since gaseous chemicals are too diluted for the laser and detector to pick up.

To overcome this limitation, Associate Professor Ling Xing Yi and PhD student Phan Quang Gia Chuong developed a special nanostructure patch made from a highly porous synthetic material known as a metal-organic framework, which actively absorbs and traps molecules from the air into a 'cage'. The nanostructure also contains metal nanoparticles, which boost the intensity of the light surrounding the molecules.



Assoc Prof Ling Xing Yi (right) with PhD student Phan Quang Gia Chuong (left) operate the gas analyser laser device that can detect gases and airborne chemicals instantly.

Image credit: NTU Singapore.

The whole process takes about 10 seconds to complete and the laser has an energy intensity of 50 mW — more than seven times weaker than in other applications of Raman spectroscopy — making the system safer to operate

The result is a million-fold enhancement in the Raman spectroscopy signals, allowing for the identification of the trapped molecules. When a laser is shone on the patch from a few metres away, the light interacts with the gas molecules, causing light of a lower energy to be emitted. When analysed, this gives a spectroscopic readout in the format of a graph chart, which acts like a 'chemical fingerprint' corresponding to various chemicals present on the patch.

These chemical fingerprints are referenced against a digital library of fingerprints to quickly determine what chemicals have been detected. The whole process takes about 10 seconds to complete and the laser has an energy intensity of 50 mW — more than seven times weaker than in other applications of Raman spectroscopy — making the system safer to operate and more energy efficient.

Assoc Prof Ling said the genesis of the invention was sparked by an incident in Singapore, where there were reports of a strong gas-like odour over certain parts of the island in 2017. The cause was only determined a few days later, and was traced to volatile organic compounds released by factories outside of Singapore.

Together with her husband, Dr Phang In-Yee, a project leader and scientist at the Institute of Materials Research and Engineering (IMRE), they conceptualised the idea of identifying gases instantly from a distance.

"Our device can work remotely, so the operation of the laser camera and analysis of chemicals can be done safely at a distance," said Assoc Prof Ling. "This is especially useful when it is not known if the gases are hazardous to human health."

The laser was tested in experiments to work up to 10 metres away and can be engineered to reach further distances. Another possible method is to use the chip to capture gases, which is subsequently analysed with a laser.

In experiments, the team showed that the device can identify airborne molecules such as polyaromatic hydrocarbons (PAH), including naphthalene and derivatives of benzene — a family of colourless industrial air pollutants known to be highly carcinogenic. It can detect PAHs at parts-per-billion (ppb) concentrations in the atmosphere as well as performing continuous monitoring of the concentration of the different types of gases like carbon dioxide (CO_2) in the atmosphere, which could be a useful application in many industrial settings.

The team has filed for a patent and is now commercialising the technology for use in pollution monitoring, chemical disaster response, as well as other industrial applications.

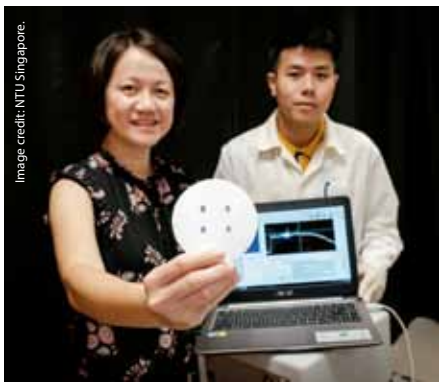


Image credit: NTU Singapore.

Assoc Prof Ling Xing Yi (left) and PhD student Phan Quang Gia Chuong (right) hold their specially designed chip that can trap gas molecules.

Mycoplasma PCR detection kit

One of the major issues in mammalian cell culture is infection due to mycoplasma contamination. It affects various cellular behaviours including metabolism, growth, viability and morphology, compromising the validity of experimental results and study data.

Up to 30–85% of cell cultures may be contaminated by mycoplasma species, so testing for mycoplasma is an essential quality control step in order to ensure correct and reproducible results. Agar cultures and DNA fluorochrome staining methods can be used for mycoplasma detection, but these methods are time-consuming (~28 days), inconsistent and difficult to interpret.

PCR-based methods have become an accepted standard protocol for mycoplasma detection to replace direct culture methods, including European Pharmacopoeia 2.6.7 and USP 63.

The Myco-Sniff-Valid Mycoplasma PCR Detection Kit has been demonstrated to be a sensitive, specific and rapid method for the detection of mycoplasma contamination in cell cultures. Using a set of primers specific for the highly conserved mycoplasma 16S-rRNA coding region including *M. pneumoniae*, *M. arginini*, *M. hyorhinis*, *M. fermentans*, *M. orale* and *A. laidlawii*, the kit is specifically designed to detect the presence of mycoplasma that might contaminate cultured cells.

The detection can be performed within 3 h with a sensitivity as low as 10 CFU/mL. An exogenous internal control is provided to control for PCR inhibition.

A positive control verifies the effectiveness of template DNA and confirms the size of PCR products for positive samples and 8-Methoxypsoralen (8-MOP) prevents cross-contamination from previous PCR products. Each kit contains 48 PCR lyophilised tubes for 20 µL reactions.

MP Biomedicals Australasia P/L
www.mpbio.com

ULT freezers

The Equitec range of ULT freezers, made in Europe, is now available in Australia.

Equitec freezers feature an innovative dual-independent compressor system (not cascade), designed to provide greater reliability. Graphic touch-screen controllers, event logging, remote alarm connections, 48 h battery backup, USB and MODBUS, vacuum release and access ports are all standard.

400, 500 and 700 L models are available in the upright configuration, as well as 90 and 110 L under-bench models and a complete range of chest configurations. Efficient high-density thin-panel insulation ensures high capacity/footprint ratios, low power consumption and good internal temperature homogeneity.

The sophisticated controller features a full suite of acoustic and visual alarms, an 88 mm touch screen with graphic display, automatic non-deletable data logging and a nickel-cadmium battery providing 48 h backup. A three-level interface (user, supervisor and service) protected via reprogrammable passwords provides good security.

The low-noise dual-independent compressors use biodegradable CFC- and HCFC-free refrigerant gases. Additional access ports and potential-free outputs are available as options, as are electronic door locks, chart recorders, additional shelves and internal doors, CO_2 and LN_2 backups.

Capella Science also supplies a full range of sliding and side-loading stainless steel racks, plastic and cardboard cryoboxes and SlimTube cryovials, which maximise storage capacity (100 per box) without the use of internal threads.

Capella Science
www.capellascience.com.au

Filter integrity tester

Sartorius Stedim Biotech's Sartocheck 5 Plus filter integrity tester is designed for use in downstream processing in the pharmaceutical industry. Based on users' needs to confirm the integrity of filters in pharmaceutical production, the product features functions for ensuring maximum data integrity and compliance with future requirements of quality risk management.

The tester is designed to improve the detectability of operator errors, improper test set-ups and out-of-tolerance environmental conditions. It is also easier to use than the company's previous models, meaning false passed and false failed test results should be relegated to the past.

Where other devices are limited in their flow measurement capability, the filter tester has been designed to cover the complete range of integrity testing from small syringe filters up to large multi-round housings and crossflow cassettes, with diffusion rates of up to thousands of millilitres per minute. In addition, the automatic test time feature for diffusion and water intrusion, along with accelerated bubble point testing, reduces overall test time. Parallel bubble point testing also saves time, enabling up to 10 small filters to be checked with the device.

User benefits include a large (12″), bright screen, an ergonomic interface, an easy-to-clean design, data integrity and inherent virus protection. The product is ATEX/IECEx/FM compliant, protecting operators by allowing safe integrity testing of alcohol-wetted filters. To prevent cross-contamination, the device can be used together with an accessory kit for external venting.

The product comes with comprehensive quality risk management documentation, including FMEA (Failure Mode and Effects Analysis). Qualification protocols are available and operational qualification can be performed by SSB's Service team for peace of mind. The company also provides onsite annual or biannual calibration along with preventive maintenance.

Purchase of the device includes a pre-established roadmap of software upgrades that come with comprehensive risk assessments. Add-on features do not require requalification. Software upgrades include features for high data integrity, QRM, HSE and usability throughout the entire life cycle of the product.

Sartorius Australia Pty Ltd
www.sartorius.com

Disposable autoinjector

The BD Intevia 1 mL disposable autoinjector is a robust platform device combining autoinjector and pre-fillable syringe in one integrated system. It is designed to effectively and safely inject a variety of drugs of different viscosities up to 35 cP and different fill volumes up to 1 mL.

The device's rigorous, patient-friendly design and control point feature enable simple two-step, push-on-skin activation allowing injection control by the patient. It is equipped with feedback indicators that visually show patients when the correct dose has been delivered and simultaneously triggers an audible click. These two considerations may enable patient treatment adherence.

The product's design enables the pharmaceutical industry to adopt it for a variety of drugs without customising the system components. Optimising combination products can help avoid problems related to poorly integrated systems — such as breakage and incompatibility — that can occur when components are purchased from multiple suppliers. This in turn can support cost efficiency and improve time to market, according to the company.

BD AUSTRALIA (Becton Dickinson)
www.bd.com

Spark-free laboratory refrigerator

The 554-litre Spark-free Laboratory Refrigerator (LKexv 5400) is a fitting choice for an intrinsically safe laboratory. The refrigerator has been manufactured to ensure the interior room is free of ignition sources and is ATEX 2014/34/EU rated II 3/-G IIB+H2 T6, making it suitable for storing flammables in partially open containers.

The 554-litre Spark-free Laboratory Refrigerator is factory set to +5°C and designed for optimal temperature stability and consistency according to EN 60068-3. Temperature can be adjusted between 0 and 'max' (+15°C) by users using the mechanical dial, with the set temperature visible on the external digital display for user convenience.

The commercial-grade polystyrol inner liner is easy to clean, and the moulded tray slides prevent the height-adjustable glass shelves from being a tipping hazard. Water from the automatic defrost cycle is collected and contained in a sealed defrost tray for laboratory safety, and a physical lock on the exterior of the refrigerator protects stored contents from unauthorised access.

The product is a large-volume fridge suitable for most laboratory conditions.

Andi-Co Australia
liebherrprofessional.com.au

Threefold approach to improving anticancer drug

Biomedical engineers at Duke University have developed a method to address failures in a promising anticancer drug, bringing together tools from genome engineering, protein engineering and biomaterials science to improve the efficacy, accuracy and longevity of certain cancer therapies. Their research has been published in the journal *Science Advances*.

More than 20 years ago, researchers discovered that the protein drug TRAIL, short for TNF-related apoptosis-inducing ligand, could effectively kill cancer cells without harming healthy cells — at least, in the lab. TRAIL works by binding to specific protein receptors on cancer cells, called death receptors, sending a signal that causes the cells to self-destruct. Although initial experiments showed the drug worked in a variety of cancer cell lines, including melanoma, lymphoma, pancreatic, prostate, lung, colon and breast cancer, TRAIL and similar drugs surprised researchers by showing limited success in clinical trials.

After more study, scientists pinpointed three reasons why the promising drug failed: TRAIL wasn't potent enough, the drug was being cleared from the body too quickly and some cancer cells were resistant to the therapy. Now, using a combination of three tools — a highly potent protein drug, a 'depot' that allows for sustained release of the drug and CRISPR/Cas9-based gene editing to pinpoint the cause of resistance to the drug — the Duke team has demonstrated how they could provide a solution to these problems and give protein-based anticancer 'biologics' like TRAIL that failed in the clinic a second chance.

"The real significance of this research for me is the true cross-disciplinary nature of it," said first author Mandana Manzari, now a postdoctoral researcher at the Memorial Sloan Kettering Cancer Center. "This is really the first example I've seen where we're bringing in pharmacology, drug delivery and genomics to pinpoint the exact circumstances that cause a biologic to fail and then develop solutions."

The first step of the process involved addressing TRAIL's limited potency. Typically, cells have multiple death receptors, but a specific receptor called death receptor 5 (DR5) is more prevalent in certain cancer cells. TRAIL, a three-part protein, binds to DR5 and

links three death receptors together, sending a signal for cells to self-destruct. TRAIL can also bind to other death receptors and 'decoy' receptors on normal cells. A more potent drug would be specific for a given death receptor, like DR5 that is present on cancer cells, and link together larger numbers of the receptor on a cell surface to send a stronger death signal to the cancer cell.

Manzari produced a highly potent, six-part death receptor agonist (DRA) that could bind six death receptors together and induce a much stronger self-destruct signal.

Next, the team examined how to prevent the super-potent death receptor agonist from being cleared from the body too quickly. They genetically fused the DRA to a temperature-responsive protein called elastin-like polypeptide (ELP), which forms a gel-like depot within a room-temperature solution. After the solution is injected under the skin, it dissolves, releasing the DRA over a longer period of time.

Finally, Manzari and Duke Biomedical Engineering Chair Ashutosh Chilkoti partnered with Kris Wood, an assistant professor of pharmacology and cancer biology, to better understand what caused certain cells to resist death by TRAIL or death receptor agonist (DRA). The team systematically disabled various genes in the cancer cells using CRISPR/Cas9 until they could deduce which were responsible for TRAIL or DRA resistance. Then they selected drugs to target the proteins produced by those genes and paired them with the DRA slow-release depot.

> With their triple-whammy tool, the team was able to effectively overcome intrinsic resistance, repress tumour growth and extend survival in mice that were implanted with colorectal cancers from human patients

"When we figured out the genes that drive resistance, we were able to map them to commercially available drugs that could specifically target the proteins that come from those genes," Manzari said. "It basically gave us a platform to figure out what drugs we can combine with the DRA in cases where this drug or other protein drugs don't work well to nip that resistance in the bud."

With their triple-whammy tool, the team was able to effectively overcome intrinsic resistance, repress tumour growth and extend survival in mice that were implanted with colorectal cancers from human patients that are highly resistant to treatment with TRAIL. Now the researchers are considering how they could apply this method to other protein and small-molecule drugs that face similar barriers that limit their effectiveness.

"I think the thing that really sets this approach apart is designing each piece of the platform rationally to address a specific problem and bringing them all together holistically to solve three critical problems that limit not just TRAIL, but many new cancer therapies," Chilkoti said.

Robotic liquid handling instrument

Tecan's Cavro Magni Flex OEM robotic liquid handling instrument is a modular and scalable development platform intended for low- to medium-throughput workflows, offering the flexibility and functionality to quickly and easily create innovative automation systems for life sciences applications, from immunoassay processing to molecular diagnostics.

The product provides the core robotic architecture for the development of complete automation solutions, with a configurable workdeck designed to accommodate a wide range of labware formats and devices to meet specific workflow requirements. A variety of carriers, cut-outs and custom grids are available to create any number of layouts, and the system is available with a choice of two, four or eight independent pipetting channels. The platform's liquid handling arm offers variable tip spacing capabilities, to suit different labware types and enable reformatting activities, and can act as both a pipettor and gripper, optimising use of the available space.

Featuring the robustness of the Tecan Cavro range of OEM liquid handling components, the device provides a comprehensive, modular liquid handling framework that allows seamless integration into any system. Supplied with Tecan's MAPlinx development software kit — which includes high-level functional commands for straightforward programming, a worktable editor with virtual library and drag-and-drop features, and a 3D simulator to simplify software testing — the product is designed to accelerate instrument development and time to market.

Tecan Australia

www.tecan.com.au

Ultrafast sCMOS camera

The Photometrics Kinetix back-illuminated sCMOS camera combines 95% quantum efficiency with a low 1.2 e- read noise to deliver a sensitive sCMOS camera at over 400 fps. The camera delivers ultrafast speed and a large field of view with balanced pixel size. This makes it suitable for use in fluorescence microscopy, high content imaging, biochip, microarray and genomic applications.

Taking advantage of an 8-bit readout mode, the camera delivers a full frame with a 29.4 mm diagonal field of view. The optimised line time allows the speed to outperform typical sCMOS devices, according to the company, delivering over 4000 MP/s — an almost 10-fold improvement.

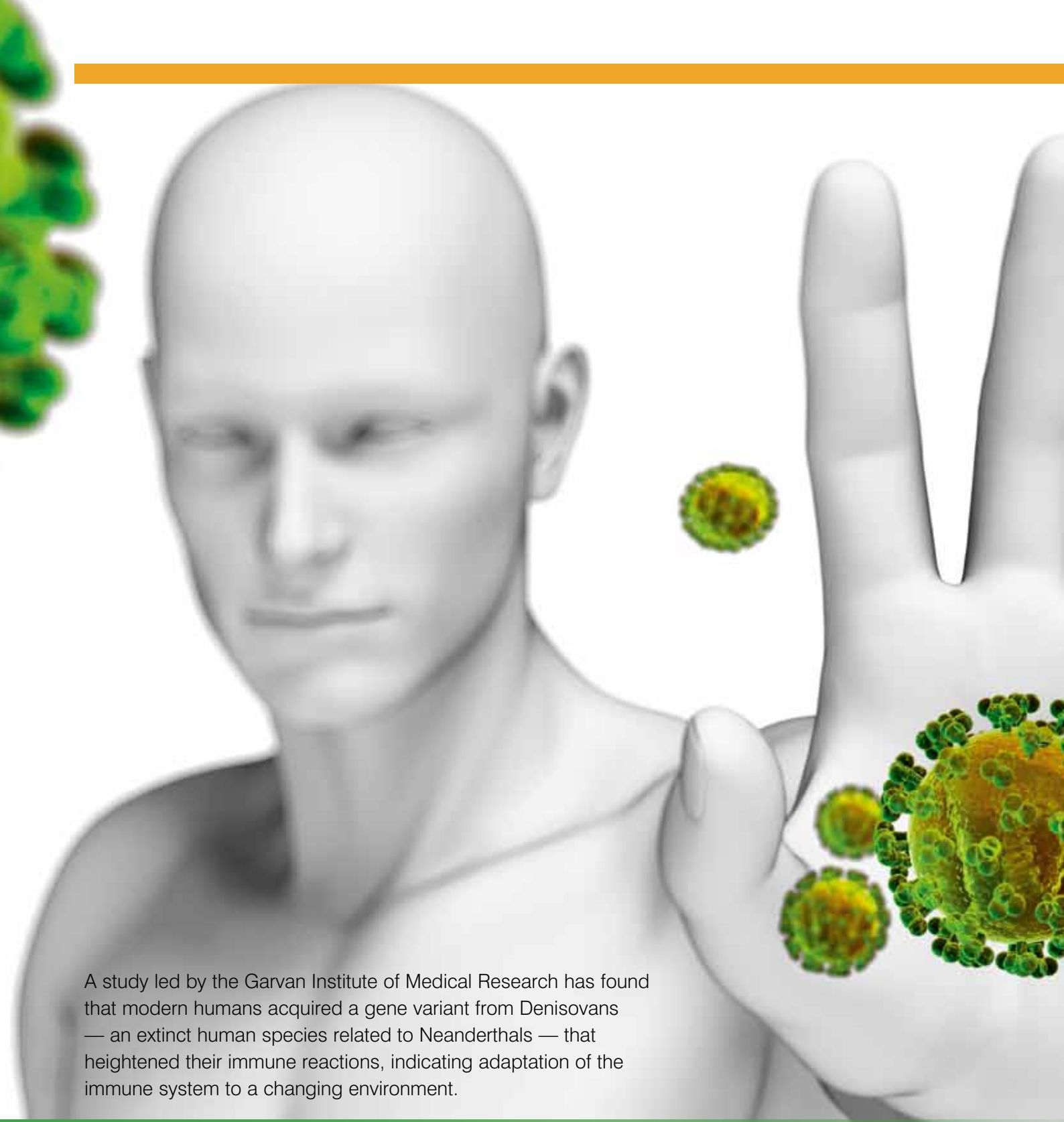
The camera features 6.5 x 6.5 μm pixels, the accepted standard for most live cell applications using 40x and 60x magnification. This pixel size provides detailed images across the imaging plane and is suitable for a broad range of microscope objectives.

The 29.4 mm^2 sensor of the Kinetix sCMOS camera is designed to increase throughput, maximise the amount of data captured in a single frame and take full advantage of larger field-of-view microscopes. At 29.4 mm diagonal, the Kinetix sensor has a 2.4x larger imaging area than typical sCMOS cameras, the company says, allowing the user to speed up data acquisition.

By bringing the light in from the back of the sensor, photons land directly onto the light-receiving surface, maximising light collecting capability.

The product features pattern noise reduction technology and correlated noise reduction technology to ensure that it delivers clean, pattern-free images with minimal pixel defects, delivering improved image quality in low light conditions.

SciTech Pty Ltd
www.scitech.com.au



A study led by the Garvan Institute of Medical Research has found that modern humans acquired a gene variant from Denisovans — an extinct human species related to Neanderthals — that heightened their immune reactions, indicating adaptation of the immune system to a changing environment.

Immunity boost provided by extinct human species

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Published in the journal *Nature Immunology*, the study is said to be the first to demonstrate a single DNA sequence variant from an extinct human species that changes the activity of the modern human immune system.

The Denisovans interbred with modern humans ~50,000 years ago, during the migrations of modern humans from Africa to what is now Papua New Guinea and Australia; indeed, up to 5% of the genome of people indigenous to Papua New Guinea is derived from Denisovans. The Garvan study reveals that modern humans acquired a gene variant from Denisovans that increases a range of immune reactions and inflammatory responses — including reactions that protect humans from disease-causing microbes.

"Previous research has found collections of gene variants from extinct human species that appear to have provided an advantage to humans living at high altitudes or to resist viruses, but have been unable to pinpoint which if any were actually functional," said co-senior author Associate Professor Shane Grey, who heads the Transplantation Immunology Lab at Garvan. "This study is the first to identify a single, functional variant, and suggests that it also had an evolutionary benefit on the human immune system."

Harmful versions of a gene called *TNFAIP3* have long been associated with the overactive immunity in autoimmune conditions, including inflammatory bowel diseases, arthritis, multiple sclerosis, lupus, psoriasis and type 1 diabetes. The *TNFAIP3* gene codes for a protein called A20 that helps 'cool' the immune system by reducing immune reactions to foreign molecules and microbes.

As part of a collaboration between Garvan, the Sydney Children's Hospital, Randwick, The Children's Hospital at Westmead and the Clinical Immunogenomics Research Consortium of Australasia (CIRCA), researchers analysed the genomes of families in which one child presented with a severe and unusual autoimmune or inflammatory condition.

"Four separate families had the same DNA variant in the *TNFAIP3* gene, changing one amino acid in the A20 protein from an isoleucine to a leucine (I207L)," said Professor Christopher Goodnow, Executive Director of the Garvan Institute and co-senior author of the study. "However, the presence of this variant in healthy family members indicated it was not sufficient to cause inflammatory disease on its own."

The researchers extracted immune cells from the families' blood samples and found that, in cell culture, they produced a stronger inflammatory response than the immune cells of other individuals.

Using datasets made available through the Simons Genome Diversity Project, the Indonesian Genome Diversity Project, Massey University and the Telethon Kids Institute, which includes genome sequence data on hundreds of diverse human populations, co-first author and Flinders University senior researcher Dr Owen Siggs investigated the worldwide distribution of the *TNFAIP3* variant.

The I207L variant carried by the Sydney families was absent from most populations but common in indigenous populations east of the Wallace Line, a deep ocean trench passing between Bali and Lombok and separating Asian fauna to the west from Australian fauna to the east. The I207L variant was common in people throughout Oceania, including people with Indigenous Australian, Melanesian, Maori and Polynesian ancestry.

"The fact that this rare version of the gene was enriched in these populations, and displayed genetic signatures of positive selection, means it was almost certainly beneficial for human health," said Assoc Prof Grey.

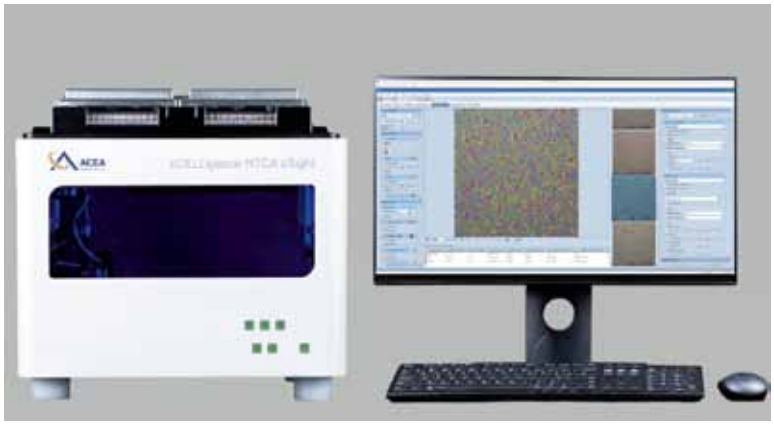
The team also discovered the I207L variant in the genome sequence of an extinct human species, extracted from a 50,000-year-old finger bone of a Denisovan girl, found inside the Denisova cave in the Altai Mountains of Siberia. The variant was present in two copies in the Denisovan girl but absent from Neanderthal remains from the same cave, indicating that the immunity-enhancing gene variant arose after the divergence of the Denisovan and Neanderthal lineages ~400,000 years ago.

To investigate the Denisovan gene variant's effects on the immune system, co-first author Dr Nathan Zammit replicated the I207L variant in a mouse model. He said, "When exposed to a pathogenic coxsackievirus strain — a virus which was originally isolated from a fatal case of human infant infection — mice with the Denisovan variant had stronger immune reactions and resisted the infection better than mice without the Denisovan gene."

According to Prof Goodnow, "Our study indicates that the Denisovan variant, and others like it, acts on a 'temperature control' dial in the immune system, turning up the temperature to change how we respond to different microbes."

Assoc Prof Grey added, "It was previously thought that A20, a gene that's central to the immune system, is binary — either it's switched on or off. We've found it in fact tunes us as individuals to optimal 'Goldilocks points' in between — where immune reactions are neither too hot nor too cold — and that blows the field wide open."

Real-time cell analysis



The xCELLigence RTCA eSight is a versatile system that combines the power of ACEA Biosciences' label-free xCELLigence Real Time Cell Analysis technology with the benefits of live cell imaging in three colours: red, green and blue.

Users can generate physiologically relevant data, easily monitoring cell health, strength of adhesion, changes in morphology, proliferation and cytolysis in primary cell cultures, or with standard tissue culture cell lines. The eSight provides insight into cellular mechanisms of action and functionality.

Offering informative live cell imaging, the eSight provides brightfield capabilities, the flexibility of three fluorescence channels, a plethora of well plate formats and the capability of user-defined schedules. Each cradle can be run and scheduled independently, which makes the system suitable for a multi-user environment.

The product works quickly, enabling the user to read a 96-well plate in ~15 s with xCELLigence biosensor technology. The user can then gain further insight into their studies with image-based measurements live, simultaneously and in real time.

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Living skin with blood vessels can now be 3D printed

Researchers at Rensselaer Polytechnic Institute have developed a way to 3D print living skin, complete with blood vessels. Published in the journal *Tissue Engineering Part A*, their work serves as a significant step towards creating grafts that are more like the skin our bodies produce naturally.

As explained by Associate Professor Pankaj Karande, a member of Rensselaer's Center for Biotechnology and Interdisciplinary Studies (CBIS), "Right now, whatever is available as a clinical product is more like a fancy Band-Aid. It provides some accelerated wound healing, but eventually it just falls off; it never really integrates with the host cells."

A significant barrier to that integration has been the absence of a functioning vascular system in the skin grafts. Assoc Prof Karande has been working on this challenge for several years, previously publishing one of the first papers showing that researchers could take two types of living human cells, make them into 'bio-inks' and print them into a skin-like structure. Since then, he and his team have been working with researchers from the Yale School of Medicine to incorporate vasculature.

The researchers have now found that if they add key elements — including human endothelial cells, which line the inside of blood vessels, and human pericyte cells, which wrap around the endothelial cells — with animal collagen and other structural cells typically found in a skin graft, the cells start communicating and forming a biologically relevant vascular structure within the span of a few weeks.

"As engineers working to recreate biology, we've always appreciated and been aware of the fact that biology is far more complex than the simple systems we make in the lab," Assoc Prof Karande said. "We were pleasantly surprised to find that, once we start approaching that complexity, biology takes over and starts getting closer and closer to what exists in nature."

Once the Yale team grafted it onto a special type of mouse, the vessels from the skin printed by the Rensselaer team began to communicate and connect with the mouse's own vessels. Assoc Prof Karande noted, "That's extremely important, because we know there is actually a transfer of blood and nutrients to the graft which is keeping the graft alive."

In order to make this usable at a clinical level, researchers need to be able to edit the donor cells using something like CRISPR technology, so that the vessels can integrate and be accepted by the patient's body. According to Assoc Prof Karande, "We are still not at that step, but we are one step closer."

Assoc Prof Karande said more work will need to be done to address the challenges associated with burn patients, which include the loss of nerve and vascular endings. But the grafts his team has created bring researchers closer to helping people with more discrete issues, like diabetic or pressure ulcers.

"For those patients, these would be perfect, because ulcers usually appear at distinct locations on the body and can be addressed with smaller pieces of skin," Assoc Prof Karande said. "Wound healing typically takes longer in diabetic patients, and this could also help to accelerate that process."

CBIS Director Deepak Vashishth concluded, "This significant development highlights the vast potential of 3D bioprinting in precision medicine, where solutions can be tailored to specific situations and eventually to individuals. "This is a perfect example of how engineers at Rensselaer are solving challenges related to human health."

Bioinformatics platform helps manage biospecimen library

The Auckland Region Tissue Bank (ARTB) is a critical component in New Zealand's medical research infrastructure. As a central facility for storing blood and tissue samples, the tissue bank has a library that could hold the secrets to unlocking cures for existing and future chronic diseases and illnesses. These samples could be made available to researchers from the University of Auckland as well as throughout New Zealand and to collaborators further afield.

Having a collection of samples for medical research is highly desirable, as it acts as a repository that researchers can access at any time. The ARTB currently houses around 125,000 samples, with the number having grown exponentially in the last four years. Without a facility like ARTB, collecting samples would be a tedious and onerous task that uses a lot of researcher time and slows medical research. However, having the samples is just one part of the equation. Being able to access the right samples with specific clinical parameters to isolate specific strains, genetic traits or tissue types is of equal importance.

"When the University of Auckland created the ARTB and acquired the existing library of samples from Middlemore Hospital Tissue Bank, there was a need to unify the bioinformatics system and we were looking for a robust and structured system able to manage our biobank in a constructive way," said Phillip Shepherd, Regional Tissue Bank Manager. "We chose OpenSpecimen as the system was able to be customised to our specific needs and the developers, Krishagni, were dedicated to biobanking and had a vast depth of experience that we could tap into."

Originally developed by Krishagni Solutions with funding from the National Cancer Institute (NCI) in the US to aggregate and manage biospecimen data, OpenSpecimen has continued to evolve into a comprehensive open-source bioinformatics platform. It is now used in over 65 biobanks around the world.

ARTB engaged with Krishagni right from the start of its journey. By being involved in ARTB's workflows and practices, Krishagni was more easily able to advise and customise OpenSpecimen to the tissue bank's requirements.

"The open source nature of OpenSpecimen allows us to make changes to the system by ourselves and not be locked into using the developer for every change that we need," Shepherd said. "Of course there are modifications that we get Krishagni involved with, and they are always very accommodating and responsive."

Alice Rykers, the ARTB's OpenSpecimen super user and Tissue Bank Technician, said, "I really enjoy using it and have been thoroughly impressed with how it works. It gives us excellent visibility and the query module is a Godsend with its ability to quickly generate reports and display data."

While the ARTB's collection of tissue samples is strategically focused on medical research areas such as blood cancers, cardiac, breast, sarcoma, melanoma and endometriosis, the organisation is always open to collaborating with other research groups where it can offer a service. This will no doubt see its valuable library continue to grow, increasing the relevance of ARTB — all with the knowledge that OpenSpecimen will be able to grow with it.

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*Proposal entries must be submitted by 30-Mar, 2020. Additional Terms and Conditions apply as per project proposal.

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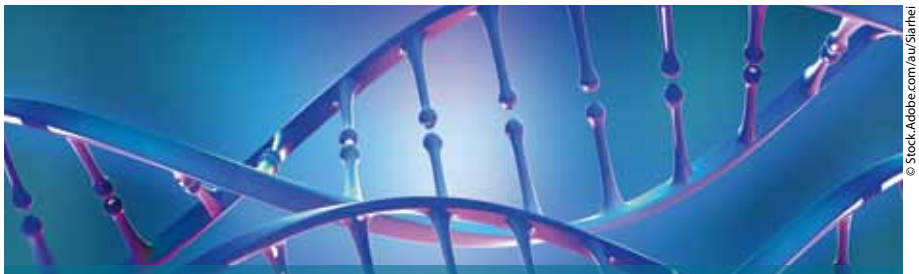

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The Human Genome Meeting has evolved from a small targeted meeting into an international scientific conference for genetic and genomic researchers; biotechnology and pharmaceutical companies; and established and young investigators. Its stimulating program of plenary lectures, symposia, workshops, poster presentations, lectures and social events covers a wide range of topics, from system biology and epigenomics to genomic technologies; from drug discovery to gene therapy, pharmogenomics and genomic medicine; and from computation genomics and bioinformatics to genetic and genomic databases. There will also be meetings specially catered for discussion on ethics, related impact on society and intellectual property.

http://hugo-hgm2020.org/

10th International Conference on Spontaneous Coherence in Excitonic Systems
January 28–31, Melbourne
http://www.fleet.org.au/icsce/

Advanced Materials World Congress
February 2–5, Sydney
https://www.advancedmaterialscongress.org/feb20/

25th Annual Lorne Proteomics Symposium
February 6–9, Lorne
https://www.australasianproteomics.org/

2020 World Congress on Oils and Fats & ISF Lectureship Series
February 9–12, Sydney
http://www.wcofsydney2020.com/index.php

45th Lorne Conference on Protein Structure and Function
February 9–13, Lorne
https://www.lorneproteins.org/

International Conference on Nanoscience and Nanotechnology
February 9–13, Brisbane
https://www.iconn2020.com/

AMOS 2020
February 10–14, Fremantle
http://amos-2020.w.amos.currinda.com/

32nd Lorne Cancer Conference
February 13–15, Lorne
https://www.lornecancer.org/

41st Annual Lorne Genome Conference 2020
February 16–18, Lorne
https://www.lornegenome.org/

26th Australian Conference on Microscopy and Microanalysis
February 16–20, Canberra
https://www.acmm26.org/welcome

Molecular Approaches to Malaria Conference 2020
February 23–27, Lorne
https://www.mam2020conference.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/

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/

AusMedtech 2020
May 20–21, Melbourne
https://www.ausmedtech.com.au/

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
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Head Office
Unit 7, 6-8 Byfield Street,
(Locked Bag 2226)
North Ryde BC NSW 1670,
AUSTRALIA
Ph: +61 2 9168 2500

Editor
Lauren Davis
LLS@wfmedia.com.au

Publishing Director/MD
Geoff Hird

Art Director/Production Manager
Julie Wright

Art/Production
Colleen Sam, Veronica King

Circulation
Dianna Alberry, Sue Lavery
circulation@wfmedia.com.au

Copy Control
Mitchie Mullins
copy@wfmedia.com.au

Advertising Sales

Sales Manager: Kerrie Robinson
Ph:0400 886 311
krobinson@wfmedia.com.au

Nikki Edwards
Ph: 0431 107 407
nedwards@wfmedia.com.au

Tim Thompson
Ph: 0421 623 958
tthompson@wfmedia.com.au

If you have any queries regarding our privacy policy please email privacy@wfmedia.com.au

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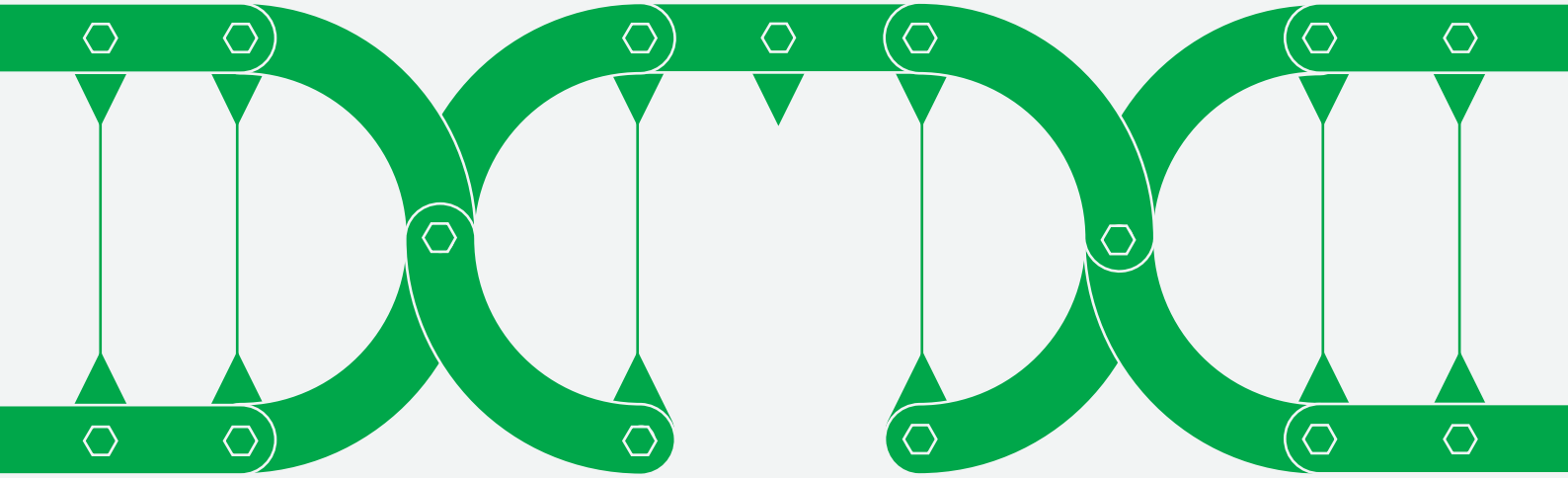

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