# Lab+Life SCIENTIST

**SOLVING THE**
GENETICS PUZZLE

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**FRANCES ARNOLD**
AT LORNE PROTEINS

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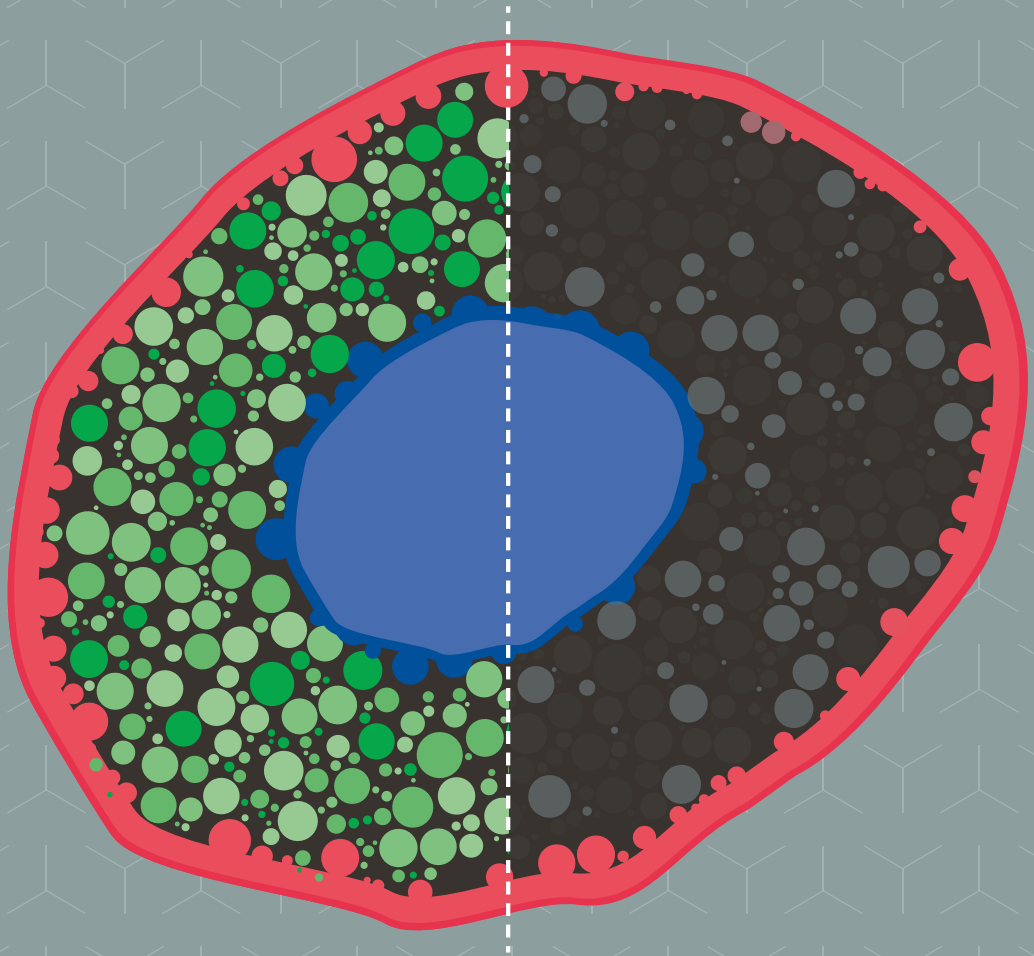

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1. Bradbury, A. and Plückthorn, A. 2015. Reproducibility: Standardize antibodies used in research. Nature. 518(7537), pp.27-29.

# Contents





## LORNE 2019






Welcome to *Lab+Life Scientist's* first issue for 2019. I hope you had a wonderful holiday period and start to the new year!

This much-awaited Lorne series of conferences — Lorne Proteomics; Lorne Protein Structure and Function; Lorne Cancer Conference; Lorne Infection and Immunity Conference; Lorne Genome Conference — will begin in a few weeks. This issue features some of the speakers presenting at the conferences. In the lead article, award-winning, Australian geneticist Melanie Bahlo — who is presenting at the 2019 Lorne Genome Conference (17–19 February) — provides insights on novel statistical techniques that are helping find genetic causes of diseases.

Professor Frances Arnold from the California Institute of Technology, a joint winner of the 2018 Nobel Prize for Chemistry, is one of the international speakers at the 44th Lorne Conference on Protein Structure and Function (10–14 February). She'll talk about protein engineering, key developments in the field and her contributions to the field. To read more on the topic, please visit page 30.

Another interesting speaker at the Lorne Proteins conference is Dr Leo James from the MRC Laboratory of Molecular Biology (LMB). Dr James and his team, along with scientists from the Max Planck Institute for Biophysical Chemistry, have recently developed a method called Trim-Away, which makes it possible to directly target almost any protein in any type of cell. At Lorne, Dr James will talk about TRIM21, a protein — discovered at his lab — that was key to the development of the new method.

In this issue, we also report on a number of other interesting projects and developments in Australia and overseas. For example, the article on page 22 features a lab-on-a-chip device that's improving blood handling, diagnostics as well as drug development. He recently received funding from the NHMRC for the project.

Stanford and SLAC National Accelerator Laboratory researchers are working on two potential treatments — one using X-rays, the other using protons — that aim to reduce the side effects of radiation therapy by vastly shrinking the length of a typical session. The idea behind both is to blast cancer cells so quickly that organs and other tissues don't have time to move during the exposure — much like taking a single freeze frame from a video. To read more on the treatments, please visit page 10.

If you're working on an interesting project, have launched a new product, would like to contribute an article or want to provide feedback, please send me an email at mgandhi@wfmedia.com.au.

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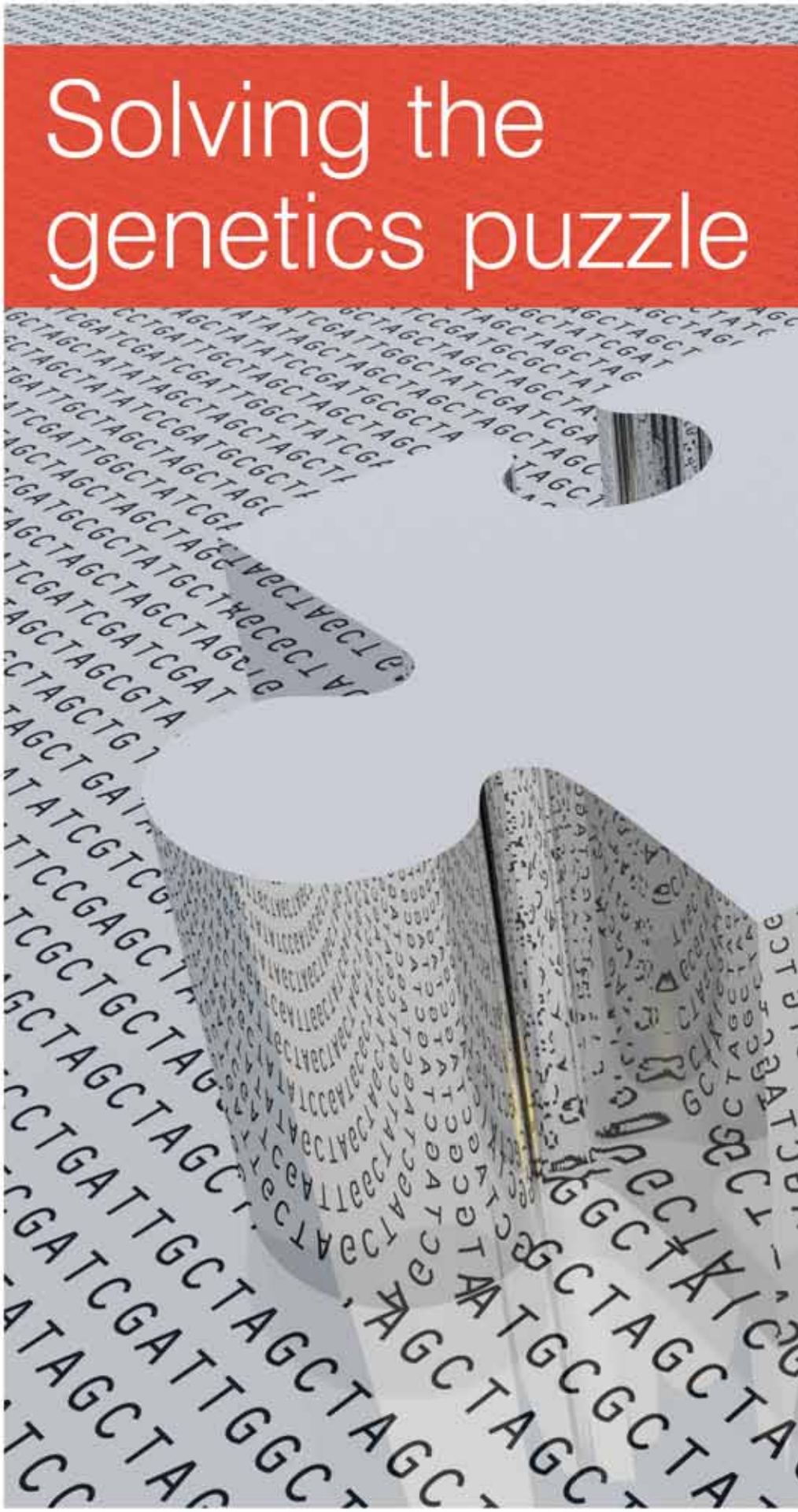
*Mansi Gandhi*

# Solving the genetics puzzle

Renowned Australian geneticist Melanie Bahlo* talks about how novel statistical methods are helping researchers uncover the causes for diseases that have previously proven intractable to analysis.



Melanie Bahlo's fascination with science and biology began to develop at a very young age. Growing up in Germany, she used to record the birds that came and visited her bird feeder in the depths of winter. She was around eight years old at the time and used to torture her friends with cryptic clues to find treasure in their natural surrounds and play elaborate games of hide and seek. The world of science has a lot of similarities. She has always loved solving puzzles and the field of statistical genetics allows her to do just that.

Bahlo's love for science and mathematics, passion, hard work and bioinformatics expertise have seen her make some great strides in identifying genetic causes of many neurological diseases.

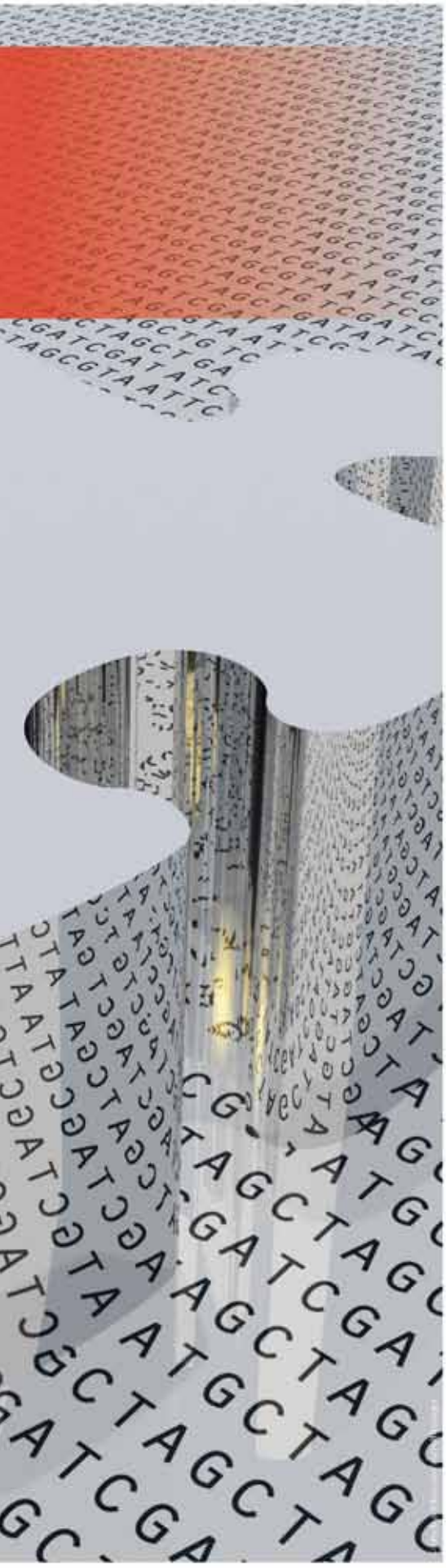
Currently the Co-Division Head of the Population Health and Immunity Division at WEHI (the Walter and Eliza Hall Institute of Medical Research), Bahlo's journey at the institute started in 1999, when she arrived as a junior postdoc. Within a short span of four years, she was already running a mini lab — with one postdoctoral student and some UROP students — in award-winning statistician and research scientist Professor Terence Paul 'Terry' Speed's lab. Bahlo officially became a laboratory head in 2007.

## Genetics and neurology

The Bahlo lab at WEHI inhabits a research space that spans statistical genetics, bioinformatics and population genomics.

"In terms of diseases our main focus are the neurological diseases, in particular epilepsy, ataxia and brain malformation disorders. But we also do a bit of work on infectious diseases, particularly malaria, and also increasingly more work on retinal disorders, which intersects nicely with our neurological disorders," said Bahlo.

The lab uses statistical methodology to describe and model genetic data, to make use of structure



Professor Melanie Bahlo is presenting at the upcoming Lorne Genome conference, where she will talk about her lab's work on MacTel.

within the data. "This allows the identification of genomic regions of interest that may harbour disease-causing mutations. We implement these models through software programming. We work on many disease identification projects simultaneously, some of which can be easily solved, others taking years before a breakthrough is achieved. We seek to identify where new technology can be combined with our genetic insights to achieve these breakthroughs in studies where we have been unsuccessful."

## Eureka moments

In a career spanning around two decades, Bahlo has had many Eureka moments. However, her favourite paper remains the discovery of the cause of action myoclonus–renal failure syndrome (AMRF), an autosomal-recessive disorder, in 2008. It was a joint project with Professor Samuel Berkovic, a long-time collaborator. Berkovic is an Australian neurologist and Laureate Professor in the Department of Medicine at the University of Melbourne, Director of the Epilepsy Research Centre at Austin Health and first author of the paper 'Array-Based Gene Discovery with Three Unrelated Subjects Shows SCARB2/LIMP-2 Deficiency Causes Myoclonus Epilepsy and Glomerulosclerosis', published in *The American Journal of Human Genetics* (2008). According to the Victorian Centre for Biostatistics, Bahlo's analyses "have led to the discovery of new genes involved in genetic diseases such as deafness and epilepsy. She has also developed new methods and software for the analysis of genetic data."

Commenting on the 2008 discovery, Bahlo said, "We used some smart analytical methods and then I had the insight to use two, at the time, very new technologies which identified the gene. My student presented this work at a conference in 2007 and I had a highly esteemed colleague tell us what we were doing was never going to work! This gene has turned out to be much more important than previously thought and has led to the genetic diagnosis of hundreds of patients. It was also another example of an early new epilepsy gene that did not encode an ion channel subunit."

Statistical genetics and bioinformatics research spans Bahlo's two favourite subjects at high school — biology and mathematics. "I still pinch myself, especially when things are tough, to appreciate that I am being paid to do work in these areas," she said.

## Retinal eye disorder

The Bahlo lab is currently at a very exciting stage with the retinal eye disorder macular telangiectasia type 2 (MacTel), she said. The researchers have some exciting datasets to analyse that should validate a number of new genetic loci and allow for further dissection of the genetic basis of this disease.

"We are continuing on our work on repeat expansions, and we are lucky to be involved in some exciting discovery projects as well as continuing to develop methods to detect repeat expansions both for known repeat expansions and trying to identify new ones as well.

"I am excited to start learning about proteomics and more metabolomics and of course keeping on learning about scRNAseq and applying it with investigators to our diseases of interest," she added.

Bahlo is presenting at the upcoming Lorne Genome conference, where she will talk about her lab's work on MacTel. Bahlo and her team published the first genome-wide association study in 2017. "This opened a Pandora's box for this really interesting eye disorder and allowed us to reinterpret metabolomics results, clinical trial results and two Mendelian disorders."

"We were able to apply many of the new exciting methods coming out of the GWAS field, such as Mendelian randomisation. This is work in collaboration with my PhD student Roberto Bonelli and a postdoc, Dr Brendan Ansell, [plus] Australian, UK and USA collaborators from the MacTel Consortium."

The team's findings established five key regions — or loci — in the genome most likely to influence a person's risk of developing MacTel. The finding will enable researchers to better understand the disease and look for ways to prevent or stop its progression.

The study, published in *Nature Genetics* in 2017, was an international collaboration led by Bahlo and Dr Thomas Scerri at WEHI. "We analysed more than six million genetic markers and identified five loci across the genome that had similar patterns in people with the disease, but not in the healthy individuals," Professor Bahlo said.

The 2017 analysis also revealed that people with the MacTel genetic risk loci identified in the study had changes in their metabolism, specifically in their glycine and serine levels. Professor Bahlo said

this meant there could be a significant relationship between the level of glycine and serine in the body, and onset of the disease.

## Bioinformatics, technology and precision medicine

Both SNP chips and next-generation sequencing have two exciting technology-related developments in the field, according to Bahlo. "What is equally amazing is that one can still extract further information from the data from these platforms and the enormous cohorts that have already been generated. An example is of course the repeat expansion detection methods that we and others have developed. I am confident that there is plenty more to find, which we can then pass onto our molecular biology colleagues to work on mechanisms and equally translate into clinical genomics pipelines to provide genetic diagnostics and predictions for patients."

Precision medicine is already possible for some diseases, but it will require substantial investment to make it transferrable to standard care, she said. "It is not clear how this can be accomplished in the current funding framework and the potential lack of workforce in bioinformatics. My lab has been fortunate enough to be involved in several cases where our findings have influenced clinical care. There are patient groups that are clearly missing out on applications of precision medicine because we lack good data. This includes Indigenous Australians. If we don't have the data, we can't detect variants and/or build population-specific predication models."

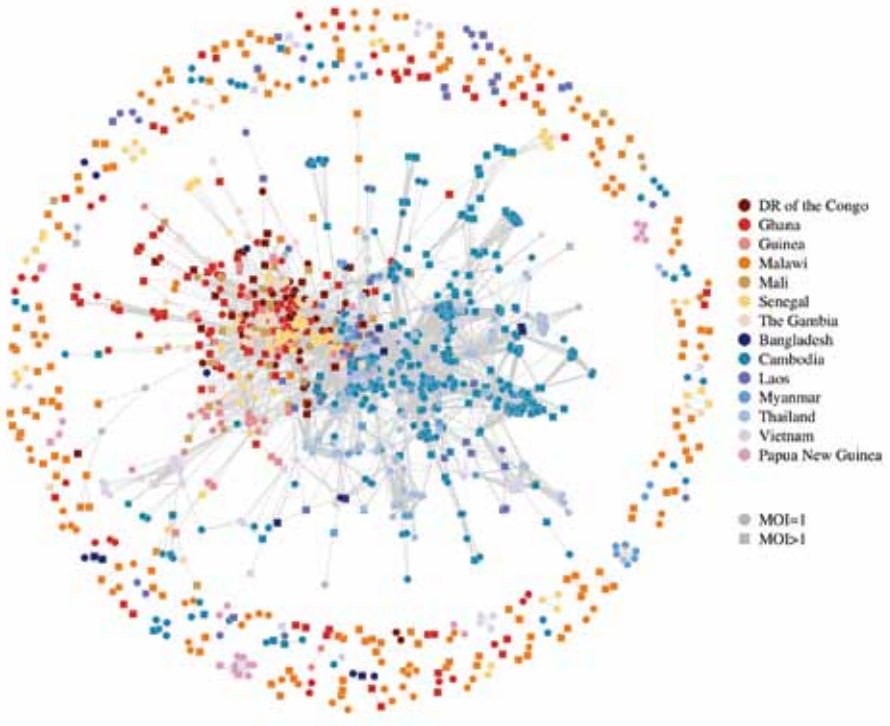
## Awards and accolades

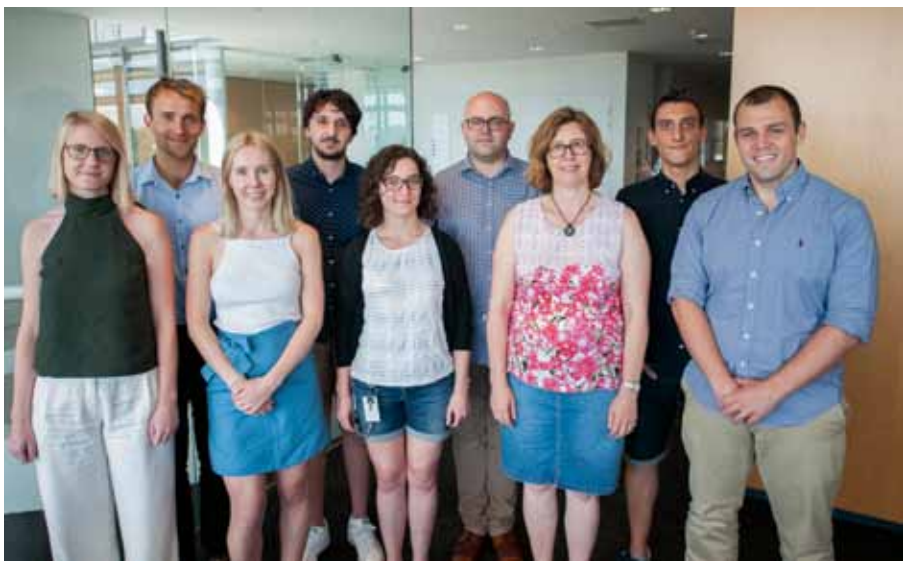
Bahlo has over 15 years' experience in the field of population genetics, genetics and bioinformatics and has contributed to discovering 22 genes involved in human disease.

In 2015, she received the Ross Crozier Medal from the Genetics Society of Australasia for her contributions to pinpointing faulty genes involved in human diseases. The medal commemorates evolutionary geneticist, past president and an avid lobbyist for the Genetics Society of Australasia, Ross Crozier. It recognises outstanding contributions to the field of genetics research by a mid-career Australasian researcher.

Bahlo's work has also contributed to the discovery of genes involved in mitochondrial diseases, leading to kidney failure, and identifying genetic variations that can alter the immune response to hepatitis C viruses, leading to a revolution in hepatitis C treatment, according to WEHI. Bahlo's work has also contributed to improved bioinformatics methods for the diagnostic screening for Down syndrome using cell-free DNA from the mother's blood. "We developed a method of tweaking the computational analysis to tune out unwanted noise that could hide signals that indicate chromosomal abnormalities," said Bahlo.

Bahlo enjoys using her bioinformatics and statistical background to solve real-world problems. "Our analysis of data produced by new genomic technologies is identifying genetic causes for diseases that have previously proven intractable to analysis," she said.



Professor Melanie Bahlo with her team at the Walter and Eliza Hall Institute of Medical Research.

**Professor Melanie Bahlo will be presenting at the Lorne Genome Conference, to be held from 17–19 February 2019 at Lorne,Victoria. Bahlo is an NHMRC Senior Research Fellow and the 'Healthy Ageing and Development' Theme Leader at the Walter and Eliza Hall Institute of Medical Research. She heads the statistical genetics laboratory focusing on the development of new methods to analyse complex genetic data. Bahlo's laboratory is highly collaborative, working closely with clinical researchers to understand the causes and mechanisms of genetic disorders. The software and analytical methods developed by Bahlo's team have led to the discovery of >20 novel genes. Bahlo also heads the bioinformatics analysis of the MacTel Consortium, an international consortium that is seeking to identify causes and treatment of MacTel, a rare but complex eye disorder.*

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# Cannabis compound may benefit children with epilepsy

Researchers reviewing studies around the medical use of cannabidiol — a non-psychoactive compound in cannabis — have found the treatment to be moderately effective in two forms of childhood epilepsy.

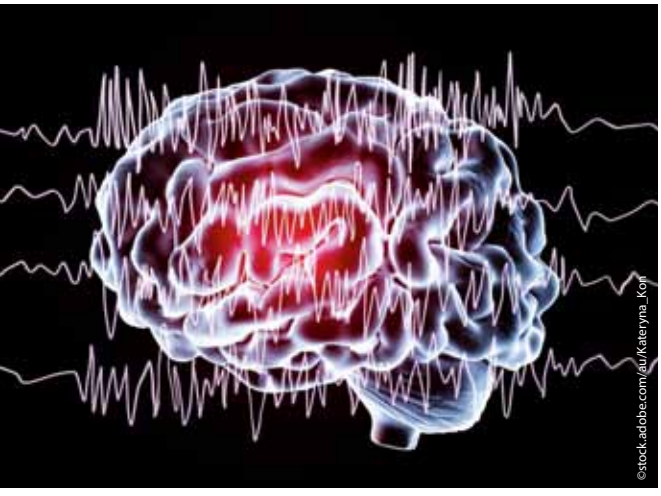
In recent years, cannabinoids — the active chemicals in medical marijuana — have been increasingly touted as a potential treatment for a range of neurological and psychiatric disorders. In particular, the cannabinoid known as cannabidiol (CBD) has the most evidence of antiepileptic efficacy and does not have psychoactive effects; yet there has been little evidence for its use apart from anecdotal reports, until the last year.

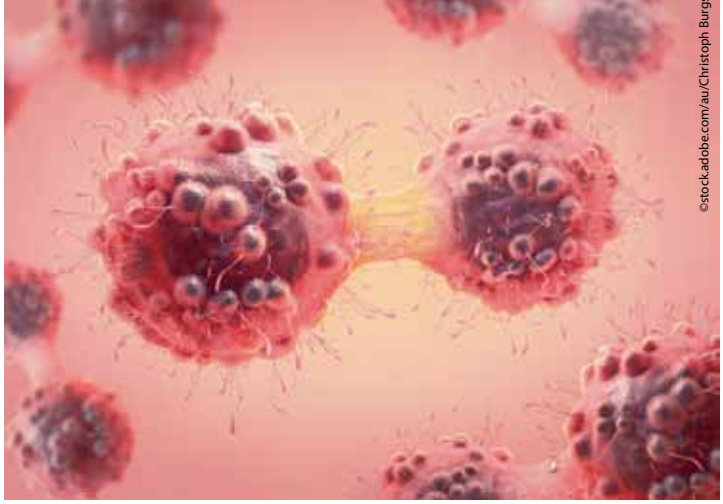
Investigators from the University of Otago and the University of Melbourne recently compared the efficacy of cannabinoids with antiepileptic drugs for children with epilepsy. The results of their review were published in the journal *Developmental Medicine & Child Neurology*.

The review notes that in three randomised, placebo-controlled, double-blind trials in Dravet syndrome and Lennox–Gastaut syndrome (two forms of childhood epilepsy), CBD produced a 38–41% median reduction in all seizures, compared with 13–19% with placebo. Similarly, CBD resulted in a 39–46% responder rate (50% convulsive or drop-seizure reduction) compared with 14–27% with placebo.

CBD was thus found to show similar efficacy to established antiepileptic drugs, the researchers concluded. They also said the compound was well tolerated in patients, although sedation, diarrhoea and decreased appetite were frequent.

"Community debate about the use of CBD and access to this antiepileptic therapy has been heated," the authors wrote. "With further trials and greater understanding of its role, the place of CBD in our antiepileptic armamentarium and its impact on comorbidities will become clearer."




# Zapping tumours in less than a second

Two potential treatments — one using X-rays, the other using protons — aim to reduce the side effects of radiation therapy by vastly shrinking the length of a typical session.

The idea behind both, by Stanford University and SLAC National Accelerator Laboratory, is to blast cancer cells so quickly that organs and other tissues don't have time to move during the exposure — much like taking a single freeze frame from a video. This reduces the chance that radiation will hit and damage healthy tissue around tumours, making radiation therapy more precise.

"Delivering the radiation dose of an entire therapy session with a single flash lasting less than a second would be the ultimate way of managing the constant motion of organs and tissues, and a major advance compared with methods we're using today," said Billy Loo, an associate professor of radiation oncology at the Stanford School of Medicine.

Sami Tantawi, a professor of particle physics and astrophysics and the chief scientist for the RF Accelerator Research Division in SLAC's Technology Innovation Directorate, who works with Loo on both projects, said, "In order to deliver high-intensity radiation efficiently enough, we need accelerator structures that are hundreds of times more powerful than today's technology. The funding we received will help us build these structures."

The project called PHASER will develop a flash delivery system for X-rays. In today's medical devices, electrons fly through a tube-like accelerator structure that's about a metre long, gaining energy from a radiofrequency field that travels through the tube at the same time and in the same direction. The energy of the electrons then gets converted into X-rays. Over the past few years, the PHASER team has developed and tested accelerator prototypes with special shapes and new ways of feeding radiofrequency fields into the tube. These components are already performing as predicted by simulations and pave the way for accelerator designs that support more power in a compact size.

"Next, we'll build the accelerator structure and test the risks of the technology, which, in three to five years, could lead to a first actual device that can eventually be used in clinical trials," Tantawi said.

The Stanford Department of Radiation Oncology will provide about $1 million over the next year for these efforts and support a campaign to raise more research funding.

In principle, protons are less harmful to healthy tissue than X-rays because they deposit their tumour-killing energy in a more confined volume inside the body. However, proton therapy requires large facilities to accelerate protons and adjust their energy. It also uses magnets weighing hundreds of tons that slowly move around a patient's body to guide the beam into the target.

"We want to come up with innovative ways to manipulate the proton beam that will make future devices simpler, more compact and much faster," said Emilio Nanni, a staff scientist at SLAC, who leads the project with Tantawi and Loo.

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# TRIM21 and antibody immunity

Scientists from MRC Laboratory of Molecular Biology (LMB) and the Max Planck Institute for Biophysical Chemistry recently developed a method which makes it possible to directly target almost any protein in any type of cell.

The new method, called Trim-Away, involves TRIM21, a protein discovered at Dr Leo James lab at the MRC LMB. The protein recognises antibodies that enter the cell attached to viruses. It binds to these antibodies, tags the antibody-virus-complex as 'garbage' and hands it over to the cell's 'garbage chute', the proteasome.

Dr James, who classifies himself as a host-pathogen biologist, is one of the speakers at the 44th Lorne Conference on Protein Structure and Function, to be held at Lorne Cumberland from 10–14 February, 2019. Here, he talks about host-pathogen interaction and TRIM21.

*What's your lab's current research focus?*

The relationship between hosts and pathogens is fascinating because of the endless evolutionary struggle


between the two, as first one and then another seeks an advantage. Viruses relentlessly evolve unexpected and ingenious ways to exploit their host, while hosts have to continuously match these schemes with stratagems of its own. The resulting evolutionary battle has been described as the 'Red Queen Paradox' after the conversation between Alice and the Red Queen (from Lewis Carroll), who said: "it takes all the running you can do to say in the same place".

One current focus of my lab is a protein called TRIM21, which we discovered a few years ago is a cytosolic antibody receptor. Our discovery was unexpected because until this time it was always thought that antibodies function exclusively outside of cells. What we were able to show is that, during infection, viruses enter our cells with antibodies attached to their surface. Once inside the cell, TRIM21 detects each virus via their associated antibodies and alerts the host that it is under attack. What is particularly cool about TRIM21 is that it both raises the alarm and attempts to destroy the virus immediately. TRIM21 can do this because, as well as being an antibody receptor, it is also a highly efficient enzyme that catalyses a process called ubiquitination. TRIM21 uses ubiquitination to label viruses for degradation by the cell's recycling machinery, such as the proteasome, thereby preventing infection.

*Can you please share your Eureka moment with our readers?*

I would say the discovery of this hidden world of intracellular antibody immunity, mediated by TRIM21, was definitely my Eureka moment. It was unexpected because our view of antibodies as purely extracellular had been held for over a century. Remarkably, it turns out that TRIM21 is actually the highest affinity (most efficient) antibody receptor in humans and is expressed in almost every cell in our body. It's been protecting us from infection for millions of years and we didn't even realise it was there.

The cool thing about TRIM21 is that it works against anything with an antibody stuck to it — this makes it effective against a broad range of viruses, bacteria and also pathogenic proteins that are the cause of neurodegenerative diseases like Alzheimer's. We realised early on that we might be able to exploit this activity and get TRIM21 to selectively remove proteins from the cell, as both a research tool and ultimately a powerful therapeutic. Eventually we were able to get this concept to work in practice, leading to the development of 'Trim-Away', which combines electroporation of off-the-shelf antibodies with TRIM21 in order to deplete individual proteins from the cell in less than an hour. Trim-Away works in primary cells as well as cell lines and offers an alternative to siRNA but which works faster and at the protein level. We'd like to extend this concept to make therapeutics and that is part of ongoing work.

*What according to you are the top three developments in the field?*

I would say Edward Jenner's discovery that vaccination protects against infection has had a larger impact on human health than any other research before or since. Subsequent to Jenner, the race to develop the polio vaccine in the 1930s–1950s to my mind is equivalent to, and more important than, the later 'space race' and shows what science can achieve with proper encouragement and investment. As these two moments are so pivotal, I'm going to take them as separate achievements and two of the top three! For the final top development, I would say the engineering of therapeutic antibodies by phage display and humanisation. I may be slightly biased because my own work revolves around antibodies, but their use in therapy is now a multibillion-dollar industry, with antibody-based therapeutics now outselling traditional small molecule drugs. The scientist, and recent Nobel Prize winner, who made this possible, Greg Winter, is an ex-director of the LMB and has been inspirational to many of us in the field.

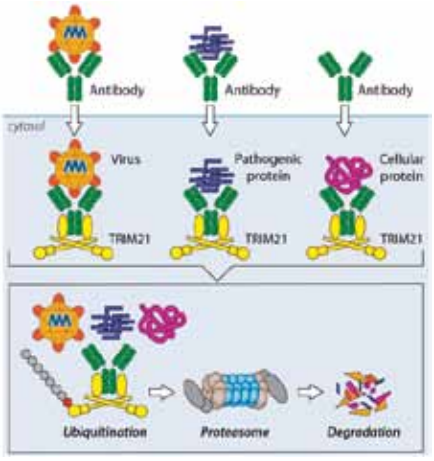


Figure 1: TRIM21 is the highest affinity antibody receptor in mammals. It intercepts antibody-coated viruses in the cytosol and mediates their proteasomal degradation to prevent infection. TRIM21 has an unusual mechanism of ubiquitination that allows it to target any antibody-bound molecule for degradation, including proteopathic agents such as tau or cellular proteins.

*What are you going to talk about at the 44th Lorne Conference on Protein Structure and Function?*

At Lorne, I plan to introduce TRIM21 and provide an overview of how this has changed our understanding of antibody immunity. I will explain why it is important, how it works and how we are exploiting our understanding to develop tools and eventually new therapeutic treatments.

# What can flying insects contribute to neuroscience?

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Insect neuroscience specialists are looking to unlock the mystery of how flying insects can rapidly respond to visual and other sensory cues, given that their tiny brains bear no comparison to the super capacity of their flying skills and speed.

Just like in humans, the brains of hoverflies and even tiny predatory robberflies have hundreds of thousands of neurones which give them survival abilities for hunting and pollen collecting, unparalleled even in the most advanced human technologies. And just like humans, the descending nerve (or 'spinal cord') in flies narrows down to channel only a few hundred neurones at a time.

So how can these extraordinarily rapid insect responses occur when the body's pre-motor pathways run into such a bottleneck linking messages from the brain to the wings and body?

Funded by the US Air Force Office of Scientific Research and an Australian Research Council Discovery grant, researchers from Flinders, Cambridge and Minnesota universities are looking for future directions in neuroscience from the study of highly advanced flying insects, such as predatory robberflies and dragonflies, and non-predatory hoverflies and bees.

Their latest study, which analyses the descending nerve in flies, has been published in the *Journal of Neuroscience* and is expected to lead to more research to mimic the response time in predatory and non-predatory insects in their natural environment in the wild.

"Humans are quite poor at responding to small stimuli in a busy or cluttered field of vision, such as catching a ball while running in a forest," said Associate Professor Karin Nordström from Flinders University.

"So how can flies see each other in similar environments?

"Clearly, there is something in their evolution that still enables incredibly fast responses in their behaviour when their brain registers a trigger (such as pollen, a potential mate or a yummy meal)."

As well as recording responses in the brain, the researchers are also looking at how the animals' neurones dictate behaviour and translate into their super sophisticated capabilities. Research findings will help to inform future technologies such as driverless cars and more efficient modes of air travel.

"This latest study is also fascinating because the tiny robberfly and larger (bee-size) hoverfly have very different evolutionary coding but very similar descending nerve cords, so we are now working on understanding the common blueprint for target detection," Associate Professor Nordström said.

"Indeed, animal brains can be seen as biological computing machines, and many current machine learning tools, including deep neural networks, are heavily inspired by neuroscience using a similar architecture with many layers of non-linear interactions."

# Neuroscientist finds hidden region of the human brain

Scientia Professor George Paxinos AO has just discovered a hidden region of the human brain, located near the brain–spinal cord junction and now dubbed the *Endorestiform Nucleus*.

A world-renowned brain cartographer currently based at Neuroscience Research Australia (NeuRA), Prof Paxinos first suspected the existence of the *Endorestiform Nucleus* 30 years ago but has only now been able to see it with better staining and imaging techniques. He properly noticed it when he introduced the use of chemical stains, combined with imaging techniques, in the production of his latest atlas.

"There is nothing more pleasant for a neuroscientist than identifying a hitherto unknown area of the human brain," he said of the find.

The discovery of new brain regions helps researchers to explore cures for diseases including Alzheimer's, Parkinson's disease and motor neuron disease. The *Endorestiform Nucleus* is located within the inferior cerebellar peduncle, an area that integrates sensory and motor information to refine our posture, balance and fine movements.

"I can only guess as to its function, but given the part of the brain where it has been found, it might be involved in fine motor control," Prof Paxinos said.

Prof Paxinos said the discovery is "like finding a new star", with the added intrigue that the area in question is absent in monkeys and other animals.

"There have to be some things that are unique about the human brain besides its larger size, and this may be one of them," he said.

Prof Paxinos is the author of the most cited publication in *neuroscience* and another 52 books of highly detailed maps of the brain. These maps are uses by brain surgeons and neuroscientists alike as guides for their work, enabling exploration, discovery and the development of treatments for diseases and disorders of the brain.

The discovery of the *Endorestiform Nucleus* is detailed in his latest book, titled *Human Brainstem: Cytoarchitecture, Chemoarchitecture, Myeloarchitecture*. It is available for pre-order now.

Image courtesy of the NeuRA Communications Team.

# Lorne Infection and Immunity Conference 2019

The Lorne Infection and Immunity Conference 2019 will be held from 20–22 February at Cumberland Lorne Resort.

The multidisciplinary, international conference brings together basic and clinical researchers from immunology, microbiology and related fields, in academia and industry, working in human and animal health, host-pathogen interactions, innate and adaptive immunity, and infectious and inflammatory diseases.

The 9th annual meeting in 2019 will feature an exciting line-up of international speakers. This includes:

- Andrea Ablasser, Global Health Institute, Switzerland
- Elizabeth Winzeler, UCSD, USA
- Pascale Cossart, Pasteur Institute, France
- Shee-Mai Lok, Duke-NUS, Singapore
- Linfa Wang, Duke-NUS, Singapore
- Robert Seder, NIH/NIAID, USA
- Kim Newton, Genentech, USA
- Robin May, University of Birmingham, UK

The conference also features eminent national speakers, including:

- Elizabeth Hartland, Hudson Institute of Medical Research, Vic
- Allison Abendroth University of Sydney, NSW
- David Hume, University of Queensland, Qld
- Kirsty Short, University of Queensland, Qld
- Wai-Hong Tham, Walter and Eliza Hall Institute, Vic
- Nicole La Gruta, Monash University, Vic
- James McCarthy, QIMR Berghofer, Qld
- Andrew Currie, Murdoch University, WA
- Ana Traven Monash University, Vic

Subsidised student registrations are on offer (conditions apply), as well as more opportunities for early-career researchers and students to speak.

Visit www.lorneinfectionimmunity.org to register and/or to submit an abstract.

# Plant peptide shows promise in antifungal trial

Biotechnology company Hexima, based at the La Trobe Institute for Molecular Science, has announced promising results for its plant defensin peptide, HXP124, in fungal nail infections.

Hexima's antifungal plant defensin platform has developed from research started by Professor Marilyn Anderson in the late 1990s, when she was searching for molecules that protect flowers from fungal disease. Since then, Prof Anderson — now Hexima's Chief Science Officer — and her team have identified hundreds of plant-derived antifungal molecules that are effective against a wide range of fungal diseases.

"These molecules are exciting because they kill fungus via a novel mechanism and are active against fungal pathogens that are resistant to current drugs," Prof Anderson said.

"The HXP124 peptide was first isolated from a shrub called Bitterbush, which grows in warm climates."

HXP124 rapidly kills a broad range of fungal pathogens, including those that cause fungal nail infections (onychomycosis). As noted by Hexima CEO Dr Nicole van der Weerden, onychomycosis affects around 12% of the global population — from runners and surfers to the elderly and diabetics.

"Left untreated, patients can suffer pain and discomfort and can have difficulty walking," Dr van der Weerden said.

"Unfortunately, many of these are not treated because current available drugs work poorly and are expensive."

The first human trial of HXP124, a dose-escalation study in which the peptide was applied topically to patients with old to moderate onychomycosis, found the substance to be both safe and effective.

"We have shown that HXP124 can substantially reduce the area of infection and can do so up to four times as fast as other available treatments," Dr van der Weerden said. "Our treatment penetrates the nail and kills the fungus that causes the infection.

"Because this is the first time this drug has been tested in humans, the data are necessarily from a relatively small number of patients. However, the results are still very encouraging and demonstrate the potential of HXP124 to be a best-in-class topical therapy."

The second stage of the trial, testing the drug in a larger cohort of patients, is currently underway, with results expected early in 2019. If the results obtained in Part 1 are replicated in the larger patient population in Part 2, Hexima will proceed with a capital raising to fund the next phase of clinical development required to obtain marketing approval in key jurisdictions, including the US and Europe.



# Almost 2m Australians start taking opioids every year

Researchers from Monash University's Centre for Medicine Use and Safety (CMUS) have found that a staggering 1.9 million Australian adults begin taking prescription opioids every year — a worrying trend that suggests the USA's so-called 'opioid epidemic' has made its way down under.

Led by CMUS PhD candidate Samanta Lalic (also a pharmacist at Austin Health), researchers analysed the dispensing of opioids through Australia's Pharmaceutical Benefits Scheme (PBS) from 2013 to 2017. The results were published in the *British Journal of Clinical Pharmacology*.

The research not only reveals just how many Australians are being dispensed opioids, it also finds that 2.6% of them — or around 50,000 people — become long-term users over a year. Furthermore, an increasing proportion of patients are being started on stronger opioids.

This is where the real cause for concern lies, according to Lalic, because both long-term use and the use of strong opioids are associated with a range of adverse health outcomes. High-dose opioid use has been associated with falls, fractures, hospitalisations and motor vehicle accidents — not to mention death from overdose. The Australian Institute of Health and Welfare (AIHW) recently revealed that overdose from prescription medicines has overtaken road deaths and illicit drug overdose as a cause of death in Australia, with deaths involving opioids nearly doubling in the last 10 years.

"Opioids do have an important role in managing cancer pain and acute non-cancer pain; however, their use remains less well established for chronic — ie, long-term — non-cancer pain," Lalic said.

"For the treatment of chronic pain, we need to change prescribing culture and raise the level of awareness of other treatment options among patients. The goal of care, treatment expectations and intended duration should be agreed upon by patients and prescribers prior to opioid initiation.

"In many cases the safest and most effective way to treat chronic pain will involve a combination of therapies, including exercise, physiotherapy and non-opioid painkillers."

Lalic said the next step is to determine how prescribers and patients escalate doses over time. This is important, she said, "because international research has demonstrated a strong link between prescribed dose and overdose deaths".

Australia's Therapeutic Goods Administration (TGA) released a consultation paper earlier this year inviting comments on options for a regulatory response to the potential misuse of prescribed opioids in Australia. These submissions and planned next steps can be viewed on the TGA website.

## Liquid handling system

The INTEGRA ASSIST PLUS pipetting robot streamlines routine pipetting tasks.

The fully automated liquid handling system with spanning head capability includes: PCR and RT-PCR set-up and clean-up, cell culture, serial dilution, ELISA and reagent addition. Using INTEGRA electronic multichannel pipettes and the GripTips Technology to assist in uniform pipetting, the system automates pipetting tasks, eliminates physical strain and ensures error-free pipetting.

It can incorporate a range of commonly used labware including 0.5, 1.5, 2.0, 5.0 and 15 mL tubes and 24-, 48-, 96- and 384-well plates as well as a wide range of reservoirs in its workflows.

With three deck positions, the system reformats samples automatically, taking advantage of VOYAGER pipette's adjustable tip spacing to process tubes and plates fast.

Other features and benefits include: performing tedious serial dilutions ensures critical parameters — such as pipetting heights and mixing speeds — remain consistent; the process could be optimised with tips change after every transfer to minimise the risk of carryover; the system allows the user to set up various assays with reagent addition in plates and tubes with ease; the VIALAB software allows the user to create and modify complex workflow programs with simple step-by-step method development.

***BioTools Pty Ltd***

***www.biotools.com.au***

## Electronic batch record execution platform

Lonza's next-generation electronic batch record execution platform, the MODA-ES Software Platform, offers a flexible solution for consolidating and managing batch and quality data produced across cell and gene therapy manufacturing processes.

The software platform has been designed to consolidate all cell and gene therapy manufacturing batch data, as well as batch-related quality control data, into a single record with an easy-to-use review and approval interface for expedited product release. With data integrity compliance and traceability at its core, the platform captures trends key quality and performance metrics, while eliminating errors associated with manual and paper-based approaches. It is flexible, easy to configure and scalable from clinical through to commercial production.


The product enables workflow-driven data entry applicable to batch records, sterility tests and cleaning forms. Its modular design allows individual modules to be created, validated and used across different processes.

Standard methods are available for processing products of the same family, with the flexibility to vary the raw materials, fill volumes and equipment types used. An electronic checklist enables real-time review and approval, while a data-integrity alert capability is available to trigger timely intervention and resolution of issues.

The platform seamlessly integrates with other cGMP compliant electronic systems, as well as with analytical equipment, for effortless data transfer.

***Lonza Australia Pty Ltd***

***www.lonza.com***



# How to tackle the reproducibility crisis: validation and quality

The scientific community is currently facing a reproducibility crisis. Over 70% of researchers are failing to reproduce published experiments[1].

With so much research built on previous work, this represents a substantial amount of time and funding wasted because of reproducibility issues. Some estimates put the cost of unreliable, irreproducible research as high as $28 million each year in the US[2]. Although there are several causes of this "crisis", it can't be denied that the quality of scientific reagents is a core issue we need to address.

Reagents are the essential building blocks for all life science research. It's crucial that reagents work as specified and provide accuracy and consistency so that scientists can generate robust data. One push in the right direction is the use of recombinant technology in the production of antibodies.

Abcam's catalogue has seen a massive increase in the number of recombinant antibodies on offer. These are developed in vitro using a synthetically produced gene construct, so antibody production is controlled, reliable, and avoids common issues such as gene mutations. We currently offer a range of over 13,000 recombinant monoclonal antibodies, all ensuring high specificity and batch-to-batch reproducibility.

Scientists need products that they can rely on; products that work as expected and don't lead to wasted time and funding. Vendors need to rigorously test reagents for reproducibility and specificity across a range of applications. We've heavily invested in knockout (KO) validation techniques — the gold standard in antibody validation — to give our customers confidence in the products they buy from us.

KO-validation confirms antibody specificity by testing the antibody of interest on a KO sample or cell line that doesn't express the target protein. KO-validation serves as a true negative control to help confirm specificity to the protein of interest. We're conducting this KO-validation program at a scale beyond anyone else in the industry with over 1,600 KO validated antibodies in our catalog and growing.

To ensure that researchers using kits rather than antibodies alone benefit from our specificity testing, we use the same validated antibodies in our range of immunoassay kits as well. Our SimpleStep ELISA® and multiplex FirePlex® kits, for example, make extensive use of our own recombinant monoclonal antibody pairs, to deliver specific and reproducible data within and between batches.

Transparent product data gives scientists confidence that the reagents they purchase have worked well in the hands of their peers. We upload all customer reviews to the Abcam site — there are no edits, whether a review is positive or negative. We continually test existing products in our catalogue, adding new testing data and removing outdated products, so researchers always have the best available options and information. On our website, you can also find information on how our antibodies compare to equivalent alternatives from our top competitors (see figure 1 for an example). We carry out these tests in an entirely fair and comparable manner showing all the data we get, even if the competitor reagents are just as good as our own.

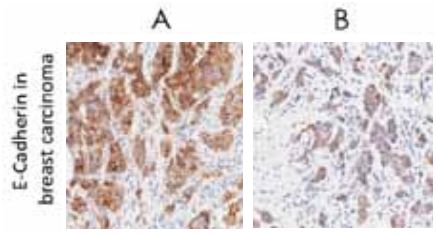


*Figure 1. E-cadherin immunohistochemistry staining in breast carcinoma. A) Abcam RabMAb® E-cadherin monoclonal antibody (ab40772). B) Competitor E-cadherin rabbit monoclonal antibody. Antibody dilution for A 1/1,000 and B 1/200.*

We're trying to change the problem of reproducibility and advance scientific research by setting new standards for reagent validation and testing. Our products perform to exceptionally high standards, and that's why researchers are choosing to buy their reagents from us. Since January 2015 Abcam products were cited in 33% of all life science publications[3]. We're driven to improve antibody reliability and specificity, and with the help of the scientific community and other vendors, the reproducibility crisis could soon become a thing of the past.

For more information:

www.abcam.com/qualityvalidation

*References*
1. Baker, M. Nature 533, 452–454 (2016)
2. Freedman L.P. et al. PLOS Biology (2018)
3. CiteAb: https://www.citeab.com/ accessed 14/09/2018

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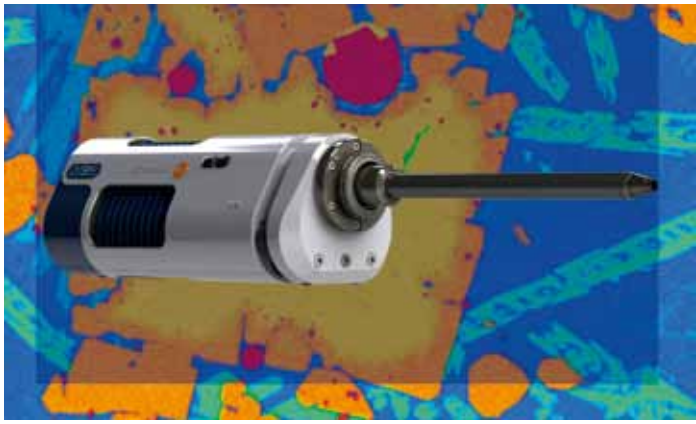
## Automated sample preparation system

Biotage's Extrahera is a powerful, user-friendly automation system for analytical sample preparation in plate or column formats. It is a compact, eight-channel automation instrument, designed for speed and flexibility and with end-user operation in mind.

An SLE and SPE automation system for analytical professionals, the product processes a full standard SPE plate method in less than 30 min, including sample pre-treatment, conditioning, equilibration, load, wash and elution steps — even when using volatile and low surface tension solvents.

The dual-format design enables users to switch from processing 96-well plates to 1, 3 or 6 mL columns in a matter of minutes. It thus ensures that the product is a suitable for analytical laboratories, providing the option of working in 96-well plate or column formats.

***Shimadzu Scientific Instruments (Oceania) Pty Ltd***
***www.shimadzu.com.au***



## SEM-EDS detectors

The Oxford Instruments Ultim Scanning Electron Microscopy/Energy Dispersive X-Ray Spectroscopy (SEM-EDS) detectors feature big sensor sizes and fast electronics that deliver high sensitivity and speed.

The Ultim Max 65 $mm^2$ and 40 $mm^2$ models have been released to complete the Ultim range and join the 170 $mm^2$, 100 $mm^2$ and the ultra-high sensitivity windowless Ultim Extreme detector, launched in 2017, to provide a complete range of microanalysis system.

Paired with Oxford Instruments AZtecLive real-time EDS analysis software as standard, live sample navigation by chemistry in an electron microscope is possible. This capability changes EDS from a traditional static approach to dynamic, interactive analysis.

The solution offers live imaging, X-ray mapping and element identification, and the range of Ultim detectors makes the most challenging analysis possible.

***Scitek Australia Pty Ltd***
***www.scitek.com.au***

## Analyser

The Gerhardt DUMATHERM system allows users to easily determine the nitrogen content of solid and liquid samples in three minutes using the Dumas method.

Suitable for food and animal feed laboratories, the system provides valid reference results quickly in almost any location with the appropriate gas infrastructure.

The combustion process is fully automated and stoichiometric. The system adds the precise quantity of oxygen required for each sample. The chrome-free reactor provides outstanding catalytic characteristics. This technology can handle samples with a low nitrogen content, highly concentrated and saline samples, and samples with a high water content.

The DUMATHERM Manager software provides clear guidance. All analytical and device data is saved, forming documentation that enables you to trace at any time all combustion processes that have been carried out. It supports quality assurance in an accredited laboratory and takes care of compiling the majority of documentation. It also includes different user levels and password protection.

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

## Liquid handling system

The bio molecular systems myra liquid handling system features an integrated miniature camera and advanced vision technology.

It automates and simplifies plate calibration to make it easy even for first-time users. Designed directly into the system's pipette head is a miniature pressure sensor, enabling both liquid level sending using conventional tips as well as real-time monitoring of aspirate and dispense process for errors.

myra offers accuracy of less than 10% CV for 1 $\mu$L pipetting volumes. The system's pipette head is designed to be easily interchangeable. Users can send the head away for annual calibration to ensure samples are always pipetted accurately. The design incorporates high-precision pipette tip positioning for small aperture tubes such as 384-well plates and Mic tubes. It comes complete with UV LED lights and a compact HEPA filter to ensure a clean qPCR set-up environment.

***Gene Target Solutions Pty Ltd***
***www.genetargetsolutions.com.au***

## Fume hood

The UniFlow LE AireStream Fume Hood is available in 3′, 4′, 5′, 6′ and 8′ widths. The fume hood incorporates a unitised superstructure, with non-metallic dual-wall construction for chemical and corrosion resistance, strength and durability. The integral one-piece fume chamber is smooth glass with all coved corners.

The AireStream baffle system with vector airflow slots directs the air through the fume chamber and through the exhaust outlet with minimum turbulence and maximum airflow efficiency, for low flow constant volume performance. Other features include: vapour-proof LED strip light fixture and control switch pre-wired to a single point junction box, 115 V/60 Hz AC. ASHRAE-110, NFPA-45, U.L. 1805 Classified and SEFA Recommended Practices.

***HEMCO Corporation***
***www.hemcocorp.com***

*Lauren Davis*

# Better blood analysis

## with lab-on-a-chip devices

Dr Warwick Nesbitt is on a mission to bring blood analysis out of the pathology lab, developing a family of lab-on-a-chip devices in an effort to improve blood handling, diagnostics and even drug development.

A biochemist based at RMIT University and the Australian Centre for Blood Diseases, Monash University, Dr Nesbitt has a particular interest in platelet biology — platelets of course being the blood cells that stop us from bleeding. Looking for ways to model how blood flows and how this affects platelet function in disease, he turned to microfluidics. Now, he's won a grant from the National Health and Medical Research Council (NHMRC) to develop his own device to measure platelet function.

"In terms of platelet function testing, there aren't really any good automated platelet function tests," Dr Nesbitt told *Lab+Life Scientist*. "There are a number of pathology-based tests, but they're quite labour-intensive, and they're not used that frequently because of the labour-intensive nature of them.

"The device that we're trying to develop is really designed to measure how platelets from patient blood samples behave, and then use that information to either predict bleeding or clotting risks," he said. This will be particularly useful for patients suffering from von Willebrand disease, which is the most prevalent heritable bleeding disorder.

Image credit: RMIT University.

"There are a series of pathology-based tests … used to identify the type of von Willebrand disease that somebody has, but there isn't a single device that can do all of that testing," Dr Nesbitt said. "And those tests aren't really great measures of platelet function in the context of von Willebrand disease.

"So we're trying to develop a microfluidic lab-on-chip device that does that better, and can potentially be used at the point of care as well. So it doesn't require a lot of operator expertise or a large pathology lab to do the testing."

The device in question contains tiny channels, pumps, valves and processors, enabling precise and flexible manipulation of fluids. It is also fast, portable and able to handle very small volumes of blood — which, according to Dr Nesbitt, is not as easy as it sounds.

"Blood's designed to clot when you take it out of the body — that's what it wants to do — so developing or engineering systems that can handle blood without that happening is really a big focus, particularly developing the blood-pumps-on-chip," he said.

With the device for von Willebrand disease now at the prototype stage, Dr Nesbitt and his team are looking at adapting the technology for people who might be prone to thrombosis, heart attack or stroke as a result of clotting.


"For example," Dr Nesbitt said, "diabetic patients often show hyper-responsive platelets, and often suffer from peripheral vascular disease as a result. So we might be able to use the device to screen the likelihood that diabetic patients might suffer peripheral vascular disease or thrombosis in the future."

The technology could even be used to monitor patients on antiplatelet therapy, with Dr Nesbitt noting that a lot of people are resistant to antiplatelet drugs such as aspirin and clopidogrel.

"These patients receive the standard dosing, and then their platelets don't respond, so they're still in danger of clotting," he said. "We're hoping that our device will enable clinicians to monitor how effective their drug treatment is, and they can tailor the dose or change the drugs that they're giving the patients."

It's an ambitious series of projects which has required a big collaborative team, including researchers at Monash University; microtechnology experts within the MicroNano Research Facility (MNRF) headed by Distinguished Professor Arnan Mitchell at RMIT University; researchers with the Department of Mechanical Engineering at the University of Melbourne; and clinicians at Alfred Hospital's Department of Clinical Haematology, headed by Professor Harshal Nandurkar. This multidisciplinary approach has allowed the collaborative team to cover all aspects of required research — from device technology, to drug development, to basic biology and clinical translation.

Now, with various projects all at various stages of completion, the researchers are currently focused on increasing the system's level of automation. This will be useful across multiple applications, enabling the device to deal with a larger numbers of samples and increasing the rate at which the user can screen those samples.

"If we want to use the system, for example, to discover new anticlotting therapies, we need a system that can analyse very large numbers of blood samples, and is also able to assess how potentially hundreds of different chemical compounds affect platelet function, to screen out and identify target molecules that might be better than current antiplatelet therapies," Dr Nesbitt said.

"So the main thrust at the moment is getting that automation — how you pump blood through the system, developing little paths-on-chip to pump the blood to the different assays, and how you kind of shunt really small-volume blood samples around on that lab-on-chip system."

## Laboratory recording instrument

The eDAQ EPU452 Quad Multi Function isoPod with USB is a four channel, user-configurable data recorder capable of recording data from common laboratory transducers directly to the personal computer.

This portable USB-based unit has four isolated input channels which can be configured by the user to record data from any combination of pH/mV, temperature, conductivity, dissolved oxygen and biosensors.

The unit is suitable for applications requiring the accurate recording of multichannel laboratory experimental data. Each precision channel can be independently configured and calibrated for a particular type of sensor using its MF Configurator software. The instrument can have four pH channels, or one each of pH, conductivity, dissolved oxygen and temperature, or any other combination. Pod-Vu, a graphical and tabular display application, is provided as a high-level recording and display tool. In addition, serial commands are available for use with NI LabView to control the system.

***eDAQ Pty Ltd***
***www.edaq.com***

## Field metrology wells

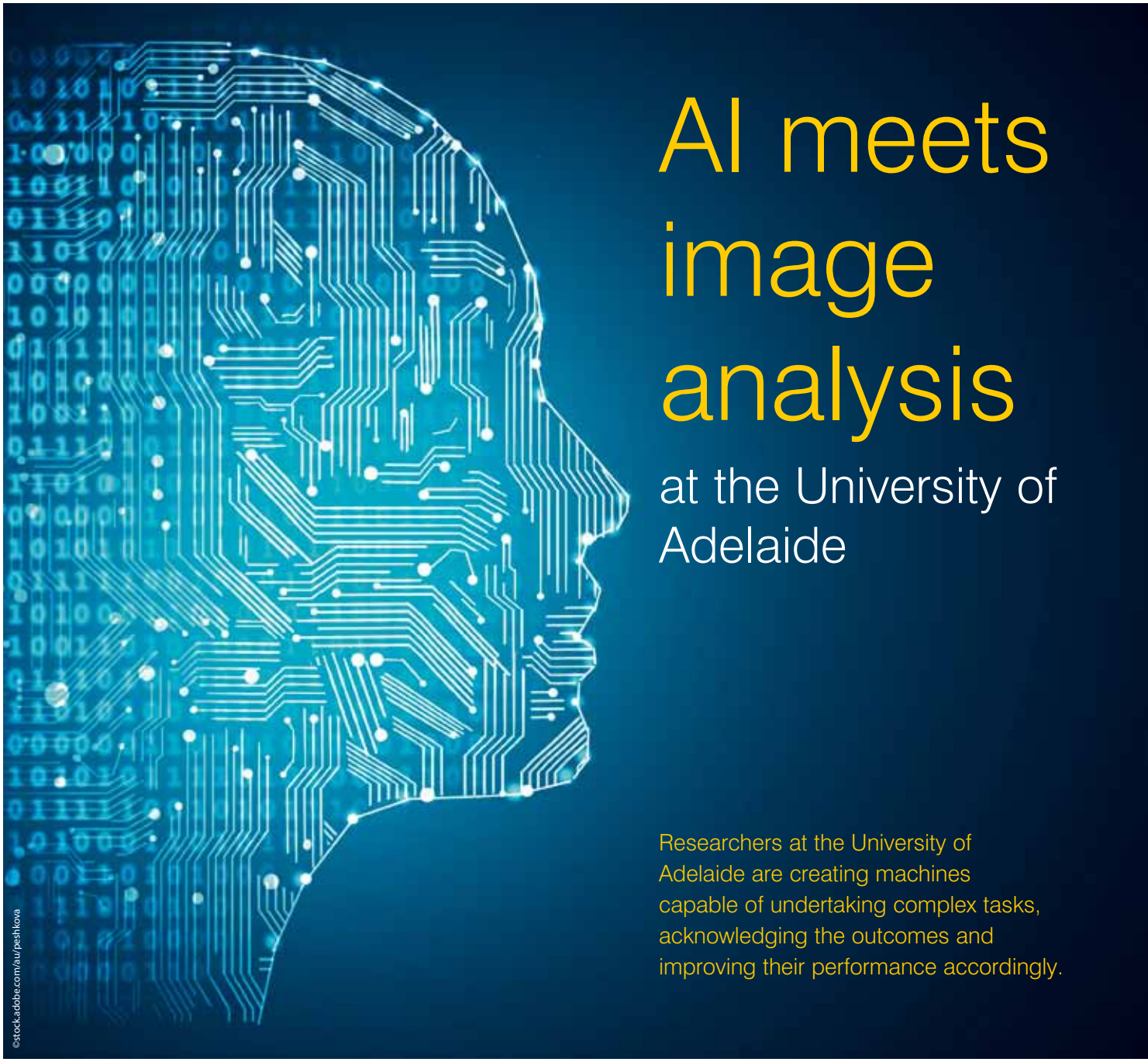
The Fluke Calibration 9142, 9143 and 9144 Series Field Metrology Wells extend high performance to the industrial process environment by maximising portability, speed and functionality without compromising measurement quality.

Field metrology wells are easy to use, lightweight, small and quick to reach temperature setpoints, yet they are also stable and uniform. The calibrators cover a wide range of temperature instruments, including RTDs, thermocouples, transmitters and thermal switches. Fluke Calibration's field metrology wells can cool to -25°C or heat to 660°C in 15 min.

Field environment conditions are typically unstable, having wide temperature variations. Each field metrology well has a built-in gradient-temperature compensation (patent pending) that adjusts control characteristics to ensure stable performance in unstable environments. In fact, all specifications are applicable over the environmental range of 13–33°C.

Measurement equipment drifts over time. Imprecise calibration results in less than optimal processes, exposure to audit risk, increased troubleshooting, shorter calibration intervals, more unplanned downtime, increased operational costs and reduced productivity. Sending tools out to third-party calibration labs may exacerbate delays and outsources a critical component to quality.

***Fluke Australia Pty Ltd***
***www.fluke.com.au***




# AI meets image analysis

## at the University of Adelaide

Researchers at the University of Adelaide are creating machines capable of undertaking complex tasks, acknowledging the outcomes and improving their performance accordingly.

Professor Anton van den Hengel, Director of the Australian Institute for Machine Learning (AIML) said the university's technology can "compete with, and sometimes exceed, human capabilities in tasks like recognition, statistical analysis and classification".

The breakthrough, according to Prof van den Hengel, has been the advent of 'deep learning' technology — a form of machine learning (itself a subset of artificial intelligence) based on the human brain's neural networks. "That's enabled machines to distil and interpret huge amounts of prior and incoming information, and particularly visual information," he said.

Prof Ian Reid, a senior colleague of Prof van den Hengel's and Deputy Director of the Australian Centre for Robotic Vision, agrees. "Artificial neural networks, together with vast computing power and data volume, have enabled step-change in the level of intelligence machine learning can achieve," he said.

### Faster disease diagnosis

For example, the University of Adelaide recently collaborated on the creation of the world's first AI microbiology screening technology for use in pathology laboratories. Developed in partnership with healthcare company LBT Innovations, the Automated Plate Assessment System (APAS) went into production in 2017 and is attracting international interest.

"APAS will enable doctors to order more tests, which will give them more information, sooner," said Prof van den Hengel, who led the six-person APAS software development team. "It could even allow country or developing-world hospitals to run their own tests without having to ship samples to a central lab. That would save a huge amount of time, and potentially many lives."

The system automates the traditionally time-consuming functions performed by microbiologists in screening culture plates after incubation. It takes high-quality images of the plates, then analyses and interprets any microbial growth, matches

In routine microbiology testing, up to 70% of plates may be negative. Removing them automatically will give microbiologists more time to spend on complex decisions, enabling even greater accuracy and allowing more tests to be run.

this against key patient data, presents a diagnosis and continually updates its own knowledge base.

Significantly, APAS also removes non-pathogenic plates from the workflow. "This is very important," said LBT co-founder Lusia Guthrie, now Chair of Clever Culture Systems — the joint-venture company bringing APAS to market. "In routine microbiology testing, up to 70% of plates may be negative. Removing them automatically will give microbiologists more time to spend on complex decisions, enabling even greater accuracy and allowing more tests to be run."

LBT CEO Brent Barnes believes the system will ultimately mean faster recovery for millions, saying, "More and more accurate testing will see patients getting the right treatment earlier and spending less time in hospital."

Keen to build on the foundation laid with APAS, the university and LBT are now jointly developing three other related medical devices utilising the university's AI image-analysis technology.

## Accelerating crop farmers' adaptation to climate change

Another application of the AI image-analysis technology lies in the agricultural sector, with Prof van den Hengel tailoring the technology to accurately estimate potential new cereal varieties' yields after only very short periods of growth, enabling rapid identification of robust varieties able to thrive in harsh conditions.

"This novel approach promises to transform crop breeding," Prof van den Hengel said.

"By using image analysis to understand plants' shape and structure at all stages of growth, we'll be able to identify and automatically measure attributes associated with high yields very early in test plants' lifespans."

The system uses multiple images taken from numerous angles to construct computerised 3D models of the plants for analysis. Once completed, it will be incorporated into the university's Plant Accelerator facility, which provides important complementary capability.

"The Plant Accelerator's fully robotic plant management system allows automatic and repeatable control of growing conditions for up to 2400 plants at a time, and enables automatic delivery of those plants to our imaging stations," Prof van den Hengel said.

"That's going to allow rapid, detailed and accurate estimations of vast numbers of crop varieties' potential yields under all kinds of climate-change-related stresses, such as high salinity or drought. We've no doubt it will expedite the development of hardy, high-yield varieties and help improve global food security."

Industry partner Bayer Crop Science has signed on to help commercialise the technology for this application.

## Emulating nature's perfect pursuit

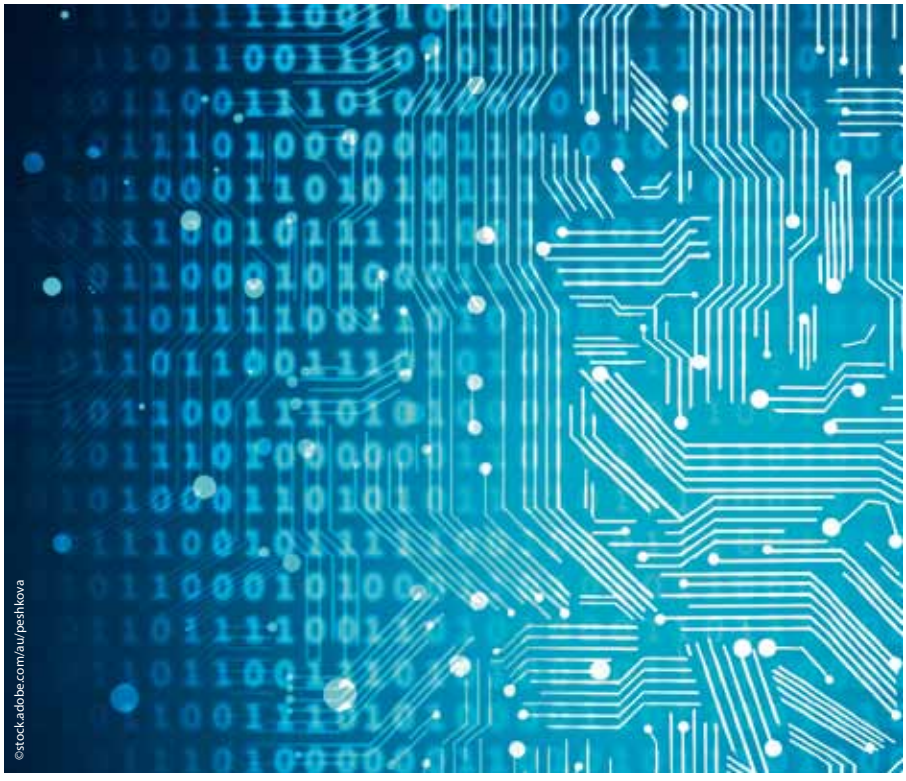
The technology is also enhancing autonomous-pursuit capabilities, with computer scientists, engineers and neuroscientists at the university adapting dragonflies' neuronal processes into an algorithm that emulates the insect's phenomenal visual tracking capability. Widely considered nature's most effective predator, dragonflies are able to target, pursue and capture tiny flying prey in mid-air at speeds of up to 60 km/h — even if that target attempts to disappear within a seething swarm — with an impressive hit-rate of over 95%.

"Tested in various nature-mimicking virtual reality environments, our pursuit algorithm matches all other state-of-the-art pursuit algorithms' accuracy, but achieves that while running up to 20 times faster," Prof Ben Cazzolato said. "So it requires far less relative processing power."

Mechanical engineering researchers at the university have also incorporated the algorithm in an autonomous robot that, in testing, has effectively and efficiently pursued targets in unstructured environments.

The interdisciplinary project is being led by neuroscientist Dr Steven Wiederman, whose team first identified how the dragonfly is able to focus on a single moving target and shut out all else. He and his team are now collaborating with Professor Reid to develop neurobiology-inspired machine-learning drone-tracking systems.

"We're excited to further define the principles underlying neuronal processing," Dr Wiederman said. "Translating them into advanced artificial vision systems could result in some incredibly effective autonomous robotics and drones, as well as neuronal prosthetics and many more applications."



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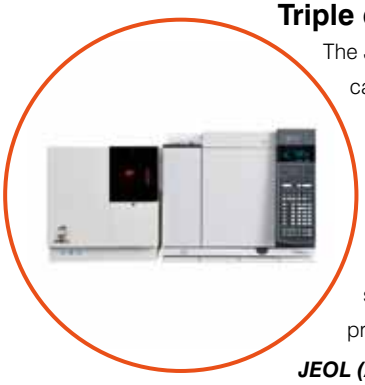
## Triple quadrupole mass spectrometer



The JEOL JMS-TQ4000GC is a gas chromatograph-triple quadrupole mass spectrometer system with capabilities of high throughput and high sensitivity, based on the short collision cell technology.

These capabilities allow users to improve the productivity for routine analysis such as residual pesticides analysis in agricultural materials or monitoring of trace amount of chemicals regulated by tap water quality standard and environmental criteria.

Features include: short collision cell technology facilitates high-speed data acquisition without crosstalk; high sensitivity achieved with ion accumulation and pulsed ion ejection at short collision cell; simple operation for data acquisition and analysis with a combination of pre-installed SRM condition file and multi-target quantitative analysis software.

***JEOL (Australasia) Pty Ltd***
***www.jeol.com.au***

## Fluorescence microscope for live cell imaging

The Nanolive 3D Cell Explorer-fluo combines fluorescence microscopy with high-resolution holo-tomographic microscopy, allowing users to non-invasively see how their cells function in response to various stimuli over long time periods. This ultimately gives researchers a comprehensive understanding of cellular behaviour and cell biology.

Using 3D holographic tomography microscopy pioneered by Nanolive, users can differentiate sub-cellular components in real time, enabling them to carry out dynamic behavioural studies of cells. Multichannel fluorescence microscopy is a well-respected technique in biology and its incorporation into the 3D Cell Explorer platform opens up several possibilities in scientific research and live cell imaging.

The Nanolive 3D Cell Explorer-fluo enables scientists to use up to four different fluorescent markers in parallel with the holo-tomographic imaging. This addition to the holo-tomographic image allows cellular researchers to correlative gene expression (via fluorescence) to provide deep insights into cellular functions at the organelle level.

The addition of these complementary imaging modalities within the one instrument results in a comprehensive imaging tool suited to stem cell research, drug development, cancer research and many other applications requiring detailed information on cellular responses.

***AXT Pty Ltd***
***www.axt.com.au***

## Test instrument

The Hysitron PI 88 SEM PicoIndenter is an in-situ nanomechanical test instrument for SEM and FIB/SEM.

The instrument's modular design also supports the company's full suite of testing techniques for future upgradability, now including 800°C heating, scratch testing, 5-axis sample positioning, electrical characterisation, dynamic fatigue testing and an interchangeable extended range (500 mN, 150 $\mu$m) transducer.

Built on Bruker's capacitive transducer technology, the PI 88 comes standard with advanced XYZ sample positioning stages which provide greater travel range (>8 mm) for accessing more sample area with high resolution and linearity. These stages also provide the foundation for the various upgrade modules available for the PI 88. Coupling the stages with a variable-load frame transducer design featuring user-changeable load cells allows users to meet evolving research demands.

The PI 88 mounts easily to the SEM stage without being a permanent fixture in the microscope. The compact design of the instrument allows for maximum stage tilt and minimum working distance for optimal imaging during testing.

***Bruker Pty Ltd***
***www.bruker.com***

## Light-sheet microscope

The Luxendo MuVi SPIM (Cleared Sample) is an extension of the MuVi SPIM capabilities and enables 3D imaging of optically cleared samples. It brings together light-sheet fluorescence microscopy and tissue clearing techniques and provides solutions in terms of sample mounting, sample size and optics to enable fast, high-quality 3D imaging of cleared samples.

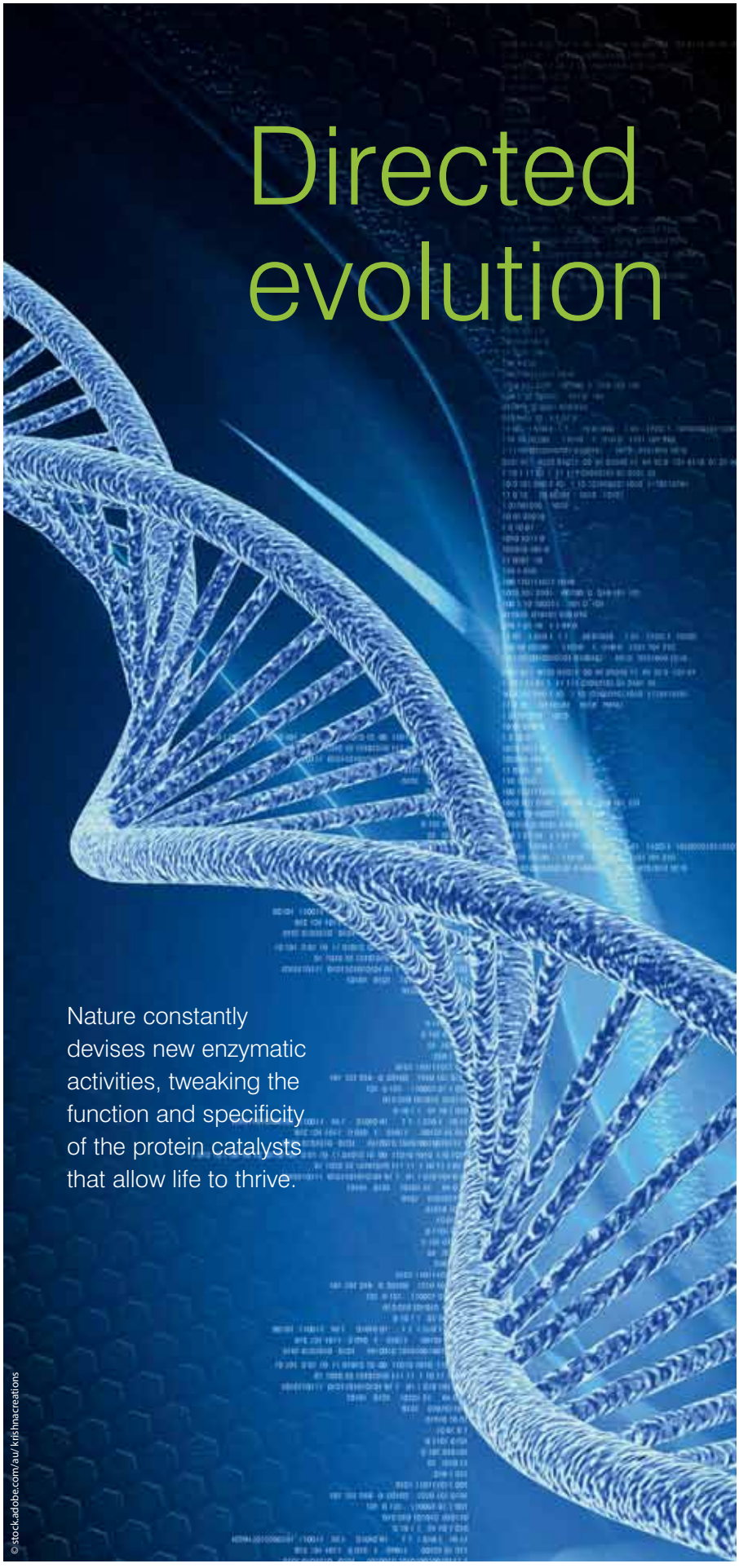
The MuVi SPIM CS is optimised for 3D imaging of intricate tissue structures, relevant to study the brain or the central nervous tissue in neuroscience, to analyse organ development or to investigate tumour structure and genesis in oncology. It enables imaging of optically cleared tissues, compatibility with various clearing methods, imaging of large samples, large samples and large accessible volume, high-speed image acquisition, high sensitivity and minimal noise.

The sample chamber, the illumination and the detection unit in the octagon are adapted to match the experimental needs in terms of sample size, refractive index, field-of-view and resolution, adding high flexibility to the system. The MuVi SPIM CS can achieve a resolution down to 300 nm in 3D (at a wavelength of 500 nm), enabling imaging of optically cleared samples.

Two Nikon 10x 0.3 NA air objective lenses project two aligned light-sheets from opposing directions on the sample. Detection includes high numerical aperture, multi-immersion objective lenses, with 20x and 10x magnification. An additional magnification changer results in a total magnification that ranges from 7.5x to 30x. The user can choose the set of illumination and detection objective lenses according to the experimental needs.

***SciTech Pty Ltd***
***www.scitech.com.au***

# Directed evolution






Protein engineering — taking this process and harnessing it to build novel activities that are desirable from a technological or medicinal perspective — is an exciting area of research, recently recognised with the 2018 Nobel Prize for Chemistry.

One half of the Prize was awarded to Professor Frances Arnold from the California Institute of Technology "for the directed evolution of enzymes" and the other half jointly to George P Smith, University of Missouri and Sir Gregory P Winter, MRC Laboratory of Molecular Biology "for the phage display of peptides and antibodies".

It's also one of the key topics to be covered at the 44th Lorne Conference on Protein Structure and Function, to be held in Lorne, Victoria, from 10–14 February 2019. Nobel Laureate Professor Frances Arnold will deliver a special evening lecture on protein engineering, key developments and her contributions to the field.

## Developments and trends

Recent years have seen several important developments in the field of protein engineering. The first, and the discovery for which Professor Arnold was awarded the Nobel Prize, is directed evolution — a methodology by which proteins can be randomly mutated, screened for improvements, recombined and screened again in an iterative process. This has been shown to produce remarkable improvements in activity and stability of proteins and the possibility to devise enzymatic activities that have never been observed in nature. The second major advance, for which Professor Gregory Winter and Professor George Smith shared the Nobel Prize, has been in high-throughput screening methods, such as phage display, which have allowed enormous numbers of protein variants to be quickly screening for improved properties. For example, this has been instrumental in engineering new antibodies that can be used in the treatment of cancer or autoimmune disease.

Lastly, the increase in computational power and increasingly sophisticated algorithms have resulted in drastic improvements in the field of computational protein design, which allows tailor-made proteins to be created for a specific task, whether it be a novel enzyme to break down a toxin or a binding protein to sense changes in the environment.

At Lorne Proteins, this year is also unique in that there is a concurrent symposium, the first Lorne Satellite on Drug Discovery and Design, which has substantial overlap with the field of protein engineering. In particular, a number of engineered proteins are now making their way into the clinic as biotherapeutics.

Engineered proteins, especially antibodies, have been shown to have particular value when used to treat chronic diseases.

## Where does Australia stand?

The global protein engineering market is predicted to be worth over US$1bn by 2020, and is growing by up to 20% per annum. Australia has a presence in this industry, through companies such as CSL, but overall, is less advanced than other global centres, such as the USA, Europe and Asia. Much of the demand for engineered proteins is in health care, with many new antibody-based treatments having undergone some level of engineering. Of the top five best-selling drugs of 2017, four were 'biologics' (humira, enbrel, rituxan, herceptin). Engineered proteins, especially antibodies, have been shown to have particular value when used to treat chronic diseases. For example, humira (adalimumab) was successfully engineered to bind and block the Tumour Necrosis Factor alpha, and in doing so can be used to treat many autoimmune conditions, such as rheumatoid arthritis, ankylosing spondylitis and Crohn's disease. There is also increasing demand for engineering enzymes in chemical manufacturing, environmental remediation, the production of biosensors and the food, beverage and textile industries.

## Challenges

There are many challenges in protein engineering still to overcome. As Professor Arnold notes in a recent review article in the Wiley journal *Angewandte Chemie* (International edition) "… designed enzymes don't yet have the sophistication of nature's products, and design struggles with the metals and other cofactors that drive so much interesting chemistry." It is clear, however, that our increasing ability to conduct both directed evolutionary and computational design driven protein engineering studies means that these complications should soon be addressed. Professor Arnold sums up the prospect for protein engineering in her review: "A treasure trove of new enzymes is just waiting to be discovered and used for chemistry that we could only have dreamed of just a few years ago."


## Mass flow controllers

Aalborg Instruments' DPC series precision digital mass flow controllers provide stable control of the mass flow rate of process gases. Inherent simultaneous displays of mass flow, volumetric flow, pressure and temperature parameters promote applications in a variety of industries such as scientific and analytical applications, bioreactors and surface depositions, gas sampling, manufacturing and metrology activities.

The precision digital mass flow controllers incorporate multigas functionalities allowing users on site to select up to 30 different gases locally via the optional OLED/joystick interface or remotely via the RS232/RS485 interface or optional Modbus RTU interface.

The flow controllers support various functions, including: user-selectable local, analog, digital or program set point control; two programmable flow totalisers; low, high or range flow; temperature and pressure alarms; automatic zero adjustment (activated via local or communication interface); programmable SSR relay; programmable 0–5 VDC, 0–10 VDC or 4–20 mA analog inputs and outputs; user-programmable pulse output (via SSR); and extensive self-diagnostics functionality.

***AALBORG***
***www.aalborg.com.au***

## Next-day *Salmonella* detection

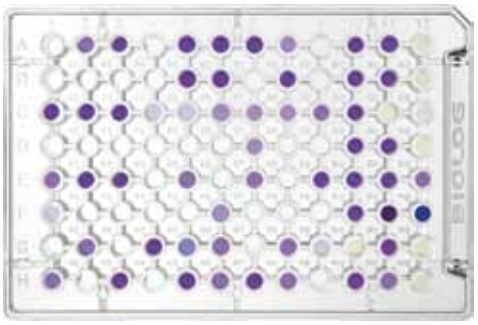
Solus One ***Salmonella*** offers laboratories a single enrichment step method to screen samples for ***Salmonella*** spp in just 24 h. Awarded by AOAC for the detection of ***Salmonella*** spp in environmental and selected food products, the product enables quality control personnel to confidently release product to the market, reducing inventory levels and limiting loss through contamination.

The product is the latest addition to the Solus Scientific pathogen system range, comprising specifically designed immunoassay kits, dedicated selective enrichment media and automated liquid handling. It utilises next-generation ELISA plate technology that is said to increase available antigen binding sites, allowing reduced enrichment times and improved sensitivity.

Solus has partnered with Dynex DS2 to provide a fully automated testing solution, providing high throughput and reducing technicians' hands-on time. A barcoding system provides full traceability of each sample, designed to reduce the possibility of human error.

The complete Dynex DS2 automated system allows for total testing flexibility and scalability. At any one time the DS2 can read two 96-well plates, allowing up to 186 samples to be processed simultaneously with a maximum of 372 samples in a day with only 2 h of hands-on assay time. This capability allows the laboratory to cope with any changing test loads.

***Key Diagnostics Pty Ltd***
***www.keydiagnostics.com.au***



## Plates for mitochondrial function assays

The Biolog MitoPlate S-1 and MitoPlate I-1 enable a comprehensive scan of mitochondrial function.

Mitochondria are organelles inside of human and other eukaryotic cells that produce most of the energy that cells need to survive and grow. When different cell types have mitochondrial defects, it can lead to wide-ranging energetics-related disorders including cancer and ageing, neurological disorders, metabolic disorders and immunodeficiencies.

Biolog's preconfigured 96-well MitoPlates provide powerful analytical tools leading to a comprehensive assay approach. The MitoPlate S-1 measures metabolism of 31 substrates, most of which are metabolised via the mitochondria. The MitoPlate I-1 measures sensitivity of the mitochondria to 22 diverse mitochondrial inhibitors. Rate of energy production measurements are made and analysed using Biolog's OmniLog instrument and companion software. The plates can also be read using any microplate reader that offers kinetic reading capability, thus making the assays accessible to most laboratories.

The products further expand Biolog's broad portfolio with permeabilised cell mitochondrial assays. All of these assays can be read on the versatile OmniLog instrument.

***Cell Biosciences Pty Ltd***
***www.cellbiosciences.com.au***

## Sequencing solution

The Illumina Nextera Flex for Enrichment is a fast and flexible targeted sequencing solution for DNA.

Combining the Nextera DNA Flex bead-based transposome technology with a single hybridisation enrichment workflow, users can get a comprehensive and extensible menu of content.

The solution supports a broad DNA input range (50–1000 ng) and multiple sample types, including blood, saliva, genomic DNA, and formalin-fixed, paraffin-embedded (FFPE) tissue.

Other features include: 6.5 h turnaround time and 2 h hands-on time; compatible with FFPE samples; oligo pool agnostic — work with custom panels, fixed panels and whole exome panels; works with all Illumina sequencing systems and optimised specifically for high-throughput systems.

***Illumina Australia Pty Ltd***
***www.illumina.com***

## 125L universal oven

The IKA 125L universal oven can be used for tempering, drying, ageing and heating tasks up to 250°C.

The design and material composition maximise the internal to total volume ratio allowing the user to fully use the unit. The fast heat-up time and temperature regulation provide reproducible results when in use.

The clear LED display with well laid out menu makes the unit easy to operate. The USB interface allows remote control use of the unit and the ability to record all test parameters.

The oven features a stylish glass door and a variety of accessories — including additional trays, temperature sensors and an assortment of trolleys — are available to complement the unit.

Other features include: timer, alarm and an adjustable temperature limiter.

***Labtek***
***www.labtek.com.au***

## $H_2O_2$ assay

The Cayman Hydrogen Peroxide Ratiometric MaxSpec Kit for mass spectrometry helps overcome the difficulties of directly measuring mitochondrial $H_2O_2$ in vivo.

The kit includes MitoB, MitoP and their respective deuterated standards (MitoB-d15 and MitoP-d15), plus a detailed protocol to determine the MitoP/MitoB ratio by LC-MS/MS in cell culture and animal models. MitoB (MitoBoronic Acid) is taken up specifically by polarised mitochondria and accumulates in the matrix. The selective reaction of the arylboronic acid moiety of MitoB with $H_2O_2$ forms the phenol product MitoP (MitoPhenol). Therefore, the increase in the MitoP/MitoB ratio over time indicates the level of mitochondrial $H_2O_2$. The ratio of MitoP/MitoB is measured in sample extracts by LC-MS/MS using deuterated internal standards to correct for extraction and detection variations.

Each compound in the kit is formulated as a ready-to-use, quantitative solution to streamline sample and standard preparation for mass spec analysis. These formulations are guaranteed to meet rigorous quality standards, ensuring consistency and reproducibility from run to run.

***Sapphire Bioscience***
***www.sapphirebioscience.com***

## Hygienic pressure, level and temperature transmitters

Emerson is now offering a line of Rosemount transmitters that support features required by most hygienic applications, but in a more compact form factor.

The Rosemount 326P Pressure, designed for improved efficiency and safety, is used for hydrostatic level measurement on fermenter tanks, storage tanks and silos, as well as static pressure measurements on pipes or near pumps to ensure line pressures are in tolerance.

The Rosemount 326T Temperature and Rosemount 327T Temperature, designed for improved product quality and consistency, monitor process temperature, an important factor in all steps of food and beverage processing such as fermenting or pasteurisations, storage tank temperature or ensuring clean-in-place processes are within FDA approved limits for an effective cleaning cycle.

The Rosemount 326L Level, designed to keep product lines running and reduce downtime, will monitor continuous level in small- to medium-sized storage, holding or buffer tanks.

All comply with 3-A and FDA specifications and are available with nine common industry process connections to ensure the right fit for new tanks and pipe fittings, as well as capability to be retrofitted on legacy systems. The small transmitters also can be mounted in tight locations common on packaging machinery. Conventional 4–20 mA outputs and IO-Link connectivity make the transmitters easy to integrate with automation systems.

***Emerson Automation Solutions***
***www.emerson.com/en-au/automation-solutions***

## Microscope

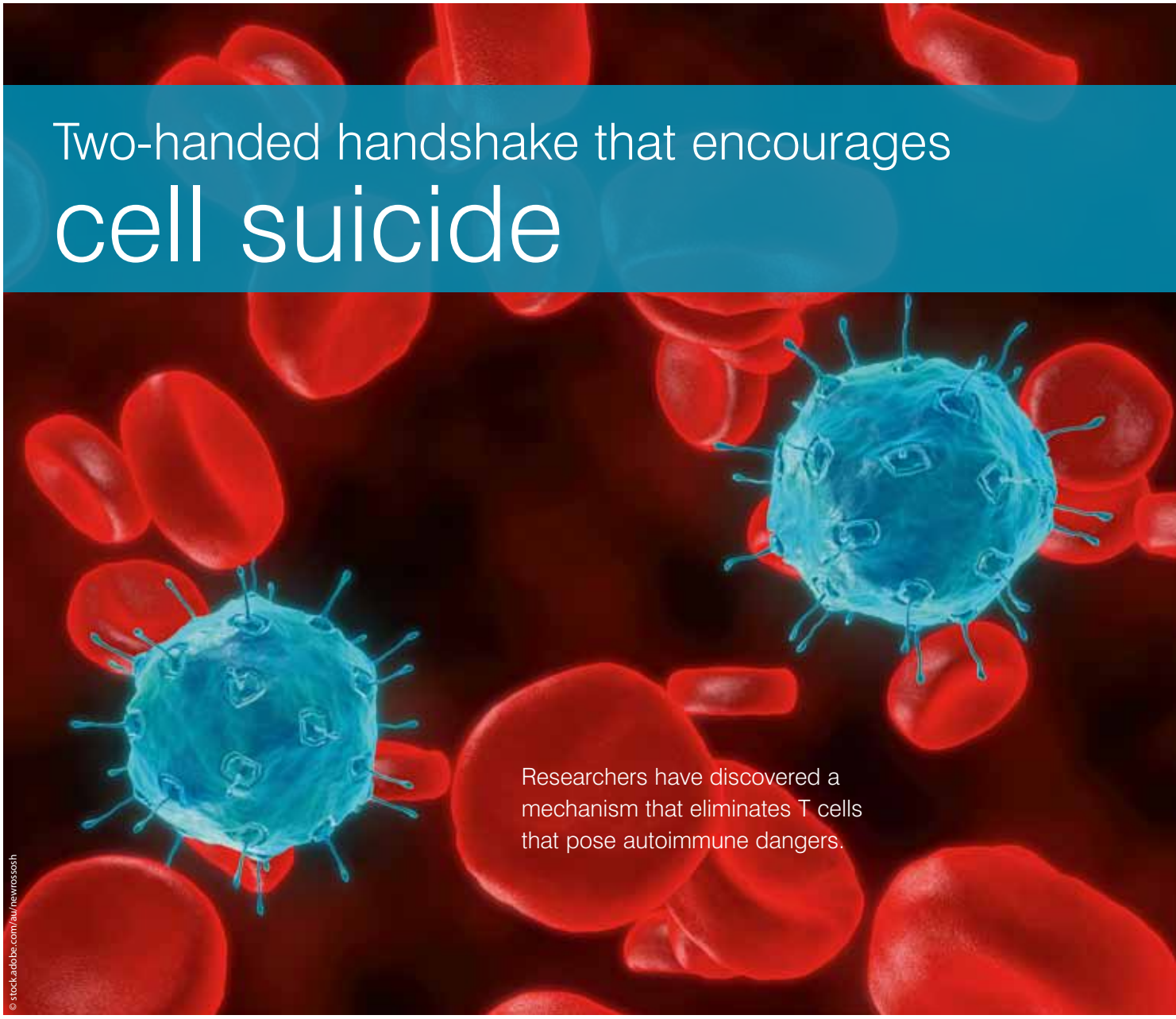
The Leica Microsystems DM6 M LIBS microscope allows users to identify the microstructure composition of interest, then trigger the LIBS analysis with a single click.

The LIBS module turns a Leica optical microscope into a 1-step solution that combines visual inspection and chemical analysis right at the user's workspace. It helps perform advanced material analysis faster because it requires no sample preparation nor transfer; no system adjustment; and no relocating the region of interest (ROI).

Other features include: surface contamination or coatings can be easily removed; chemical mapping and micro-drilling are further analytical steps; easy one-click handling; examine exactly what you see via the eyepieces or camera with a single click for fast and simple identification and interpretation; no additional expertise by the operator required; no risk of losing the link to the area of interest when transferring the sample to other devices.

***Leica Microsystems Pty Ltd***
***www.leica-microsystems.com***

# Two-handed handshake that encourages cell suicide



Researchers have discovered a mechanism that eliminates T cells that pose autoimmune dangers.



Although the mechanisms are intertwined with biochemical processes, they also work mechanically, grasping, tugging and clamping, according to Georgia Institute of Technology researchers, who measured responses to physical force acting on these elimination mechanisms.

The mechanisms' purpose is to make dangerously aggressive, developing immune cells called thymocytes kill themselves to keep them from attacking the body, while sparing healthy thymocytes as they mature into T cells. Understanding these selection mechanisms, which ensure T cells aggressively pursue hordes of infectors and cancers but not damage healthy human tissue, could someday lead to new immune-regulating therapies. The study was published in the journal *Nature Immunology*.

## Two-handed handshake

Usually, researchers pursue such mechanisms using chemistry experiments, but Georgia Tech's Cheng Zhu, who led the study, makes atypical discoveries via physical experiments to observe effects of forces between key proteins in living cells.

"Experiments where the proteins are isolated and used in chemical reactions in vitro miss this force dynamic," said Zhu, a Regents Professor in the Wallace H. Coulter Department of Biomedical Engineering at Georgia Tech and Emory University. "Before our work, force was not considered as a factor in thymocyte selection and now it is."

In this study, they discovered a loop of physical signals resembling a double-handed handshake that encourages cell suicide. It is described in further detail below.

## Thymocyte death gauntlet

Like blood cells, human thymocytes are born in bone marrow, but they travel to the thymus, a small organ just below the neck, where they run a gauntlet of selection tests. Failing any one selection means death by cell suicide; passing all selections promotes thymocytes to T cells that depart the thymus to battle our bodies' foes.

One selection checks T cell receptors (TCR), which are on the thymocyte's membrane, to ensure they are properly formed then to see if they recognise self-antigens, ie, molecules that identify

The researchers also made the novel discovery that CD8's handshake participation constitutes a signal coming from inside the thymocyte back out to the self-antigen in answer to its initial signal.

the body's own cells. Then another selection, called negative selection, tests TCRs to make sure they don't react too aggressively to self-antigens.

Cells that pass these checks then have TCRs that tolerate self-antigens yet react to enemy antigens.

"You don't want the cells with strongly grabbing receptor sites to turn against the body itself," said Zhu, whose study focused on negative selection.

## Self-antigen shakes

In negative selection, other cells extend self-antigens on their membrane to interact with the thymocytes' T cell receptors. Those interactions seal the thymocytes' fate — advance or die.

Studying forces in those interactions revealed a new signalling loop with mechanical properties analogous to a two-handed grip and tug by the thymocyte.

The first hand would be the T cell receptor itself, and the other cell presenting the self-antigen would be like someone else's hand holding a special ball out to the T cell's first hand. The handshake begins as the self-antigen gives a signal to the T cell receptor.

If the TCR reacts too strongly to the self-antigen, the thymocyte adds the second, assisting hand coming in from the side to make a two-handed handshake. The additional hand is a lever called CD8 (cluster of differentiation 8), which connects to key mechanisms inside the thymocyte and is considered part of the TCR site.

## Suicide handshakes

For about two weeks in the thymus, multiple T cell receptor sites engage in one- or two-handed handshakes, which send signals into the thymocyte that make it either mature into a T cell or commit suicide.

The researchers found that the two-handedness markedly resisted the force applied to break the grip between the T cell receptor and the self-antigen, thus prolonging the duration of the handshake. A long grip sent signals for the thymocyte to die.

"That's the study's elegant finding," Zhu said. "That the force is significant for the selection to work."

## New signalling loop

The researchers also made the novel discovery that CD8's handshake participation constitutes a signal coming from inside the thymocyte back out to the self-antigen in answer to its initial signal. "The inside-out return signal had not yet been reported for this T cell receptor," Zhu said.

Together, the outside-in and inside-out signals create a feedback loop that perpetuates the handshake — self-antigen touches receptor; receptor fires signal into cell and interacts with self-antigen too aggressively; inside cell membrane, signal pulls CD8 closer; outside cell membrane, CD8 strengthens handshake; when the self-antigen slips a bit, the double-handed grip can coax it back into the receptor, kicking off another signal, restarting the signalling cycle again and again; many feedback loops trigger cell suicide.



## Particle size analyser

With a range that spans 0.01 to 3500 microns, the Malvern Mastersizer 3000 is designed to deliver precise wet and dry particle size measurements. Intelligent software guides users through every stage of a measurement, allowing new or experienced particle sizing professionals to make measurements and get the information they need quickly and easily.

A new range of wet and dry dispersion accessories opens up more applications than ever before. The Hydro Sight is a lens-less dynamic imaging accessory that supports method development and troubleshooting by providing real-time visualisation of liquid particle dispersions. The Hydro SV wet dispersion unit is particularly useful where the amount of sample available for analysis is limited. The Aero M dry powder disperser has been specifically designed to provide reproducible dispersion of a wide range of samples, from cohesive powders to fragile materials.

For those that do not need the advanced functionality that the Mastersizer 3000 offers, Mastersizer 3000E offers an entry-level option that can be upgraded as required.

***ATA Scientific Pty Ltd***
***www.atascientific.com.au***

## Electron probe microanalyser

CAMECA has announced the SXFive-TACTIS microanalytical instrument — an electron probe microanalyser (EPMA) with a touch-screen interface. The product is designed to meet a growing demand from multi-user research facilities for instrumentation that combines sophisticated analytical options with ease of use.

Users can choose between two tool operation modes. In beginner mode, the instrument configuration and operation, as well as basic imaging and data processing, are made easy with an intuitive touch-screen interface that gives immediate access to a wealth of simplified options. In expert mode, the interface is designed for skilled users who can benefit from a full complement of different tool parameters and software options.

Among the other technological advances are an additional backscattered electron (BSE) detector for enhanced imaging especially at low voltage; a fully integrated energy dispersive spectroscopy (EDS) hyper-mapping module for ultrafast quantitative analysis; and the capability to acquire real-time wavelength dispersive spectroscopy (WDS) and EDS X-ray images. The instrument can be fully remote controlled, allowing users to run experiments from their smartphones, tablets or any remote computer.

The EPMA platform is available with a W, LaB6 or field-emission source. CAMECA has optimised the performance for challenging microanalytical applications at a sub-micron spatial resolution, extending EPMA capabilities to smaller analysed volumes.

Equipped with high-precision spectrometers for good reproducibility, the product delivers high-quality minor and trace element analysis, addressing demanding analytical tasks in mineralogy, geochronology, ore discovery and nuclear science, as well as research in materials, metals, thin films and semiconductors.

***AMATEK DESIGN***
***www.amatek.com***

James O'Brien


# Using automation to fast-track commercialisation

When it's time to move biotechnology breakthroughs towards commercialisation, specific application workflows may require a custom approach to lab automation. If the requirements are non-standard, no off-the-shelf products may be available for comparison and testing. Even custom configuration of off-the-shelf components may not be suitable. In that case, what would be the ideal approach for finding a custom solution that meets the requirements?

The solution is to use a defined process that ensures each step is thoroughly explored and evaluated. Consider these four 'I's' of custom engineering — investigate, ideate, invent and integrate. Working through a defined process that includes investigation, idea generation, invention and integration followed by comprehensive validation on delivery can help ensure users have a custom lab automation system that does exactly what is required.

## Investigate

This is the first and most critical step. When doing something that hasn't been done before, the user may have unique performance requirements, ambitions, constraints and concerns that the lab automation system must address. How will all of these challenges be solved? Whether the custom lab automation system is being developed internally or through an automation partner, the investigation should begin with listening. The process should allow all stakeholders to discuss and understand the full scope of exactly what is needed. If done well, it will result in a carefully specified list of requirements for a project and a detailed project plan that provides complete transparency into the decision-making process.

## Ideate

There can be more than one way to solve a problem. Brainstorming is one of the most effective ways to involve the whole team and get lots of ideas on the table. A brainstorming session for a lab automation solution is likely to be highly productive with a team that not only involves experts in life science and lab automation engineering, but also creative thinkers and inventors. This way, the team can bring together their collective knowledge to carefully consider all concepts, even combining elements from different ideas to create the optimal design for your custom-engineered lab automation system.

## Invent

It is possible that some elements required to automate the workflow might not exist. Off-the-shelf components that were designed for other purposes may not be suitable for your purposes, even with customised configuration. A lab's revolutionary breakthrough may require innovation. Depending on the nature of the unmet need and a team's internal expertise, a partner who is willing and able to develop and deliver new software, hardware or processes may be required.

## Integrate

An optimum custom lab automation solution might include standard products, invented components, new software elements and unique workflows. All of these elements must work smoothly together with the components and protocols. The development process should include performance validation of the complete integrated system both in your partner's facility and in your own lab.

Thorough testing along with documented procedures and performance will help to ensure that the lab automation system upholds the defined specifications, giving confidence that it will deliver reliable performance while the workflow is optimised.

## Taking time can save time

Successful development of a complex integrated lab automation solution requires clear definition and understanding of the end goal, expert creative thinking and a well-planned process to get there. Taking time to work through the four I's — investigation, idea generation, invention when needed and integration — can help to ensure successful validation and avoid multiple iterations so that the biotech breakthrough can be brought to the market with the right specifications, on time and on budget.

Tecan's Labwerx dedicated multidisciplinary teams of life scientists, engineers and software experts can help researchers through the four I's to design a custom lab automation solution from concept to completion.

*Tecan Australia*
*www.tecan.com.au*

## Desktop SEM with FEG source

The Thermo Scientific Phenom Pharos desktop scanning electron microscope (SEM) is said to be the first desktop SEM solution that includes a field emission gun (FEG) source to deliver crisp, high-brightness images.

The product offers floor model performance on a desktop microscope with loads of added benefits that make it easy to operate for any user. Suitable for a wide range of academic and industrial applications, the device covers material characterisation, metallurgy analysis, forensic investigation, process control, pharmaceutical and industrial research, and more.

As with every Phenom desktop SEM in the series, the Phenom Pharos maintains the signature functionality for speed and ease of use, providing access to sharp, high-contrast SEM imaging with minimal training. The intuitive user interface includes an optical colour microscope for a 'never lost' sample navigation while the venting/loading mechanism is designed to provide the fastest vent/load cycle for high throughput.

Advanced detectors (BSD and SED) can acquire high-quality images in less than 25 s after inserting the sample into the system, with magnifications of up to one million times and resolutions below 3 nm. In addition, fully integrated X-ray analysis (energy dispersive spectroscopy, EDS) allows users to quickly identify and assess the distribution of elements in a sample.

***ATA Scientific Pty Ltd***
***www.atascientific.com.au***

## Vacuum pumps

The Welch CRVpro vacuum pumps are suitable for use in life sciences and biotechnology research applications such as Schlenk lines, freeze dryers, vacuum concentrators, HVAC applications, degassing, vacuum ovens, glove boxes and mass spectrometers.

The pumps feature gas ballast, forced oil lubrication, anti-suck-back valve mechanism, thermal overload protection and low noise level.

Benefits include: reduced risk of chemical attacks and oil breakdown by diluting chemical vapours with a larger oil chamber; slowing down corrosion by cool running operation; provides a measure of protection from sublimed chemical vapours with coating on pump module and oil case; less oil consumption by cool running operation; and extended usability of oil due to high dilution effect by a larger oil chamber.

***AVT Services Pty Limited***
***www.avt.net.au***

## Class 1 ductless workstation

The MicroFlow III is a Class 1 ductless carbon filtered workstation, equipped with particle pre-filter and activated carbon filtration. It is suitable for fumes, odours and non-hazardous chemical vapours. Measuring 61 x 53 x 61 cm, the unit is completely self-contained with an integral recessed work surface to contain spills.

A convenient clear viewing sash surrounds the work area for user protection. The sash can be conformed for use with a microscope and is easily removable. Variable speed fan control allows for high-speed airflow through the sash opening, or medium and low flow for sensitive operations.

Typical applications include: sample weighing; general chemistry involving small volumes of common chemicals; individual workstations; tissue staining and processing; gluing and drying operations; solvent cleaning of electronic parts; soldering fumes and odours; school demonstration workstations; and containment of forensic applications. The hood is available with a mobile table.

***HEMCO Corporation***
***www.hemcocorp.com***

## Antibody

Leica Biosystems' PD-L1 BOND antibody is designed for use on the company's fully automated BOND IHC and ISH staining platform.

The PD-L1 (programmed death - ligand 1) antibody uses the MKP1A07310 (clone 73-10) expressed by Abcam on behalf of Merck KGaA, which owns all IP rights to this antibody. It joins the ALK (anaplastic lymphoma kinase) antibody as the latest addition to Novocastra's growing lung menu of primary antibodies.

Leica Biosystems has optimised these two clones into a ready-to-use format for use on the BOND IHC and ISH staining platform. This allows labs to perform ALK and PD-L1 testing on the BOND system with rapid turnaround times, reliable staining and walk-away convenience.

***Leica Microsystems Pty Ltd***
***www.leica-microsystems.com***

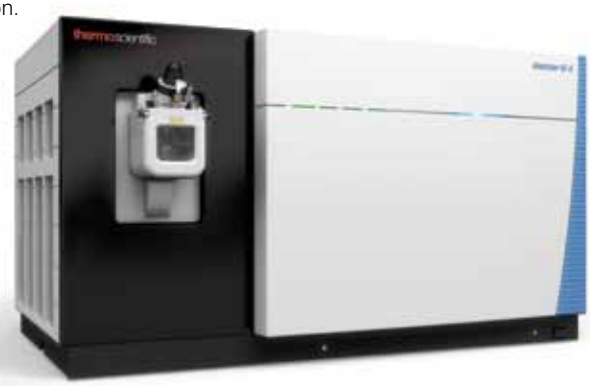
## Mass spectrometry software

Pharmaceutical scientists are now able to overcome challenges associated with the identification and characterisation of small molecules and their fragments with Thermo Scientific Mass Frontier 8.0 software, which quickly translates complex data into actionable, sharable knowledge.

The software enables analysts to rapidly deconvolute and search information-rich, MSn mass spectrometric data produced during the identification and structural characterisation of small-molecule unknown compounds and their fragments. Through its powerful algorithms and fully curated knowledge databases of spectral and fragmentation data that covers 95% of all published fragmentation pathways, the software is designed to accelerate small-molecule characterisation.

The software enables scientists to go from complex data to actionable, sharable insights by: making unknowns known through searching deconvoluted components against mzCloud, a comprehensive mass-spectral database; providing access to a fragmentation library of more than 52,000 schemes, all of which are curated from peer-reviewed scientific papers; offering access to the Metabolika biological pathway database, providing 370 curated biochemical pathways with annotated reactions and corresponding metadata for various organisms; and constructing, storing and managing spectral libraries using the Data Manager software, providing the ability to share this knowledge across a network or organisation.

In combination with the Thermo Scientific Orbitrap ID-X Tribrid Mass Spectrometer supporting the Thermo Scientific AquireX intelligent MSn data acquisition strategy, the software can be used to capture low-abundance analytes through streamlined data analysis and mass spectral prediction tools. This eliminates the labour-intensive and time-consuming steps analysts face when identifying small molecules and their respective fragments using traditional solutions, providing insights, understanding and confidence when turning data into actionable knowledge.



***Thermo Fisher Scientific***
***www.thermofisher.com.au***


## Intensified 16-bit sCMOS camera

PCO has released the pco.dicam C1, said to be the first camera to combine a high-resolution 25 mm image intensifier with a 16-bit (4.2 MP) sCMOS sensor via an ultra-efficient tandem lens. The product delivers enhanced extinction ratio gating and has the ability to detect individual photons at the short exposure times of 3 ns–1 s.

The pco dicam C1 camera has the capacity to achieve 104 fps at full resolution (2048 x 2048 pixels) while ensuring an ultralow readout noise of 1.1 e- (said to be the lowest readout noise of any gated intensified camera system). It incorporates a high-speed tandem lens to deliver high-quality images with high transmission efficiency. Camera Link HS ensures uncompressed and secure data transfer. The latest standard of high-performance data interfaces enables the bridging of long distances via fibre-optic cable. F-mount, C-mount or EF-mount with lens control is available.

The camera has a host of different applications in the fields of life science and industrial science, including laser-induced incandescence (LII) shock wave physics, laser-induced breakdown spectroscopy (LIBS), particle image velocimetry (PIV), time-resolved spectroscopy, plasma physics, laser-induced fluorescence (LIF), ballistics and combustion.

***SciTech Pty Ltd***
***www.scitech.com.au***

## High-performance circular dichroism (CD) spectrophotometers

CD spectroscopy is generally considered an essential tool for the secondary structure analysis of proteins, particularly in the UV region below 260 nm. While synchrotron radiation is an effective method to measure the CD spectra of protein film samples in the vacuum-UV region, it requires access to a limited number of facilities.

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

Based on over 50 years of experience, the Jasco J-1000 series includes the J-1100 CD spectrometer, designed for routine, conventional CD applications in a compact package; the J-1500 CD spectrometer, designed as a multipurpose, flexible system with a wide dynamic range to meet demanding CD applications with high sensitivity; and the J-1700 CD spectrometer, designed for more demanding near-infrared CD applications such as magnetic CD and covering the wavelength range from UV, visible and NIR up to 2500 nm.

***ATA Scientific Pty Ltd***
***www.atascientific.com.au***


## Antimicrobials 2019
## February 21–23, Sydney

**The Australian Society for Antimicrobials 20th Annual Scientific Meeting, Antimicrobials 2019, will cover many different aspects of antimicrobials. The scientific program of the conference will include the themes Gene Editing, RNA Biology and Drug Discovery. The event will feature a number of overseas plenary presentations, society speciality lectures, poster sessions, 3-minute poster presentations and an E/MCR mini-symposium. Confirmed plenary speakers include Lingling Chen and Tom Blundell. Sessions include: Difficult to treat populations (Science and immunology); Difficult to treat/ID organisms (Laboratory and technical aspects); Technology and antimicrobial resistance; Where humans and animals collide; and AMR testing update.**
**http://www.antimicrobials2019.com**

**The 9th Australian Colloid & Interface Symposium**
February 3–7, 2019, Tasmania
https://acis.wildapricot.org/events

**24th Lorne Proteomics Symposium 2019**
February 7–10, Lorne
www.australasianproteomics.org.au

**44th Lorne Conference on Protein Structure and Function**
February 10–14, Lorne
www.lorneproteins.org

**31st Lorne Cancer Conference**
February 14–16, Lorne
www.lornecancer.org

**40th Lorne Genome Conference 2019**
February 17–19, Lorne
www.lornegenome.org

**Australian Poultry Science Symposium**
February 17–19, Sydney
www.apss2019.com.au

**Lorne Infection & Immunity Conference 2019**
February 20–22, Lorne
www.lorneinfectionimmunity.org

**Antimicrobials 2019**
February 21–23, Sydney
http://www.antimicrobials2019.com

**Hunter Cell Biology Meeting 2019**
March 18–22, Hunter Valley
http://www.huntermeeting.org.au/

**4th International Conference on Plant Science and Physiology**
March 25–26, Sydney
http://aip.org.au/event/4th-international-conference-on-plant-science-and-physiology/

**ASID Annual Scientific Meeting 2019**
May 16–18, Darwin
https://www.asid.net.au/meetings/asid-annual-scientific-meeting-2019

**AMOS-ICTMO 2019**
June 11–15, Darwin
https://www.amos.org.au/event/amos-ictmo-2019/

**International Conference on Cytochrome P450**
June 23–27, Brisbane
https://my.vanderbilt.edu/p450meetings/

**42nd MERGA Conference – 2019**
June 30–July 4, Sydney
http://www.promaco.com.au/events/MERGA/

**AMSA 2019: Marine Science for a Blue Economy**
July 7–11, Perth
http://amsa19.amsa.asn.au/

**The 2019 Australian Genomics National Conference**
September 5–6, 2019, Melbourne
https://www.australiangenomics.org.au

**ASBMB 2019**
October 1–3, Perth
https://asbmb2019.com.au/

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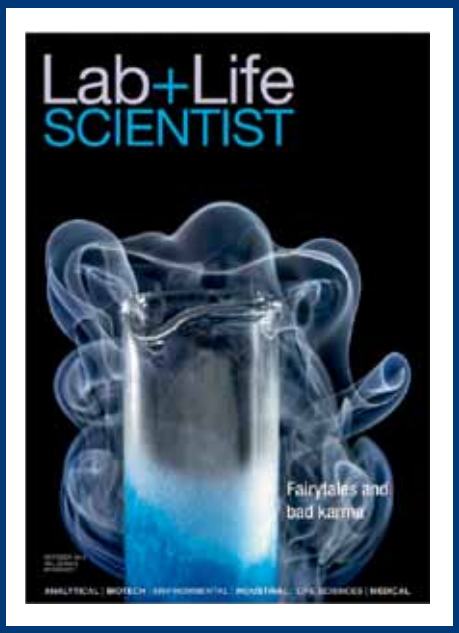


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