Lab+Life SCIENTIST

THE ROAD TO REPRODUCIBLE RESEARCH

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ANALYTICAL | BIOTECH | ENVIRONMENTAL | INDUSTRIAL | LIFE SCIENCES | MEDICAL

The special gases game has changed, and so have we.

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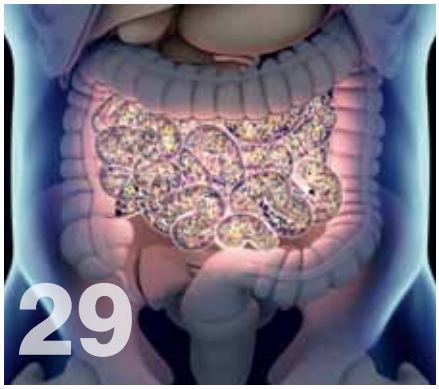

Just when I was wrapping up the April/May issue of *Lab+Life Scientis*t, a scientific paper was retracted. In May last year, a controversial study by scientists from Stanford, the University of Iowa and Columbia University claimed that CRISPR-Cas 9 could produce a number of unexpected mutations. The scientific journal *Nature* that published the paper recently retracted it saying there was insufficient data to support the claim.

The development not only highlights that CRISPR is a young research field but also reminds us about the need to improve rigour and reproducibility. Science's reproducibility problem is not new, but everybody is talking about it and efforts are being made to address the issue.

To learn about the causes of reproducibility and get some insights into how we could reduce irreproducibility, we interviewed two industry experts — Dr C Glenn Begley, the man behind the 2012 paper on reproducibility, and Dr Leonard Freedman, founding president, Global Biological Standards Institute. To read the article, go to page 10.

Quality assurance and biotech are two main themes in this issue. In the biotech article (page 18), experienced life sciences/biotech investment expert Dr Katharine Giles sheds some light on the current trends and developments in the industry and where it's headed. Dr Giles was recently recognised in the 2018 40under40 Business News Awards for her work in the medical and investment fields, and for educating and inspiring the medical innovation community of Western Australia.

There is also an article on quality control of alcoholic beverages (page 22). Scientists have developed optoelectronic noses to identify counterfeit liquor. The noses are based on colorimetric sensor arrays, which make use of the chemical diversity available in molecular sensors (specifically, chemically responsive dyes).

This issue also features what is claimed to be the world's first modular hearing aid, Facett, developed in Australia. The breakthrough took 130 prototypes to get right and saw RMIT University lecturer Leah Heiss spend 37 weeks embedded with the company behind the device, Blamey Saunders Hears. In another local success story, researchers at the Gold Coast Health and Knowledge Precinct (GCHKP) have used a 3D computer-simulated biomechanical model and an electroencephalogram (EEG) to stimulate movement — and eventually recovery — in quadriplegics. But that's not all. This issue features a number of articles on latest technologies and industry developments, as well as new product editorials. I hope you enjoy this issue of *Lab+Life Scientist* as much as I enjoyed putting it together for you.

Regards,
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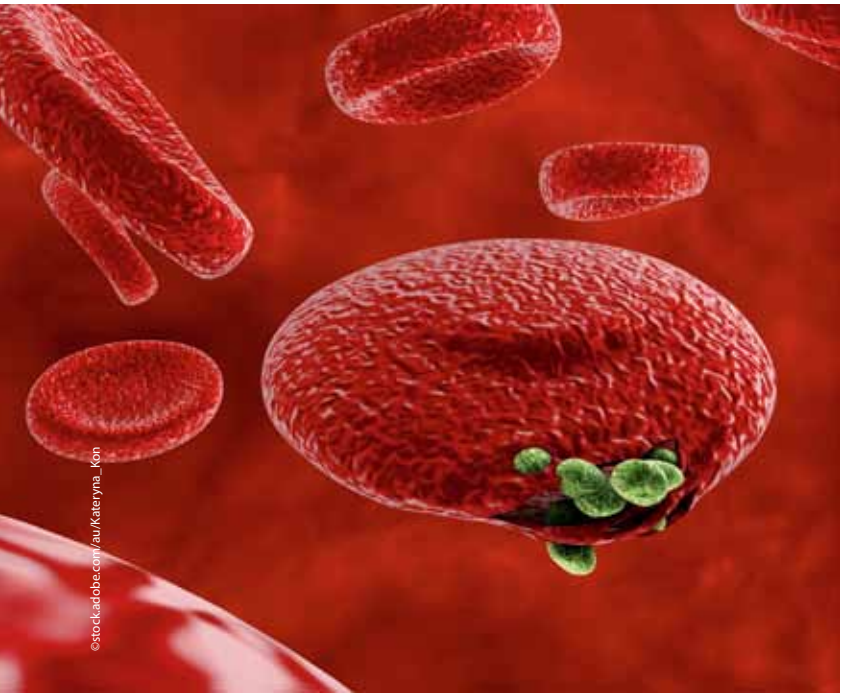

The gene mutation that wards off malaria

Scientists at The Scripps Research Institute (TSRI) have led new research into a genetic mutation that may protect people from malaria, shedding light on how humans who live in close quarters with malaria-carrying mosquitoes may evolve defences against the disease.

Writing in the journal *Cell*, the researchers explained that a mutation in the gene PIEZO1, which codes for a pressure-sensing protein, was found to dehydrate red blood cells. In a mouse model, this mutation made it harder for the malaria parasite *Plasmodium* to infect red blood cells and cause cerebral malaria (a severe neurological complication of *Plasmodium* infection).

"This study is a good example of a host/pathogen arms race playing out in real time — this time with the host a likely winner," said Kristian Andersen, an assistant professor at TSRI and co-author on the study.

This red blood cell dehydration condition, called hereditary xerocytosis, is uncommon in non-African populations and had never been the focus of a large-scale analysis — so the researchers were surprised to find it could be present in one in three people of African descent. Their findings suggest the mutation is much more common in areas where people have lived alongside selection pressure from malaria.

The PIEZO1 mutation is not the first adaptation linked to malaria resistance; people of African descent are also more likely to have a genetic condition called sickle cell anaemia, which makes it harder for *Plasmodium* to enter their red blood cells. Going forward, Andersen said, large-scale genomic association studies will be needed to confirm the PIEZO1 mutation's role in malaria resistance.

Study leader Ardem Patapoutian added that his lab plans to learn more about the biological role of PIEZO1 and how mutations in the protein could affect other health conditions. Indeed, PIEZO1 as a pressure sensor is important for cardiovascular development and function, and its deletion is proposed to cause hypertension.

"The fact that we have a mouse model will make it seamless to test mechanisms behind any association we find in humans," Patapoutian said.

Trapping the protein servants of drug-resistant bacteria

Researchers from Belgium's VIB, KU Leuven and UZ Leuven have devised a novel approach to developing antibacterial drugs, in a breakthrough that is set to combat the rise of antibiotic resistance.

A key contributor to antibiotic resistance is that most antibiotics today work according to only a few mechanisms of action, so when a bacterium becomes tolerant to one drug, it often becomes tolerant to the whole family. To solve this situation, scientists need to develop an entirely new class of drugs that shares no structural or mechanistic similarities with the existing antibiotics.

Professors Joost Schymkowitz and Frederic Rousseau of VIB-KU Leuven, in collaboration with Professor Johan Van Eldere of University Hospitals Leuven, have gone one step further: they have developed a new way of designing antibiotic drugs that can give rise to many new antibacterial molecules. Described in the journal *Nature Communications*, the drugs are designed to penetrate bacterial cells, where they induce a process called protein aggregation.

This process resembles what happens when boiling an egg, but now without heat: proteins that normally need to carry out essential functions for the bacteria — such as digesting their food — clump together and can no longer carry out their work. As this affects many proteins in the bacterial cell all at once, the bacteria rapidly succumb and die.

The scientists reveal novel molecules with a strong antibacterial (bactericidal) activity against Gram-negative bacteria. They found the approach was effective against drug-resistant clinical isolates of *Escherichia coli* and *Acinetobacter baumannii*, reducing bacterial load in a murine bladder infection model.

The technology will now be further explored and exploited by biotech start-up Aelin Therapeutics, recently founded by VIB, KU Leuven, VUB and UGent. The company plans to use the study findings to generate many more antibacterial molecules, with the aim of targeting a wide array of diseases.

New brew of beer holds the hops, keeps the flavour

How would you like to try beer that costs less and has a more consistent flavour? US scientists may have come to your rescue, engineering brewer's yeast to produce two molecules that are partly responsible for the hoppy flavour in beer — with no actual hops necessary.

The flowers of the hop plant are an essential ingredient in beer, providing its bitter taste as well as a distinctive floral aroma. They are, however, a very water- and energy-intensive crop — one that can vary considerably in essential oil content due to a combination of genetic, environmental and processing factors. This makes it challenging for brewers to achieve a consistent hoppy taste in their product.

Researchers led by the Lawrence Berkeley National Laboratory engineered brewer's yeast to increase production of linalool and geraniol — two molecules found in essential oil which have been identified as primary flavour determinants in hops. The authors did this by incorporating DNA from mint and basil into strains of brewer's yeast.

Published in the journal *Nature Communications*, the study results indicate that the engineered strain can give rise to the hoppy flavour in beer. In double-blind sensory taste tests involving 40 participants, the authors found that the engineered strain produced beer with a greater hoppy flavour than regular dry-hopped beer.

The authors note that although linalool and geraniol confer hop flavour to beer, the full flavour imparted by traditional hopping is likely to rely on a more diverse set of molecules. Nevertheless, their initial results are promising, with the scientists writing that their methodologies "provide a foundation for generating more complex yeast-derived hop flavors, and broaden the possibilities of yeast-biosynthesized flavor molecules to those throughout the plant kingdom".

Lab-grown kidneys a step closer

Chronic kidney disease is rising in incidence by 6% a year and costs the Australian economy $1 billion a year. It is estimated by Kidney Health Australia that 1 in 10 Australians will show evidence of chronic kidney disease by 2020, but only 1 in 4 patients will receive a transplant. Hence, there is an acute need to develop new therapies.

In 2015, the Murdoch Children's Research Institute's (MCRI) Professor Melissa Little and her team grew kidney tissue from stem cells that can be used in drug screening and disease. Researchers across the world now use this method.

Now, Australian and Dutch researchers have moved a step closer towards making human kidneys from stem cells.

The research — by the MCRI, University of Melbourne and Leiden University Medical Centre (LUMC) in The Netherlands — is part of a regenerative medicine project in which human stem cells are used to develop kidneys with functioning tissue as an alternative for renal replacement.

"The mini-kidney we have grown in the laboratory has all the different cell types and structures found in a 'real' kidney, but so far we haven't managed to properly attach the blood vessel system in a culture dish and achieve sufficient maturation of this kidney tissue," said LUMC researcher Cathelijne van den Berg.

In this new research, published in *Stem Cell Reports*, the research teams transplanted the stem-cell derived kidney organoid under the protective layer surrounding the kidney of a living mouse. They were able to see blood flow through the filtration units of the human kidney organoid by making this tissue using gene-edited stem cells lines of different colours. This also helped them to discover connections between the blood vessels of the mouse and the human kidney tissue. After four weeks of transplantation, the kidney tubules and blood vessels showed evidence of fully developed adult kidney tissue.

"The fact that we can make kidney tissue from human stem cells and have this develop into mature kidney tissue after transplantation is a very promising step towards developing this further for treatment," said Professor Melissa Little from the Murdoch Children's Research Institute.

"There is a long way to go to make the tissue large enough for treatment, but knowing that it will begin to function is an important step along the way," said Professor Little.

BOC to locally produce over 8000 specialty gases

Australia's manufacturing industry has had a big vote of confidence from the global gases and engineering company The Linde Group with a $35 million investment at its manufacturing site in Western Sydney.

BOC Australia, part of The Linde Group, has unveiled a new $20 million specialty gases production facility and $15 million robot cylinder automation system at its Sydney Operations Centre in Wetherill Park.

The new specialty gases facility will increase BOC's capacity to locally produce and supply over 8000 high-purity and specialty gases to many high-value industries in Australia — from science and medical research, to manufacturing and energy exports, said John Evans, BOC South Pacific Managing Director.

Image courtesy of BOC

The upgrade will allow BOC to displace imported products and service the Australian as well as the Asia–Pacific market via its Sydney facility.

"With leading-edge laboratory technology and a highly experienced team of chemists, the new facility offers the best in quality, precision and safety — allowing BOC to supply many scientific and calibration gases in almost half the time and at higher packaging pressures.

"BOC is proud to be expanding our specialty gases capability to meet future demand for high-precision gas mixtures and support Australia's vibrant research and knowledge-based economy as it continues to grow.

Embracing the era of automation, BOC also revealed a robot cylinder automation system that has transformed the way cylinders are sorted, picked and moved around the busy production site. The system, according to BOC, is a world-first application of a six-axis robot combined with four turntables that can see, pick up and handle cylinders.

Manufacturing has gone through a significant period chance and BOC, like many other companies, has had to change "what we do and how we do it", said Evans.

"The launch of this cylinder automation system is a landmark moment for BOC, driving a competitive advantage and representing a significant safety investment for the Sydney Operations Centre, which produces more than 1.3 million cylinders each year.

"Designed with global experts and local engineers, the system integrates advanced laser vision technologies, automated guide vehicles, robots and 3D cameras — which has successfully automated manual handling processes and introduced new skills of the future into BOC's workforce," added Evans.

Professor Dr Aldo Belloni, Chief Executive Officer, The Linde Group, said, "Innovation is in our DNA. The Linde Group pride ourselves on being the world leaders in innovation in the gases industry, and BOC in Australia is leading the new era of automation. With the addition of the new world-class special gases facility, the Sydney Operations Centre is not only one of the busiest production sites within the Linde Group but is now at the forefront of integration and automation in production globally."

"With increased capacity and efficient production technology, BOC's new specialty gases facility is strongly positioned to export Australian-made product to Asia's emerging electronics, manufacturing and medical markets. This will be particularly important as demand for specialty gases in the Asia–Pacific region is expected to grow significantly over the next five years," said Sanjiv Lamba, Member of the Executive Board, Linde AG, and Chief Operating Officer for Asia Pacific.

BOC has invested more than $130 million at the Sydney Operations Centre since it was opened. The site has a cylinder maintenance centre, dedicated medical gas filling facility, dissolved acetylene plant, nitrous oxide plant, specialty gases production facility and dry ice production facility.

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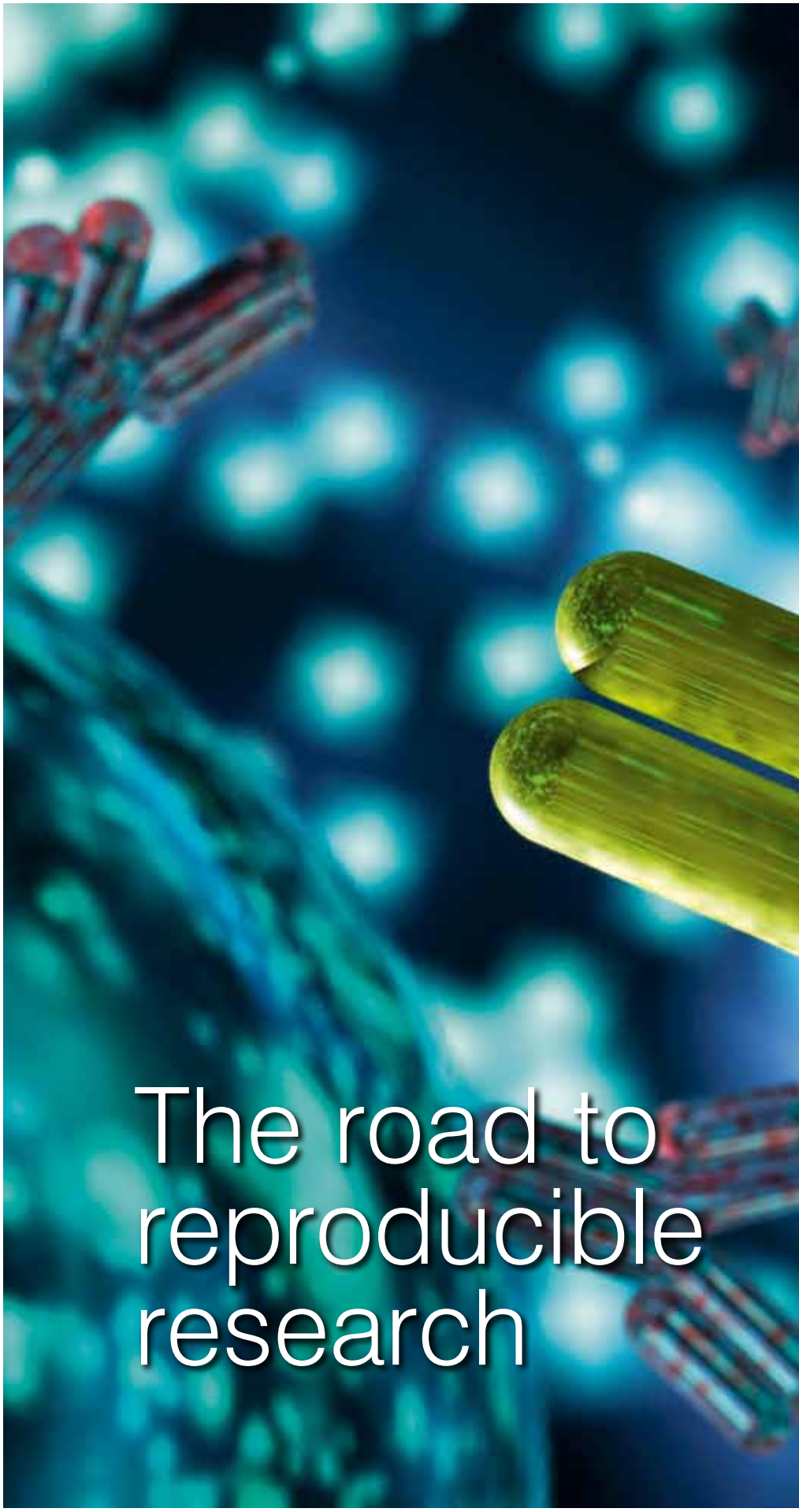
Mansi Gandhi

The road to reproducible research



The reproducibility problem has plagued biomedical science for decades, but it came into the limelight in 2012 when scientists, led by Dr Glenn Begley (former Vice President, Hematology and Oncology Research, Amgen), reported that they couldn't reproduce 47 out of 53 'landmark' publications.

When the paper was published, the scientists behind the project received threats, hate mail and were told they were "stupid and incompetent", said Begley. "When I would give a seminar there was a lot of hostility in the audience."

Six years later, things have changed. While the reproducibility problem still exists, people are now asking what they need to do to address the problem, said Begley, who is a strong advocate of rigour and reproducibility.

Journals have offered guidelines to authors with an emphasis on reproducibility. The National Institutes of Health (NIH) has rewritten its instructions to people applying for grants. Money is being invested in training students. Grants have been offered to people investigating reproducibility.

A lot has changed, but we haven't yet seen an impact of those changes, he said, quickly adding that it's probably too early to expect that to happen.

After spending 15 years in the biopharma industry in the US, Begley returned to Australia last year. Born and raised in Melbourne, Begley took up the role of CEO of BioCurate, a joint venture between Monash University and the University of Melbourne, in May 2017. Data quality and integrity are two important criteria in BioCurate's efforts to translate research from Melbourne and Monash Universities into commercial outcomes. John Brumby is the board chair of the independent company.

The combined research strengths of Monash and Melbourne Universities place them in the top 10 globally in a number of areas. The universities are in the same league as Boston University in terms of impact factor of publications but the difference in venture capital funding is

Poorly validated antibodies are a major contributor to the reproducibility problem

significant. So research judged to be of the same quality isn't receiving similar funding, said Begley.

Reducing irreproducibility

In order to enhance the quality of biomedical research, the Global Biological Standards Institute (GBSI) was launched in 2013, under the leadership of Dr Ray Cypess. In 2016 the organisation launched the Reproducibility2020 initiative, challenging industry stakeholders to improve the quality of research by 2020.

Leonard Freedman is the founding president and chief scientific officer of GBSI. The issues and drivers for irreproducibility are very complex, he said. There are issues around transparency, manipulating statistics, poor experimental design, poor methodologies and lack of validated reagents, said Freedman. It's a multifaceted issue and there isn't going to be any one quick fix, he added. The areas where action can help reproducibility include: study design and analysis; reagents and reference materials; laboratory protocols; and reporting and review, according to GBSI.

Commenting on improving reproducibility, Begley said if he could do one thing, he would insist all the experiments are blinded.

Perverse incentives

The problem is of perverse incentives, he said. For example, to receive a research grant, a researcher will need a paper in a top-tier journal. There is "no metric for quality. It's only about flashy science. It's only about something that's exciting", said Begley. We falsely believe that a publication in a top-tier journal is a measure of quality, he said.

Changes are required at multiple levels. A number of things have already begun to happen and they'll hopefully have an impact, said Begley. The development of 'mega labs', ie, labs with 50 students and postdoctoral researchers, should be discouraged in order to improve quality. It's difficult to appropriately mentor 50 people, he said.

"We need to develop some sort of metric for quality. We could have a more rigorous review system for grant application. One thing I'd like to see is people cannot submit their CV with their grant application. They can only submit the last two papers; then people would be more inclined to look at those last two papers and see if they were representing work of quality rather than something in top-tier journals."

Another thing that could help is if the names of the authors on grants applications aren't known to people reviewing papers and grants, including editors. There is very telling data from the National Health and Medical Research Council (NHMRC) indicating that women scientists do much more poorly on grant applications compared to male scientists. This reflects the intent of prejudice in our system, he said.

Antibody validation

Poorly validated antibodies are a major contributor to the reproducibility problem, said Freedman.

"Antibodies are key reagents in preclinical research for activities as diverse as protein visualisation, protein quantification, and biochemical signal disruption. Antibody performance is variable, with differences in specificity, reliability, and functionality for different types of experiments (eg, Western blotting and immunofluorescence), manufacturers, and lots, harming reproducibility," wrote Freedman and his co-authors, Gautham Venugopalan and Rosann Wisman, in the report 'Reproducibility2020: Progress and priorities [version 1; referees: 2 approved]' in 2017.

"The Antibody Validation Initiative, involving stakeholders throughout the research community and led by GBSI, is an example that could be replicated in other scientific areas (eg, both stem cells and synthetic biology are areas where a greater emphasis on development of standards and best practices are needed to ensure quality and advance discovery)," said the authors.

Stakeholder solutions include antibody databases, such as the CiteAB database, and repositories, such as the proposed universal library recombinant antibodies for all human gene products, the authors said. "In all cases, validation is a key component of the solution."

Research antibodies must demonstrate specificity, selectivity and reproducibility in the application or assay for which they are used, according to GBSI. A range of issues, including production variations, storage conditions, and improper validation techniques, can put even the best designed experiments at risk.

It typically takes Begley around 8–10 hours to read a scientific paper. Part of the time is spent checking reagents. He routinely goes back to see that the antibody being used in the experiment is recommended by the manufacturer. Begley recently found a paper where the investigators made a claim that manufacturers didn't make; ie, the investigators said that the antibody was selected for a particular protein but when he went to the manufacturer's site, he discovered that wasn't the case. Sometimes manufacturers make claims that are not substantiated. Such issues need to be addressed, insisted Begley.

Best practices and guidelines

GBSI believes that in order to accelerate the successful translation of benchside research breakthroughs into approved diagnostics and therapies, best practices and standards must be established around the development, commercial availability and widespread use of assay-specific validated antibodies in biomedical research.

In 2016, GBSI and the Antibody Society brought together industry stakeholders to share insights and weigh in on potential solutions for validating antibodies. Following the meeting, the stakeholders agreed that there needs to be greater validation, said Freedman. But antibodies are complicated — there are multiple applications and there is no simple solution, said Freedman. As a result, it's difficult to have standards but there have been efforts to create guidelines, he informed.

At the meeting, the stakeholders agreed on creating a tool — a set of criteria or scorecards — for consumers. Each one of these scorecards will be different depending on the application, so the scorecard for western blots will be different to immunoprecipitation.

GBSI has been testing the pilot scorecard system for six months to evaluate and rank research antibody performance. The scorecard is a measuring system with data that would allow researchers to select antibodies for a given application based on their intrinsic on-target, off-target and other technical characteristics, ultimately improving accuracy and resulting in more reproducible research.

After alpha testing the initial scorecards for three of the most used applications — western Blot, ELISA and immunohistochemistry — participating manufacturers and academics will meet to review the outcomes and determine what, if any, changes are needed, said GBSI.

"My personal wish is that there will be general adoption of the scoring system and that it becomes the standard when validating an antibody," said Freedman. "Consumers often rely on scoring systems to make more informed purchasing decisions, as long as the scoring is straightforward and transparent. Why should the purchase of essential reagents such as antibodies be any different?"

Training and automation

Training can also have a significant impact in improving reproducibility, said Freedman. GBSI has already received $2.34 million over five years from NIH for an experimental design training project. The project, 'Producing Reproducible Experiments by Promoting Reverse Experimental Design' (PREPaRED), is a partnership between GBSI, Harvard Medical School, Vanderbilt University, Purdue University and Massachusetts Institute of Technology (MIT). It will take the concepts of 'reverse engineering' and apply them to training for experimental design.

"Sound experimental design is a core prerequisite for rigorous and reproducible research, which forms the necessary foundation for scientific breakthroughs, and yet it is not frequently taught as a formal part of undergraduate and graduate training," said Freedman.

One of the other focus areas for GBSI is lab automation. Current lab protocols contribute around $3 billion a year to the preclinical irreproducibility issue, according to the not-for-profit body. The emergence of affordable automation tools and technology can also have a positive impact on reproducibility, said Freedman.

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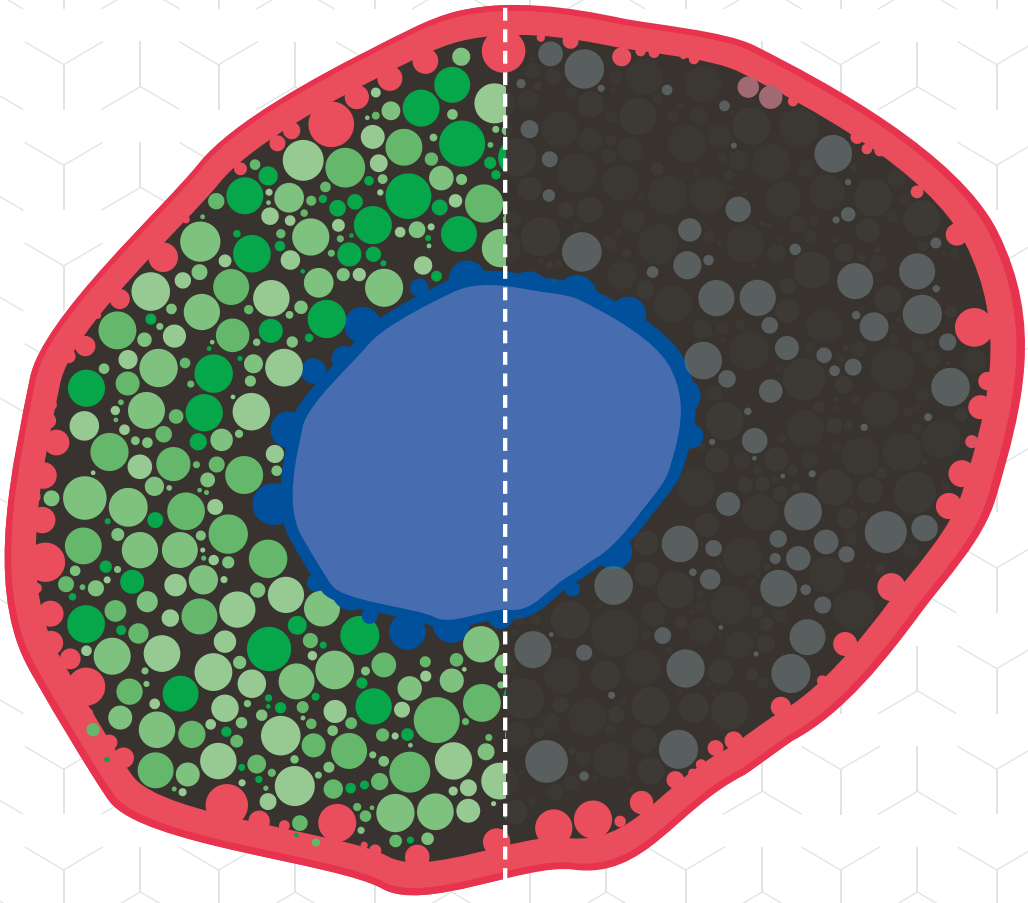

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1. Bradbury, A. and Plückthorn, A. 2015. Reproducibility: Standardize antibodies used in research. Nature. 518(7537), pp.27-29.

HIV testing in one hour or less

Advances in biosensor technology are expected to limit the spread of HIV and other sexually transmitted infections, according to market research firm IDTechEx.

1.8 million people acquire HIV each year, with the World Health Organization (WHO) estimating that one in five people living with HIV do not realise they are infected. Therefore, strategies for faster and earlier diagnosis are as important as ever to limit the spread of HIV.

Currently, the most common test for HIV looks for an immune response by looking for the antibodies the body produces in response to infection. A blood sample taken from the patient is sent to a laboratory for this test, which takes around a week, with positive results then confirmed by a second test. Alternatively, in resource-limited settings where the infrastructure is not available to conduct such tests, lateral flow devices (resembling at-home pregnancy tests) can be used to make an initial diagnosis.

The problem with testing for antibodies (the immune response) is that it can produce false-negatives when the test is conducted before the immune response has occurred. It takes around four weeks for the body to generate antibodies to HIV, called the 'window period'; therefore, tests cannot be carried out before this time. The advice is to wait three months to take an HIV test.

The most rapid and reliable way of detecting HIV is to search for the HIV genetic material directly in blood, using a process called polymerase chain reaction (PCR). This has the advantage of not requiring a long wait after exposure, being available after only three days.

Traditionally this process, known as molecular diagnostics, has been performed in a laboratory by trained personnel. Recent technological advances have, however, brought the possibility of conducting molecular diagnostics out of the laboratory and next to the patient. This is part of a wider trend in the field of biosensors, which is undergoing a shift to the point of care.

Point-of-care testing can be defined as a test which takes under an hour on a portable device, meaning samples no longer have to be sent to a laboratory for analysis, with the results fed back for follow-up treatment. It has particularly high value in the diagnosis of sexually transmitted infections, where a rapid diagnosis can demonstrably reduce the spread of infection.

The IDTechEx report 'Biosensors for Point-of-Care Testing 2017–2027' gives a complete analysis of the important trends in the field of medical biosensors and lists the new technologies and devices which are likely to be highly disruptive to the in vitro diagnostics market. With the ability to carry out tests while the patient waits, treatment can be given immediately and the spread of infection is greatly reduced.

The report is available on the IDTechEx website.

Clarivate Analytics partners with IP Australia

Clarivate Analytics has partnered with IP Australia by providing its enhanced patent data to augment its Source IP database.

The enhanced Derwent patent data will be available for a number of patents currently listed on the Source IP national initiative. The initiative was launched by IP Australia in November 2015 to help expose potential collaboration opportunities to Australian businesses seeking to work with public sector research partners and to facilitate quick and easy contact. The main goal of the initiative is to increase investment in public sector IP.

Source IP will expand its current Australian patent data with additional patent fields from the enriched patent data from Clarivate Analytics, specifically the Derwent World Patents Index (DWPI). The addition of DWPI will enable industries to search and comprehend available patents, identify what patents can be licensed from Australian universities to strengthen their own research and development efforts, and identify potential research partners.

Source IP currently features research expertise from over 67 research organisations including Commonwealth research organisations, universities, medical research institutes and cooperative research centres.

"We have always strongly supported the Australian Government's National Innovation and Science Agenda. This includes supporting the Source IP initiative with our enhanced DWPI patent data as part of our continuous efforts at Clarivate Analytics to promote greater academia–industry collaboration within the innovation communities around the world," said Jeroen Prinsen, Vice President and Head of Australasia and Southeast Asia at Clarivate Analytics.

Patricia Kelly, IP Australia's Director General, commented on the contribution from Clarivate, "We're extremely privileged to have Clarivate Analytics provide us with the Derwent abstracts. These abstracts help strengthen Source IP, which is a powerful tool helping connect IP rights holders with Australian businesses. The Derwent abstracts have increased the chance of investment in public sector IP, potentially helping many different publicly funded research parties."

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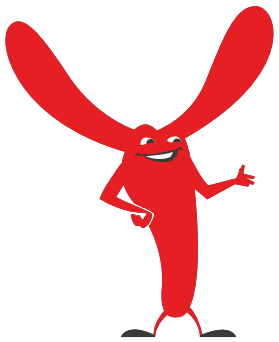

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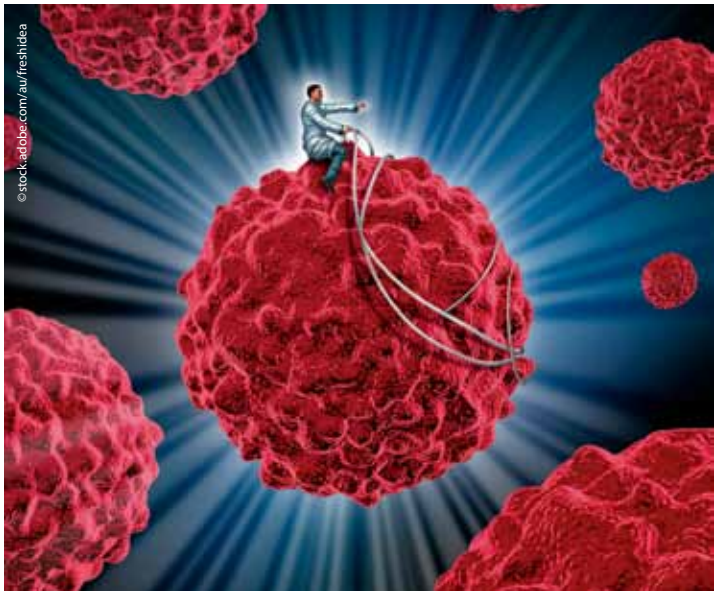

Lung cancer subtype responsive to immunotherapy

Melbourne researchers have discovered that an aggressive lung cancer subtype is susceptible to immunotherapy, thanks to the identification of special markers expressed in tumours.

The research was led by Dr Sarah Best and Dr Kate Sutherland from the Walter and Eliza Hall Institute (WEHI), working with colleagues at Metabolomics Australia at the University of Melbourne's Bio21 Institute. Their study focused on the role of two cell signalling pathways — KEAP1/NRF2 and PI3K — which are known to be involved in human lung cancers called adenocarcinomas — the most common form of the cancer, accounting for around 40% of cases.

"More than one in five lung adenocarcinomas have alterations in the KEAP1/NRF2 pathway, suggesting it is a major cancer driver," Dr Sutherland said. "These cancers are very aggressive, are resistant to standard therapies and have a poor prognosis, so new therapies are urgently needed."

Published in the journal *Cell Metabolism*, the study revealed that non-stop signalling caused by mutations in the KEAP1/NRF2 and PI3K pathways causes lung adenocarcinomas to develop.

"With this knowledge, we can further investigate how targeting those pathways could lead to therapies for these aggressive and hard-to-treat cancers," she said.

Furthermore, said Dr Best, the study found that adenocarcinomas caused by altered PI3 kinase and NRF2 pathways "express markers that leave them susceptible to immunotherapy" — a relatively new treatment that effectively "enables our immune cells to see the tumour cells again and kill them" but is not responsive in all patients.

"Using preclinical models, we showed for the first time that these tumours have the markers that respond to anti-PD-1 and anti-CTLA-4 immunotherapies, which are some of the most exciting new cancer therapies being investigated in the clinic," said Dr Best.

"But more importantly, we showed that these immunotherapies were effective in fighting the tumours and leading to tumour regression in our preclinical models."

Dr Sutherland added that the researchers have also identified what she calls "a unique 'breadcrumb' trail that the cancers leave behind in the blood" — a "molecular signature" that could be utilised as part of a simple blood test in future.

"The next steps would be to analyse human samples to prove the same is true in lung adenocarcinoma patients, but we need more funding for that work to continue and to generate results that will lead to better detection and treatments for the community."

Zelda and Curtin University expand partnership

Zelda Therapeutics, an Australian-listed biotech focused on medical cannabis, has expanded its pancreatic cancer research collaboration agreement with Curtin University.

This expansion will focus on in vivo animal studies to investigate the effect of a range of Zelda's formulations in combination with existing chemotherapy agents Abraxane and Gemcitabine.

The treatment protocols in this study will closely mirror typical standard of care protocols utilised by oncologists in treating patients with pancreatic cancer. Zelda expects the results from these studies to generate highly relevant data for potential future human clinical trials.

There is a growing body of evidence that whole plant cannabinoid extracts can impede cancer growth and potentially render the tumour more responsive to chemotherapeutic agents, the company said in a statement.

Pancreatic cancer is the 12th most common cancer globally, with over 330,000 diagnoses in 2012, according to Pancreatic Cancer World Research Fund International. With a very low five-year survival rate, the pancreatic cancer market will greatly benefit from further research and development using novel approaches, the statement said.

"The data to be generated by this new program has the potential to open new avenues of treatment for a cancer with very low survival rates," said Executive Chairman Harry Karelis. "We look forward to results being generated over coming months and progressing the body of knowledge in this important field."

Professor Marco Falasca, head of the Metabolic Signalling Group at Curtin University, added, "The expanded collaboration with Zelda is a great opportunity to provide scientific validation to the use of cannabis in combination with chemotherapy agents in cancer treatment."

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Biotech boom

The Australian life sciences and biotech industry is witnessing a resurgence in activity, which is expected to continue over the next 12 months.

To get some insights on the state of the Australian biotech industry, *Lab+Life Scientist* interviewed Dr Katharine Giles*, Brandon Capital Investment Manager. Dr Giles was recently recognised in the 2018 40under40 Business News Awards for her work in the medical and investment fields, and for educating and inspiring the medical innovation community of Western Australia.

Lab+Life Scientist: What are your thoughts on the current state of the Australian life sciences and biotech industry?

Dr Katherine Giles: The Australian life sciences industry is in a really strong position. There is plenty of world-class science and research being conducted and there is greater access to local venture capital than ever before, strengthening the whole ecosystem. MTPConnect has been great at fostering collaboration and connectivity. Through its Project Fund Program scheme, they're helping institutes get over the key early-stage barriers involved in commercialisation, such as building clinical trial capability by providing funding grants.

While Australia has a strong tradition of conducting great science, traditionally the ecosystem for supporting commercialisation and connecting researchers pursuing this pathway to impact was fragmented — there was an opportunity for greater coordination of Australia's medical research talent and capabilities. There is a lot more cohesion and support within the community now and researchers have multiple options available to upskill in the commercialisation process and engage with industry.

The Medical Research Commercialisation Fund (MRCF), a collaboration between major Australian superannuation funds, over 50 medical research institutes and research hospitals in Australia and New Zealand, has been working to bridge the gap between science and translation for over 10 years. The MRCF is managed by Brandon Capital. Our collaboration is one way we contribute to the ecosystem.

The R&D Tax incentive scheme is invaluable for encouraging companies to carry out work in Australia. It also attracts overseas companies, particularly from the UK and US, to Australia for advanced clinical development.

A key challenge, but also something that is positive and results from a surge in activity, is accessing experienced management talent.

LLS: What are currently the most exciting areas in biotech?

KG: The MRCF research members are continuing to conduct great research so exciting opportunities are coming to us all the time, covering an extremely wide range of disease areas and technologies.

In particular, the application of technology from outside the life science sector is an exciting and growing area. Technological advancements are bringing a lot more opportunities to the biomedical sector, with potential for new applications.

In Western Australia, there are a number of medical device companies being established. At OncoRes Medical, one of the MRCF's portfolio companies, we're developing a handheld imaging probe and console which will provide real-time intraoperative guidance to surgeons by assisting to delineate tumour from a healthy tissue, with the aim of improving the outcome of breast cancer surgery.

In breast cancer surgery, it's often difficult to remove the entire tumour. Around 25% of patients undergoing breast-conserving surgery will need another surgery to remove residual malignant tissue not removed in the first operation. The technology being developed at OncoRes will help surgeons identify residual cancerous tissue remaining within the breast so it can be removed during surgery, reducing the need for repeat surgery.

These additional surgeries are a $1 billion-a-year cost to the healthcare system in the US and Europe, creating a huge need for a tool that can provide real-time information on whether cancerous tissue remains, increasing the likelihood that it is completely removed during the first operation.

In life sciences, you never know where you're going to find inspiration and solutions, so you need to be open-minded.

LLS: What do you expect to be the main themes/trends for the next 3–5 years?

KG: We will see continued maturing of the sector. As the sector develops further there will be an increased need for collaboration between multidisciplinary teams. For example, if you are a scientist in the lab, and you have an idea you're trying to commercialise, having a clinician on your team is essential. With Australia's life science ecosystem becoming more cohesive, there will be more opportunities for scientists to work with those clinicians, and clinicians will also be looking for ways to collaborate.

In the next few years, more companies will successfully take products into clinical development. As Australian start-ups successfully develop therapies, tools and treatments that positively impact patient care, we will see more mid-stage, maturing companies with larger teams emerge. We also expect to see a steady flow of larger exits. Australia is likely to see more corporate activity from global companies as we are very much on everybody's radar at present.

LLS: What are some of the challenges facing the Australian life sciences industry?

KG: Australia has great fundamental research, and now has more capital for development than ever before. The $500 million Biomedical Translation Fund, which was created by the Australian Government in 2016, has been a game changer. It's a once-in-a-generation initiative to make Australia a global leader in commercialisation of biomedical discoveries. Under the initiative the government has made $250 million available, with the remainder coming from private investors, managed by three venture capital firms. Brandon Capital has been appointed to manage the $230 million MRCF BTF fund.

Access to human capital is a key issue. We're facing a skill shortage and we want to attract experienced biotech and medtech management and R&D experts to return or move to Australia to help us grow emerging companies.

LLS: What advice would you offer to emerging biotech companies looking at funding/commercialisation?

KG: Prepare yourself for a long journey and get access to as much expertise as possible — you can never have too much in this industry.

It's important to understand the clinical need you're trying to meet is vital and also have knowledge of what's already happening in the field. It's critical to know things like "Do other treatments or products exist for this area?", "Who's developing what?", "What methods are being used?", "Why is my solution better than others?" and "Who will pay for this treatment?" I'd also suggest seeking advice from intellectual property experts at an early stage during the development process in order ensure all work is protected by a patent.

To get a foot in the door with investors, try and get a warm introduction as opposed to cold calling. If you are working or studying in biotech, there will be someone who can make an introduction to an investor and it's an automatic way in.

It is never too early to start a dialogue with us. Whilst our head office — co-located with 13 of our companies — is in Melbourne, we also have team members in Perth, Sydney, Brisbane, Adelaide and Auckland.

LLS: Where are you at with MCRF 3 and MCRF BTF? How much money do you have left to invest?

KG: We are really excited by the prospects of MRCF3's portfolio. MRCF3, a fund of $200 million, was started in May 2015 and will be three years old at the end of April. So far, 18 investments have been made. Of the 18 companies, 12 are new start-ups, with the MRCF investment being the first funding round provided to the companies.

It is early days for the MRCF BTF, a $230 million fund which started in January 2017 and is focused on Australian companies developing clinical stage technologies. Through the MRCF BTF, we've been reviewing some really interesting companies and we will be making announcements on investments from this fund over the coming months.

To get a foot in the door with investors, try and get a warm introduction as opposed to cold calling.

LLS: What attributes do you look for in a potential investment?

KG: When making an investment, we look for world-class technology that has the potential to make a significant difference to patients if brought to market.

It needs a strong intellectual property position and needs to have long-term relevance, because by the time it's gone through all the research, development, trial and manufacturing phases to get to market, it may have been 10 or more years. We also look for investments where we can make a difference and add value as the manager, and where our funding will help the company progress to the next stage.

As Brandon Capital has started 32 companies of the 37 it has invested in over the last 10 years, we are very happy to work up a business plan with the entrepreneur and to even help manage the company in its early days, including recruiting the management team. Professional relationships play a large part in a company's success and one of the key competitive advantages at Brandon Capital is the networks we've established and maintained in the commercial, technical and clinical fields both here and overseas.

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LLS: Tell us about the five most exciting investments in your portfolio?

KG: There are 25 active companies in Brandon Capital's MRCF portfolio at the moment and we are excited about them all.

A few of particular note are:

- PolyActiva, a biotech company based in Melbourne, has developed a unique drug-polymer conjugate technology that enables slow release, site-specific drug delivery from medical device components directly at the site of action.
- OccuRx, a Melbourne-based company founded and led by Professor Darren Kelly, one of Australia's top life sciences entrepreneurs, is developing a drug aimed at curing retinal blindness.
- QueOncology, a University of Queensland spin-out, is creating a non-hormonal therapy for the treatment of host flushes in women undergoing endocrine therapy for breast cancer. The company also has preclinical programs in the areas of cancer-related pain, as well as two novel targeted anticancer therapies.
- Osprey Medical is developing the CINCOR System for advanced kidney protection during cardiovascular procedures. The system is designed to remove dye (contrast) from the heart before it can enter the kidneys and cause damage.
- Global Kinetics Corporation (GKC) provides point-of-care measurement and reporting of Parkinson's disease (PD) motor symptoms so that neurologists and professional carers can better manage the symptoms of PD, leading to better quality-of-life outcomes.

**Dr Katherine Giles joined Brandon Capital Partners in 2012. Before this she was an investment manager with Perth-based Stone Ridge Ventures, a fund manager specialising in seed- to early-stage technology investment.*

In addition to her investment experience, Giles has start-up experience in medical apps, diagnostics and fitness devices. She still practises as a medical doctor, mainly working within the surgical field, and also has experience as a medical officer monitoring clinical trials.

The Power of Research

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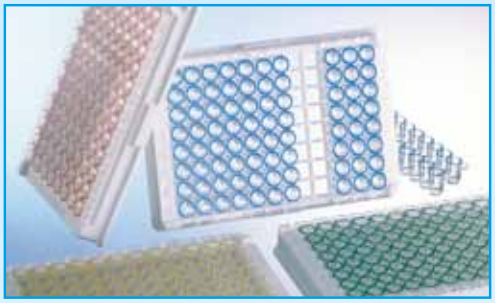
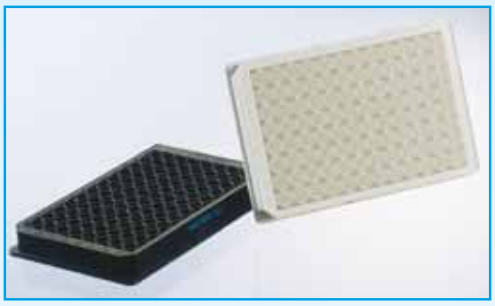
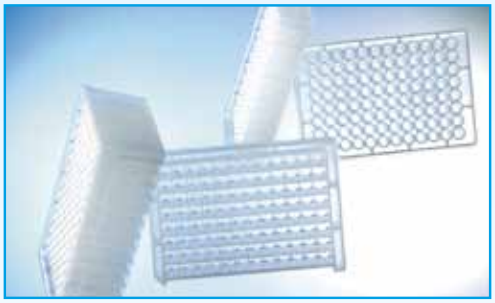


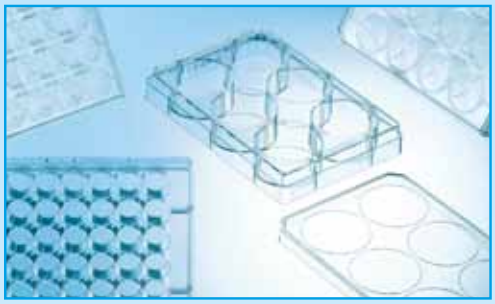
ELISA / Immunology



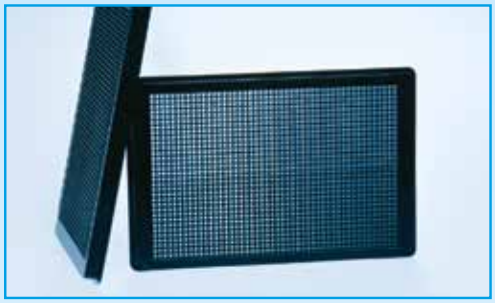
Fluorescence / Luminescence



Sample Storage



Cell Culture



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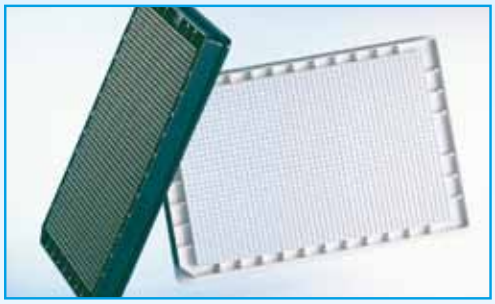

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Lauren Davis

Drink up!

Better detection developed for counterfeit liquors

When you think of counterfeit goods, the first things to come to mind are probably clothing or electronics. But there's another industry out there that has been hit so badly by counterfeiters that lives have been lost as a result — the alcohol industry.

Writing in the American Chemical Society journal *ACS Sensors*, researchers at the University of Illinois at Urbana-Champaign noted, "Counterfeiting and adulteration of foods and beverages generally, and liquors specifically, is a substantial problem worldwide." With literally thousands of liquor products available, they said, opportunities exist for unscrupulous individuals to try and make themselves a profit.

Counterfeiters may homebrew their own liquor and bottle it in official-looking packaging, with consumers none the wiser about the source of the product or its actual ingredients. As a result, the product may have been adulterated or contaminated with water, low-end liquors or other inexpensive additives, including antifreeze. The consumption of counterfeit liquors is therefore a public health problem, with deaths from contaminated alcohol having been reported in Indonesia, Mexico, China, Poland, Russia and more.

"For these reasons, the quality control of liquors becomes imperative for regulation of the liquor market and for protection of consumers' health," the researchers said. "Easy analysis of liquors in the field, outside of laboratory settings, has become an urgent need as part of such quality control monitoring, and this requires the ability to distinguish even subtle differences among liquor samples."

The scientists set out to address this growing health concern by engineering a device that can easily identify tainted products. Their work follows the development of several techniques for liquor analysis in recent years, including gas chromatography (GC), high-performance liquid chromatography (HPLC), mass spectrometry (MS), infrared or UV–vis spectrometry and solid-phase microextraction (SPME).

"Chromatographic or spectroscopic methods only gives ppm or sub-ppm level detection for most analytes; below that level, preconcentration of low-concentration components using SPME is necessary," the study authors said. "Unfortunately, due to the variation in partition coefficients among polar vs nonpolar compounds, SPME inherently gives uneven preconcentration so that the analysis gives inaccurate distribution of components in the original mixture."

Another alternative is the use of array-based sensors such as electronic noses, as first proposed in the early 1980s, which provide a composite response. As noted by the researchers, examples of electronic or optoelectronic noses employed in liquor assessment include chemiresistive metal oxides, mass-sensitive quartz crystal microbalances, photonic crystals, and UV–vis or fluorescence.

"Liquor analysis by traditional electronic nose technology has [however] often been problematic because the dominant analyte to which prior sensors respond is ethanol," the scientists said. "Consequently, subtle differences among liquors with similar alcohol contents have been difficult to detect."

Seeking to overcome these limitations, the research team developed their own optoelectronic noses based on colorimetric sensor arrays, which make use of the chemical diversity available in molecular sensors (specifically, chemically responsive dyes). Such devices have previously proven effective for the identification and quantification of analytes in both gaseous and aqueous phases, finding success in security screening, environmental monitoring, medical diagnosis and quality inspection of foods and drinks.

"Our colorimetric sensor arrays probe a broad range of chemical interactions using a set of chemo-responsive dyes immobilized in relatively hydrophobic matrices," the team wrote. "The change in colors [RGB — red, green and blue] … of the array before and after exposure to a given odorant are digitally imaged and provide a 'fingerprint' that identifies the odorant by comparison to a collected library database."

The researchers noted that the chemical composition of liquor products is "enormously complex", with 300–1500 identifiable compounds found in different liquors. The good news is, aldehydes and ketones — products produced from fermentation, the ageing process and storage — contribute substantially to the distinctive aroma of alcoholic beverages, and can therefore be used as standards for the authentication and quality assessment of liquor products.

"To target those aldehydes and ketones, we designed several colorimetric sensor elements based on acid-doped, amine-based nucleophiles that are specifically aldehyde- and ketone-sensitive," the study authors said. These were combined with 36 classes of chemical dyes that change colour upon exposure to particular components in liquor, including six aldehyde/ketone responsive dyes and 30 other classes of sensor elements from prior studies. The array therefore responded not only to aldehydes and ketones but also to a wide range of volatile organic chemicals (VOCs).

Finally, to improve sensitivity and increase discriminatory power, the team developed a way to partially oxidise the liquor vapour stream before exposure to the array. This would result in the production of more chemically reactive species such as aldehydes, quinones and carboxylic acids, they explained — which was vital to their research, as the colorimetric sensors used in the array were not especially sensitive to alcohols.

"This provides a much more sensitive and distinctive signature than simply detecting the vapor of the pristine liquors," the study authors said.

This preoxidation was carried out with the help of a disposable tube that was simply attached to the handheld image analyser. Head-gas vapours were drawn through the tube and over the array located inside the analyser. This enabled in situ collection and real-time analysis of sensor images within 2 min.

The team tested their colorimetric sensor array against a library of 14 commercial liquor products across five categories: scotch, bourbon, rye, vodka and brandy. By mapping their colour difference profiles, the researchers were able to correctly identify the alcoholic content and brand of each of the 14 different liquors — with greater than 99% accuracy.

The scientists went on to investigate the effect of the dilution of liquors on the sensor array response, in a demonstration of what could be a real-world application. This time, the colour difference profiles were found to change with increasing degrees of dilution. This enabled the researchers to distinguish among different dilutions of the liquor — even when that dilution was as little as 1%.

The researchers believe that the "extremely high discriminatory power" of their colorimetric sensor array may make it suitable for quality assurance for the beverage industry, given its high accuracy rate and successful discrimination between pristine liquors, adulterated liquors and aqueous ethanol samples. Furthermore, they suggest that additional research could lead to discrimination between a more complete list of alcoholic beverages — including wines, ciders and beers — according to their type and method of preparation, country of origin and degree of spoilage, adulteration or contamination.

Combined laboratory fridge-freezer

The small footprint of the LIEBHERR Laboratory Fridge-Freezer Combo makes it suitable for labs that have limited space. Configured with the user in mind, the 254 L fridge compartment is stacked on top of the 107 L freezer compartment, giving users easy access to samples and reagents.

Samples and reagents can be optimally stored between +3°C and +16°C in the fridge compartment and between -9°C and -30°C in the freezer compartment, with temperatures set to 1/10°C accuracy using the digital display of the Comfort electronic controller. Temperature remains uniform in the fridge compartment due to the fan-forced, dynamic cooling system and stable in the freezer compartment because of the static cooling system.

The product comes with an access port for feeding external temperature sensors via the back of the unit. This maintains the integrity of the door seal and permits temperature control, when the external temperature sensor is used in conjunction with the 1-point calibration function of the Comfort controller.

The unit is fitted with locks, equipped with visual and audible alarms to warn users when temperature limits are exceeded, and has an integrated data memory to record min/max temperature as well as the last three alarm events. Temperature and alarm data can also be transferred to a building management system via RS 485 interface and alarms forwarded to an email, phone, etc via volt-free contact.

Energy consumption and running costs are low due to the efficient compressor, insulation and eco-friendly refrigerant (R600a) used.

Andi-Co Australia
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All-in-one detector

Gentec's BLU series all-in-one detectors combine a detector and a meter with Bluetooth connectivity in one convenient product. This means there is only one calibration required and no need to carry a meter.

The small but powerful BLU series meter features a Bluetooth connection so the user can display the results on their mobile device with the Gentec-EO BLU app, available for both iOS and Android systems. If they need to use it with a PC, the user can simply plug in the included Bluetooth receptor and be ready to make power or energy measurements within seconds.

The BLU range of detectors is designed to offer a safer work environment as operators can be far from the detector while making measurements (up to 30 m, depending on the environment and barriers). With fewer cables in the workspace, accidents are less likely to happen.

Users can receive data at up to 30 m from the detector, with the same performance as the usual detector–monitor combination. By going wireless, there is no need to worry about cable length or monitor location.

The USB-rechargeable Li-ion battery lasts up to five continuous days with the device running.

Lastek Pty Ltd
www.lastek.com.au

Upright microscope

The Eclipse Ci upright microscope is described by Nikon as a big step forward in the evolution of ergonomic microscopes that can adjust to multiple users, reduce fatigue and increase comfort during operation, while providing bright, sharp and clear images.

The Ci offers simultaneous, motorised switching of objective lens, condenser and light intensity. The system incorporates an Eco-illumination power saving, 60,000 h, high-intensity LED optical system, which offers low power consumption and heat generation and eliminates colour temperature changes. The advanced ergonomic features allow the user to sit in a natural, relaxed posture throughout their workday. The advanced ergonomics are further evolved in the Ci-E model, representing Nikon's first automated microscope model for clinical laboratory use.

The system is suitable for darkfield, polarising and sensitive colour polarising for gout testing and phase contrast. Additional features include the Nikon's CFI60 infinity optics; an advanced tool menu for annotations and measurements; split-screen capability for live comparisons; and an image sharing capability via firmware.

Coherent Scientific Pty Ltd
www.coherent.com.au

Osmometer

Now with a self-cleaning thermocouple, the Vapro osmometer brings simplicity and convenience to the routine determination of osmolality to help meet the demands placed on today's laboratories. Auto-calibration, self-diagnostics, statistical analysis and computer interface/printout capabilities make the osmometer suitable for any busy laboratory. The small sample requirement allows users to assay hard-to-get samples using the vapour pressure method.

Vapour pressure measurement is the method of choice for most fluids in biology in which water is the solvent. The vapour pressure method determines osmolality at room temperature with the sample in natural equilibrium. Cryoscopic artefacts due to high viscosity, suspended particles or other conditions that can interfere with freezing point are avoided with vapour pressure determinations, giving the Vapro osmometer a broad range of error-free applications. Functions are user-friendly, selected from a simple and logical menu.

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Droplet digital PCR (ddPCR) system

The QX200 Droplet Digital PCR (ddPCR) System from Bio-Rad provides absolute quantification of nucleic acids. It is particularly useful for detection of targets in complex backgrounds or for monitoring subtle changes or low nucleic acid abundance not easily detected/quantified with traditional qPCR.

Based on water-emulsion droplet technology, the system fractionates a DNA sample in 20,000 droplets. PCR amplification of the template subsequently occurs in each individual droplet, and counting the positive droplets gives precise, absolute target quantification.

The product covers a range of applications including copy number variation, rare mutation detection and liquid biopsy for research and now clinical diagnostics. Scientists are also investigating new application uses in genome editing detection, pathogen detection and quantification, environmental monitoring and more.

In conjunction with the instrumentation, Bio-Rad offers digital PCR assays that were designed by experts in the digital biology field. Every assay has been experimentally validated to ensure optimal performance for its target application and feature precision and sensitivity in providing an absolute measure of target DNA molecules.

Bio-Rad Laboratories Pty Ltd
www.bio-rad.com

Single plane illumination microscope

Luxendo's MuVi-SPIM is a single plane illumination microscope designed to facilitate rapid in-toto fluorescence imaging of biological specimens with subcellular resolution.

The system utilises a sheet of laser light to illuminate only a thin slice of a fluorescently labelled sample. A wide-field fluorescence microscope, placed perpendicular to the light sheet, serves to collect the fluorescence signal and images the observed region by means of an sCMOS camera. Optimised combinations of the sCMOS camera and objective lenses enable users to obtain multiple views of large samples at high speeds. The product is suitable for applications such as developmental biology, embryonic development, marine biology, neurobiology, functional imaging, long timelapse imaging and large specimens.

MuVi-SPIM provides four simultaneous orthogonal views on large living specimens, without the need for sample rotation, in order to dispel shadowing effects and facilitate long-term imaging at ultrahigh acquisition speeds. It is claimed to be the fastest SPIM on the market for analysing dynamic processes, enabling four simultaneous views at 65 fps.

The microscope avoids sample phototoxicity by sequentially illuminating a stack of small slices of an organism. It integrates modular software concepts in order to enhance flexibility in designing complex experimental layouts, and 3D image data is employed, in real time, and directly streamed to a storage and data processing server.

Features include: large field of view; close-to-confocal resolution; high imaging speed; good sample handling; low phototoxicity; high sensitivity; low noise; 360° illumination and detection; a Hamamatsu ORCA-Flash 4.0 high-speed sCMOS camera; a laser combiner with six laser positions; 2x Nikon CHI Plan Fluor 10XW 0.3NA water immersion for illumination; 2x Nikon CFI LWD 25XW 1.1NA water immersion for detection; and a mounting chamber with temperature control (15 to 40°C).

SciTech Pty Ltd
www.scitech.com.au

New method to quickly screen fentanyl and other drugs of abuse

Researchers at McMaster University have developed a new drug screening technique that could lead to the rapid and accurate identification of fentanyl, as well as a vast number of other drugs of abuse, which up until now have been difficult to detect by traditional urine tests.

The method, outlined in the current edition of the journal *Analytical Chemistry*, addresses a serious public health emergency related to opioid addiction and unintentional overdose deaths: the lack of a reliable and inexpensive test that allows for comprehensive surveillance of synthetic drugs flooding the illegal market.

The new method would eliminate a two-stage process currently in use for drug monitoring by allowing technicians to run many tests at once in a high throughput manner — dramatically cutting processing time while improving screening accuracy with quality assurance. Importantly, this mass spectrometric method can also screen for a wider range of drugs of abuse, as well as identify designer drugs that elude conventional tests.

New technologies are urgently needed, given a worldwide epidemic of prescription and illicit drug abuse and its devastating impacts on public health. According to a recent report by the United Nations Office on Drugs and Crime approximately 35 million people worldwide used opioid drugs in the year 2014. In 2016, the Public Health Agency of Canada reported an estimated 2,800 people died of opioid overdoses alone. It expects that number to rise to at least 3,000 in 2017.

Conventional tests using immunoassays fall short because they cannot detect the alarming assortment of drugs, which include synthetic opioids, tranquilisers, stimulants and anti-anxiety agents. Additional confirmation tests are also required due to a high rate of false positives and false negatives, which slows the process further.

"Drug testing is always behind the times since screening relies on antibody reagents that target only known drugs and they are prone to error, which contributes to higher health care costs and delays to clinical decision making," explains Phillip Britz-McKibbin, a professor in the Department of Chemistry and Chemical Biology at McMaster and lead author of the study.

"Current technologies are not specific, accurate nor comprehensive enough, which impairs a physician's ability to properly care for patients, such as monitoring for drug compliance, potential substitution or polydrug usage," he says.

This problem extends beyond pain management; take, for example, a clinically depressed patient. Prescribed anti-anxiety medications can be harmful if taken at the wrong dosage or not taken at all, leading to a higher risk for self-harm especially if mixed with other drugs. Only accurate urine tests can show whether or not the patient is following a doctor's prescription or taking other harmful substances that can compromise treatment efficacy and patient safety, explains Britz-McKibbin.

Researchers plan to validate the method relative to conventional screening tests for a broad spectrum of drugs of abuse on a cohort of in-patients, currently under physician care.

The work was funded by the Natural Sciences and Engineering Research Council of Canada and involved a collaboration with Seroclinix Corporation and Agilent Technologies Inc.

Chillers

Huber Minichillers and Unichillers are suitable for environmentally friendly cooling in laboratory and industry applications. There are several air- and water-cooled models available, with cooling powers from 0.3 to 20 kW and efficient energy management.

The chillers are now available with an OLÉ controller, combining state-of-the-art technology with simple operation. OLÉ models are suitable for routine tasks in research and industry and are convincing as practice-oriented basic equipment. They are equipped with USB and RS232 interfaces and have a bright, large OLED display. A Pt100 sensor connection to display the process temperature, for example, is available as an option.

The compact chillers have a stainless steel casing and reach operating temperatures of -25 to +40°C. The technical equipment includes an illuminated level indicator, as well as status symbols for pump, cooling and heating. All models are available with integrated heating to extend the temperature range to +100°C.

The chillers are designed for non-supervised permanent operation at ambient temperatures of up to +40°C. They are equipped with a circulating pump with 1 bar pressure for best flow rates. For applications with significant pressure loss, 'P' models with stronger pressure pumps (2.5 bar) are available.

Scitek Australia Pty Ltd
www.scitek.com.au

Multiplex immunoassays

Abcam's FirePlex-HT immunoassays offer a no-wash workflow in 384-well plate format, enabling multiplex quantification of up to 10 protein analytes per well from as little as 6.25 µL of plasma, serum or cell culture supernatant. A two-step protocol limits hands-on time and can be easily automated, making the assay suitable for high-throughput studies.

Data from FirePlex particles can be collected using any high-content imager at scan speeds of less than 20 min/plate. Subsequent analysis is performed using Abcam's free integrated FirePlex Analysis Workbench software.

Available as pre-designed panels or user-designed custom panels, researchers can select from a growing catalogue of over 800 antibody pairs, the majority of which have been developed using Abcam's recombinant monoclonal antibody technology. Quality antibodies combined with FirePlex particles enable consistent assays with a dynamic range of 3–4 logs, sensitivity down to 1 pg/mL and <15% intraplate CVs.

Abcam Australia Pty Ltd
www.abcam.com

Medication caught meddling with the gut microbiome

One in four pharmaceuticals have been found to inhibit the growth of bacteria in the human gut, according to a large-scale international study.

It has been known for some time that the human gut contains a large number of species of bacteria, collectively referred to as the gut microbiome, whose composition has a noticeable effect on human health. It is also well known that antibiotics have a substantial impact on this microbiome, eg, causing gastrointestinal side effects.

However, recent studies have suggested that various non-antibiotic drugs — including antidiabetic, non-steroidal anti-inflammatory and atypical antipsychotic medications — can also change the composition of the gut microbiota, despite being designed to act on human cells rather than against bacteria. Until now, the full extent of this phenomenon has been unknown.

An international research team led by the European Molecular Biology Laboratory (EMBL) set out to systematically profile direct interactions between marketed drugs and individual gut bacteria. The team screened over 1100 drugs — including antibacterials, antivirals, drugs that act on human cells and veterinary drugs — against 40 representative bacteria from the human gut.

Published in the journal *Nature*, the study results found that 27% of the tested drugs and 24% of the drugs designed to act on human cells — including members from each therapeutic class — inhibited the growth of at least one species of gut bacterium. In addition, examination of previous cohort studies revealed that the human-targeted drugs have antibiotic-like side effects.

"The number of unrelated drugs that hit gut microbes as collateral damage was surprising," said EMBL co-group leader Peer Bork. "Especially since we show that the actual number is likely to be even higher. This shift in the composition of our gut bacteria contributes to drug side effects, but might also be part of the drugs' beneficial action."

"This is just the beginning," added co-group leader Kiran Patil. "We don't know yet how most of these drugs target microbes, how these effects manifest in the human host, and what the clinical outcomes are. We need to carefully study these relationships, as this knowledge could dramatically improve our understanding and the efficacy of existing drugs."

The study also highlights the previously unnoticed risk that consumption of non-antibiotic drugs may promote antibiotic resistance, as the general resistance mechanisms of microbes to human-targeted drugs and to antibiotics seem to largely overlap.

"This is scary, considering that we take many non-antibiotic drugs in our life, often for long

periods," said co-group leader Nassos Typas. "Still, not all drugs will impact gut bacteria and not all resistance will be common. In some cases, resistance to specific non-antibiotics will trigger sensitivity to specific antibiotics, opening paths for designing optimal drug combinations."

The good news is that the findings may help refine medications and reduce side effects, alongside possibly leading to the repurposing of human-targeting drugs as new antibacterials or as microbiome modulators. And with each human harbouring a unique gut microbiome — including different bacterial species and strains — many drug-microbe interactions are likely to be individual, opening paths for personalised drug therapies aimed at the individual gut microbiome.

"We are excited to move on and explore drug-microbe interactions in complex gut microbial communities, as this will help us understand how individuals sometimes respond differently to the same medication," said co-group leader Georg Zeller.

Commenting on the results of the study, Dr Hannah Wardill from the Adelaide Medical School was interested to learn that bacteria are not only sensitive to culture additives, but also to commonly prescribed drugs.

"It has always been known that antibiotics negatively affect the good bacteria that reside in our gut, but this study has shown that a number of non-antibiotic drugs also affect the viability of certain bacteria," she said. "Although only shown in vitro, without the complexities of the human body, results showed that a number of antidiabetic, anti-inflammatory and antipsychotic medications affected bacterial viability.

"These results are critically important as it suggests that a wider group of medications may also be driving antibiotic resistance, a looming threat to the health of our current society."

Ramiz Boulos, CEO of Boulos & Cooper Pharmaceuticals, has meanwhile provided his own interpretation of the results, saying the study's actual findings were that "bacteria that were resistant to antibacterial drugs were more likely to be resistant to non-antibacterial drugs".

"This correlation is not the same as saying the use of these non-antibacterial drugs leads to or causes antibiotic drug resistance, but highlights an area of interest that should be watched until more data becomes available," Boulos said.

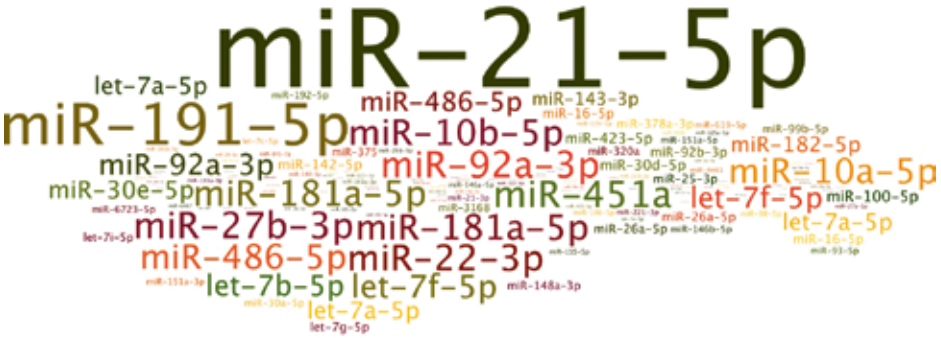
"Finally, it is important to stress that the studies were carried out in isolation in plates that contained at any one time no more than one bacterial species and one drug. Biological systems such as our guts are much more complicated, with tens of trillions of bacterial cells in competition and where there are complex relationships between bacteria, acid levels in the gut, biomolecules such as carbohydrates, enzymes, hormones and others.

"An important question that is yet to be answered is therefore whether these findings can be reproduced in holistic biological systems."

microRNA signature for osteoporosis diagnosis

osteomiRs are circulating microRNAs that serve as novel biomarkers for bone quality and musculoskeletal diseases and can improve early diagnosis of osteoporosis.

Bone densitometry (DEXA) provides the criterion for diagnosis of osteoporosis, but is not sufficiently sensitive to identify patients at immediate fracture risk. In addition, patients of type 2 diabetic osteopathy exhibit elevated fracture risk in spite of elevated bone marrow density.



The osteomiR microRNA signature is intended to assess the risk of a first fracture in female patients of postmenopausal osteoporosis and type 2 diabetes. This information enables timely interventions and can help to avoid fractures.

Biomedica has identified 11 microRNAs in human serum of osteoporotic patients, which are informative about fracture-risk in primary and secondary osteoporosis.

The osteomiR test from Biomedica is a minimally invasive and novel fracture-risk assessment tool, requiring only 200 μL of serum. It has a fast and simple workflow and includes software facilitating data analysis.

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

Automated imaging system

Automated morphological imaging is now an established technique for gathering statistically relevant particle size and shape data, and when combined with Raman spectroscopy it also provides comprehensive chemical analysis. This is particularly useful for the precise identification of particles within a blend that cannot be differentiated on the basis of size and shape alone. The ability to isolate a particle population on the basis of particle size and shape allows the efficient direction of spectroscopy to those particles of interest, providing complete and time-efficient characterisation.

The Morphologi 4 automated static imaging system and Morphologi 4-ID, with integrated Morphologically-Directed Raman Spectroscopy (MDRS), are powerful tools for every scientist seeking absolute analysis and understanding of their samples.

The Morphologi 4 is a fully automated system for characterising particles ranging in size from less than 1 μm to over 1 mm. Sharp Edge analysis, an automated segmentation algorithm, makes it easy to detect and define particles.

The 18 MP camera and enclosure of the sample during imaging has led to high measurement sensitivity. These advances make it possible to measure light-sensitive and low-contrast samples, such as proteins and certain mineral and chemical species, and deliver enhanced shape parameter sensitivity for samples.

The Morphologi 4-ID delivers Morphologically-Directed Raman Spectroscopy (MDRS), integrating the static imaging capabilities of the Morphologi 4 with Raman spectroscopy to enable the component-specific morphological characterisation of different chemical species in a mixture.

ATA Scientific Pty Ltd
www.atascientific.com.au

Lauren Davis

'Thought control' enables spinal injury patient to ride a bike

It's an old adage that as human beings, we can do anything we want if we believe in ourselves. Now researchers at the Gold Coast Health and Knowledge Precinct (GCHKP) are bringing this cliché to life, using a 3D computer-simulated biomechanical model and an electroencephalogram (EEG) to stimulate movement — and eventually recovery — in quadriplegics.

Dr Dinesh Palipana, a junior doctor at Gold Coast University Hospital and graduate of Griffith University, has a vested interest in the research. A quadriplegic himself, he wants to see a cure for spinal cord injury in his lifetime. He is thus quite happy to be the "guinea pig" of the GCHKP project, teaming up with Griffith's Professor David Lloyd and Dr Claudio Pizzolato in what is said to be the first step towards a world-first integrated neuro-musculoskeletal rehabilitation program.

As noted by Professor Lloyd, the development of these neuro-mechanical models has been a project 25 years in the making. It is only recently, however, that the research team has succeeding in personalising these models and making them work in real time. "And so we're going to take those models and create a twin of a patient who is a quadriplegic like Dinesh," he said.

"We will use that model to help us understand how to activate these muscles through stimulation to do rehabilitation on a bicycle or a reclined bicycle, which you can use for people who are quadriplegic. We're also connecting it to EEG equipment.

"The idea is that a spinal injury or neurological patient can think about riding the bike. This generates neural patterns, and the biomechanical model sits in the middle to generate control of the patient's personalised muscle activation patterns. These are then personalised to the patient, so that they can then electrically stimulate the muscles to make the patient and bike move.

"It's all in real time, with the model adjusting the amount of stimulation required as the patient starts to recover."

"We've had equipment for many years where people passively exercise using stationary bikes, and stationary methods where people get on and the equipment moves their legs for them," Dr Palipana explained. "The problem is you really need some stimulation from the brain.

"As the years go by we're starting to realise that the whole nervous system is very plastic and it has to be trained, so actually thinking about moving the bike or doing an activity stimulates the spinal cord from the top down and that creates change."

This top-down, bottom-up approach effectively provides a substitute connection between the limbs and the brain where it was previously broken when the spinal cord was injured. And while the study is still in its early stages, Professor Lloyd said the researchers "have shown our real-time personalised model works", with Dr Palipana successfully moving himself along on a specially adapted recline bike simply by thinking about pushing its pedals.

Dr Dinesh Palipana with Professor David Lloyd (left) and Dr Claudio Pizzolato (right).

The neuro-rehabilitation research is also set to dovetail with a related study by Griffith's Associate Professor James St John, who has had seen promising results for his biological treatment using olfactory cells to create nerve bridges to regenerate damaged spinal cords. Professor Lloyd explained, "You use the modelling to recreate the connection, and over time, with the science of Associate Professor James St John, you establish new neural pathways.

"So over time patients will be less dependent on the model to control the bike movement and it will move back to their own control, with their regenerating spinal cord and their reprogrammed neural pathways."

Associate Professor St John aims to move into human clinical trials in the GCHKP within the next 2–3 years. Professor Lloyd and his team meanwhile hope to refine their rehab testing and develop the technology with leading global companies in exoskeleton design.

Griffith University
www.griffith.edu.au

Back-illuminated sCMOS camera for low-light microscopy

The pco.panda 4.2 bi camera incorporates the latest 16-bit sCMOS back-illuminated sensor to offer up to 95% quantum efficiency without the need for active cooling. It is suitable for low-light microscopy such as GSDIM, PALM, STORM, SPIM, SIM, live cell microscopy, single molecule detection, light sheet microscopy, spinning disk confocal microscopy, FRET, FRAP, fluorescence spectroscopy, bio- and chemi-luminescence and high content screening.

The 4.2 MP camera delivers high resolution of 2048 x 2048 pixels, in conjunction with a 6.5 x 6.5 μm^2 pixel size and facilitates good detail diversity and highly qualitative images. It has the capability to capture full-resolution images at 40 fps and offers exposure times between 100 μs and 5 s. The addition of a USB 3.1 interface provides power delivery, while the compact dimensions of 65 x 65 x 65 mm make the camera suitable for a range of applications in the fields of microscopy and life science.

SciTech Pty Ltd
www.scitech.com.au

Cell sorter

The S3e Cell Sorter is an automated cell sorter with real-time monitoring and smart features equipped with up to two lasers and four fluorescence detectors plus forward-scatter and side-scatter detectors. The compact system, with dimensions of only 70 x 65 x 65 cm, includes onboard fluidics and a temperature control system.

Among the many innovations of the S3e Cell Sorter, two key advancements are ProDrop Technology and the AutoGimbal System. ProDrop Technology simplifies and automates drop delay calculation and droplet break-off monitoring through direct counting of bead events, producing precise results. The AutoGimbal System automates alignment of the nozzle tip and stream to optics by combining picomotor fine motion positioning, imaging and software for hands-free alignment at all points on the stream and consistency in stream position from day to day.

The system is suitable for sorting cells expressing fluorescent proteins or for cells labelled with fluorescent markers excited by the 488, 561 and 640 nm lasers. The cell sorter provides good sort purity, recovery and yield without compromising performance and sensitivity.

Bio-Rad Laboratories Pty Ltd
www.bio-rad.com

High-capacity microbalance

The Cubis MSA116P high-capacity microbalance has been designed to weigh small samples directly into large laboratory containers. This procedure eliminates critical process parameters entailing the risk of inaccuracy, such as quantitative transfer of samples.

The balance is defined by the flask volumes users would like to use and the minimum sample quantity they need to attain. It accommodates vessel volumes of up to 250 mL while achieving an optimal minimum weight of only 1.64 mg in compliance with USP Chapter 41.

Based on the high weighing capacity of the balance, users will no longer need to transfer samples using weigh boats or paper. This not only saves time, it also eliminates the risk of sample loss during transfer when using significantly reduced samples or those only available in small quantities.

Supplied with an adjustable sample holder and a large, 50 mm diameter titanium weighing pan, the balance is prepared to accommodate nearly any standard shape of laboratory vessel.

Sartorius Australia Pty Ltd
www.sartorius.com

Ubiquitination TR-FRET kits

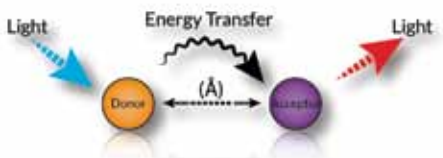
South Bay Bio's real-time TR-FRET ubiquitin conjugation assays are simple: the format is 96- or 384-well low-volume plates and assays are 'set and forget'.

A mixture of ubiquitins labelled with cryptate and acceptor fluorophore are combined with UBA1 activating enzyme, E2 conjugating enzyme, E3 ligase, substrate protein (optional) and 10x reaction buffer, and initiated with addition of ATP. As donor and acceptor ubiquitins become incorporated into chains they come into close proximity, resulting in energy transfer (FRET) and signal detection. Readout can be collected in real time, facilitating enzyme kinetics or endpoint if preferred. Assay performance is typically unparalleled: Z' are usually >0.8 and signal-to-noise is commonly >3000%.

The kits enable the study of auto-ubiquitination kinetics for several human recombinant E3 ligases: MDM2, ITCH and Parkin. Coupled with the assay's short development time (as no antibody development is required for assay optimisation), the assay platform is suitable for a wide variety of academic and industry screening applications.

Kit components are also available separately.

Sapphire Bioscience
www.sapphirebioscience.com



Live cell imaging and analysis using quantitative phase imaging (QPI)

The Livecyte is an imaging system for live cell analysis, used to study cell functions and behaviour. It can reveal the inner details of transparent structures without the need for staining or tagging.

Based on ptychographic quantitative phase imaging (QPI) technology, individual cells and cell populations can be automatically tracked and analysed for phenotypic and kinetic behaviour over several hours or days.

A large field of view ensures that highly motile cells are not 'lost' during long time-courses. High-contrast images and videos can be generated which are artefact-free and quantitative in the absence of labels or high-intensity light imaging which can potentially disturb normal cell functions.

With the ability to automatically analyse multiple parameters simultaneously from a single experiment, scientists can efficiently define the impact of experimental conditions on each and every cell. This makes the Livecyte pertinent across a wide range of application areas including immunological, neurobiological, cancer and basic cell biology research.

ATA Scientific is the local distributor for the Livecyte Cell Imaging and Analysis System, developed by UK-based company Phasefocus.

ATA Scientific Pty Ltd
www.atascientific.com.au

Cell culture system

A common issue faced by drug discovery scientists who use conventional in vitro culture systems is their poor translatability to humans. To address this problem, Kirkstall's Quasi Vivo system consists of interconnected cell-culture chambers and a peristaltic pump to create a continuous flow of media over cells. As a result, cultures are exposed to more physiologically relevant conditions, helping researchers improve the predictive value of in vitro experiments.

The system is available with three different culture chambers (QV500, QV600 and QV900) to support a wide range of applications, including submerged cell culture, co-culture and modelling of air-liquid and liquid-liquid interfaces. Not only is the system easy to set up, it also enables close monitoring of variables during an experiment. Furthermore, the large scale and user configurability of the system allow assays to be performed that are not possible using microfluidic systems.

Lonza Australia Pty Ltd
www.lonza.com

Drug delays disability

in secondary progressive MS

A new drug, called siponimod, is said to slow the progression of disability in secondary progressive multiple sclerosis (MS), according to a double-blind, randomised, phase III trial published in ***The Lancet***.

MS is a condition that affects the central nervous system and involves the nerves losing their protective coating of myelin. Most cases of MS present as relapsing-remitting MS, and more than half of these patients later develop secondary progressive MS within 15–20 years.

The Novartis EXPAND study of BAF312 (siponimod) is a placebo-controlled Phase III trial, comparing the efficacy and safety of siponimod versus placebo in people with secondary progressive multiple sclerosis (SPMS). The study was funded by Novartis and conducted by researchers from University of Basel, University of Pennsylvania, McGill University, University of California San Francisco, Cleveland Clinic, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, St Josef-Hospital/Ruhr-University Bochum, University of Lille, NeuroRx Research and Novartis Pharma AG, Lycalis.

The trial involved 1645 patients aged 18–60 who had moderate or advanced disability from 292 centres in 31 countries. They were either given 2 mg of siponimod once a day (1099 patients) or a placebo (546 patients) for up to three years or until their disability had progressed after six months. Patients whose disease progressed were offered open-label siponimod.

Progression to higher levels of disability was more common in people given a placebo, compared to those given siponimod. After three months, a quarter of patients saw their disability progress on the drug compared to a third of those given a placebo. Further research into the long-term use of the drug is ongoing. The authors also note that the drug had some side effects.

The drug may directly prevent degeneration of the nerve fibres, suppress the autoimmune attack causing the damage and promote recoating of the nerves in the central nervous system. The patients had assessments of their disability levels every three months in the trial, as well as MRI scans at the start of the trial, and after 12, 24 and 36 months.

At the start of the trial, on average, patients had had MS for 17 years and had had secondary progressive MS for 4 years. More than half of the group needed walking assistance (55%, 918/1651 people). 1327 people completed the study (including 903 given siponimod and 424 people given placebo). On average participants of the study took the study drug for 18 months. Of the 424 people given placebo, 11% switched to open-label siponimod after their disability progressed as confirmed after six months.

The risk of a patient's disability getting worse was 21% lower for people given siponimod, compared to people given placebo — around a quarter of people given the drug saw their level of disability increase after three months (26%, 288/1096 people), compared with a third of people on placebo (32%, 173/545 people).

In addition, secondary outcomes of the trial suggest that, from the start of the trial to 24 months, the reduction in brain volume was less severe for people given the drug, compared to placebo. Loss of brain volume is a marker for tissue damage in MS.

The drug had no effect on maintaining patients' walking speed, and both the group taking the drug and the placebo group became slower after three months when doing a timed walk of 25 feet. However, the authors note that most of these patients already relied on walking aids, and this might have affected the test.

More patients given the drug than the placebo experienced adverse events (89% vs 82% patients), such as a slower heart rate (4% vs 3%), high blood pressure (12% vs 9%), reduced white blood cell count (1% vs 0%), macular oedema (2% vs less than 1%), increased liver enzymes (6% vs 4%) and increased numbers of convulsions (2% vs less than 1%).

The authors say that this safety profile is similar to other drugs in the same class and conclude that siponimod could be a useful treatment for secondary progressive MS.

"So far, no drug has consistently reduced disability progression in people with secondary progressive multiple sclerosis. These patients often have a high level of disability, and preventing further progression is important for their quality of life," said lead author Professor Ludwig Kappos, University of Basel, Switzerland.

"Although the effects of the drug on disability progression after three and six months are impressive, our study does not yet look at the long-term effects of siponimod, which we are investigating in the long-term follow-up of the study patients."

The authors acknowledged some limitations, including that results for people who were originally given a placebo and chose to have open-label siponimod after their disability progressed were still included in the study. This may have reduced the effect size of siponimod for some secondary outcomes of the study.

Although the authors attempted to analyse it, the treatments people were given before the study may have affected their response to siponimod.

Dr Luanne Metz, University of Calgary, Canada, expressed caution because the drug did not have an effect on all of the secondary outcomes. She said, "Relapsing-remitting multiple sclerosis (RRMS) has been treatable for over 20 years and increasingly effective therapies continue to be developed. Unfortunately, therapies that convincingly affect the progressive phase of MS have yet to be identified… Although siponimod seems to reduce the time to confirmed disability in SPMS, the treatment effect was small. In our opinion, the reduction in the proportion of participants reaching the primary endpoint of only 6% and the absence of a significant difference for the key secondary clinical outcome are disappointing results and do not suggest that siponimod is an effective treatment for SPMS. Confidence in the treatment benefit of siponimod in progressive MS will, in our opinion, require confirmation in a second trial. Trials of other novel treatments that target non-inflammatory mechanisms are still needed."

Novartis plans to file for regulatory approval of siponimod for SPMS with the US Food and Drug Administration (FDA) in early 2018. Novartis has initiated a scientific advice consultation with the European Medicines Agency (EMA) and, pending its outcome, plans to file in Q3 2018. The EXPAND results have previously been presented at scientific congresses.

High-purity gas equipment

When using gas for analysis and high-tech production, it's essential to maintain the integrity of gas between the gas source and point of use — and the quality of the gas is only as good as the quality of the distribution system. BOC offers two ranges of high-purity gas equipment — BASELINE cylinder regulators and REDLINE gas supply systems. The latter is available when installed by BOC Customer Engineering Services.

BASELINE cylinder regulators are designed for more stable operation than industrial equipment can provide. The range is suitable for gas purities of up to 5.0 and is designed to complement the specialty gases supplied by BOC. As such, both stainless steel and brass options are available to suit corrosive and non-corrosive gases.

REDLINE gas supply equipment is suitable for high-performance and purity-sensitive specialty gas applications. According to the company, the REDLINE system ensures that the integrity of the HiQ specialty gas in the user's system is not jeopardised. As a one-stop solution provider, BOC designs and installs these systems in accordance with the user's requirements.

BOC Limited
www.boc.com.au

2D barcode scanner for liquid handling systems

Ziath's 2D barcode rack scanner, the DataPaq Mirage, is a camera-based scanner with a low-profile design.

Researchers working in biotech, academia and pharma frequently manage a large number of samples and, as a result, require automated solutions to assist with routine techniques, such as liquid dispensing. Many camera-based scanners are too tall for use on liquid handling workstations; however, the DataPaq Mirage utilises a mirror to give the scanner a more compact design.

The low-profile design enables easy integration with liquid handling systems, as well as other laboratory automation solutions, allowing samples in SBS format racks to be efficiently scanned and recorded at the point of processing. Despite the compact nature of the product, its powerful camera system means the depth of image focusing is not compromised, ensuring that a variety of 2D-barcoded tubes can be quickly scanned.

Pathtech Pty Ltd
www.pathtech.com.au

Sequencing solution

Thermo Fisher Scientific has partnered with Illumina to make the former's suite of AmpliSeq chemistry products compatible with the latter's next-generation sequencing (NGS) platforms. The end result, AmpliSeq for Illumina, enables fast, robust, targeted library prep for all Illumina sequencers.

The solution offers a highly multiplexed polymerase chain reaction (PCR)-based workflow for use with targets ranging from a few to hundreds in a single run. Users can prepare DNA or RNA libraries from as little as 1 ng input in just 5 h, with a comprehensive menu of panels and a wide variety of sample types.

Panels are optimised for clinical cancer and genetic disease research applications, and are available as ready-to-use, community or custom panels. AmpliSeq panels can accommodate high-quality samples such as blood, cell culture or fresh frozen tissue, and also challenging samples such as formalin-fixed paraffin-embedded (FFPE) tissue. Users can select from predesigned panels or customise their content for a variety of genomes and flexibility.

AmpliSeq for Illumina sequencing offers high-confidence data to researchers in a wide variety of application areas.

Illumina Australia Pty Ltd
www.illumina.com

BRUKER

ALPHA II

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The ALPHA II is the further development of the very successful ALPHA spectrometer. It combines the highest quality with little space requirement and maximum operating comfort. With the integrated touchpanel PC and the intuitive OPUS-TOUCH software, IR analysis is easier than ever before.

Thanks to technical innovations, the ALPHA II is now even more powerful and more robust than before. The ALPHA II is particularly suitable for quality control of industrial products.

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Innovation with Integrity

FT-IR

Document management software

LTech presents its latest standalone module, specifically designed for centrally managing laboratory documents as well as a framework for archiving on an enterprise level.

DocuVault is secure, robust and enterprise-friendly document management software that supports major documents' formats and allows for seamless integration with ERP systems and accounting software. It is designed to be user-friendly, enabling lab staff to use it intuitively and focus on what they are trained to do.

The product enables laboratory documents in any format to be securely (SSL) stored in and accessed from one repository, thus simplifying paperwork. It is said to enable secure data sharing, enhance documents' control, simplify documents' review and move labs one step closer to being paperless.

The software is claimed to optimise the user's intellectual control and ensure compliance to good data and record management, which is the first crucial step to good-quality management. Version controls and an advanced search function provide laboratories with a flexible way to track changes and enhanced data mining capability.

The product can be seamlessly integrated with Lims1.

LTech Australia Pty Ltd
www.lims1.com

Fluorescent glycerolipids

Fluorescent lipids are useful for visualising lipid structures and processes in vivo. Avanti Polar Lipids' glycerolipids enable the study of lipid droplets (LDs).

LDs can be found in most eukaryotic cells and are organelles that store lipids as reservoirs of metabolic energy and membrane lipid precursors. LDs are unusual organelles in that they are bound by a monolayer of surface phospholipids into which specific proteins are embedded, such as perilipins and metabolic enzymes. The cell biology of LDs as cellular organelles is only beginning to be unravelled.

Avanti's fluorescent lipids are >99% in purity and rigorously designed to mimic native function. In addition to glycerolipids, they offer fluorescent fatty acid and omega labelled sphingolipids, as well as fatty acid and headgroup labelled phospholipids and sterols.

Sapphire Bioscience
www.sapphirebioscience.com

Women in STEM:

pay improving but opportunities lacking

Female scientists are not getting the same opportunities for promotion or seniority as their male peers with similar qualifications and experience, a national survey has revealed.

Overall, STEM salary increases have crept ahead of the national average and conditions have slightly improved over the last 12 months for the STEM workforce, but women have fewer opportunities for promotion, according to the annual Professional Scientists Remuneration Survey conducted by Professionals Australia and Science & Technology Australia (STA).

STA CEO Kylie Walker said it's clear this inequity still needs to be urgently addressed.

"There are important national programs underway to address structural and systemic inequities, such as the SAGE program, but they will take time to have an effect on wage and promotion inequities," Walker said.

"I believe a step-change is called for, such as that created in Iceland for example, where wage equality has been protected through legislation. The gap is historic and enduring, and requires bold and significant action if we are to see change in the near future," Walker said.

"It's great to see that our STEM professionals are being rewarded for their hard work through strong average wage increases, but we must ensure that these increases are delivered in a way that levels the playing field."

Australia's most comprehensive snapshot of science and technology working conditions, the Professional Scientist Remuneration Survey, also found that job security remains a longstanding issue for scientists and technologists.

"More than 40% of Australian scientists surveyed were thinking about leaving their job in the next 12 months, and many of them have cited a lack of job security as the prime reason," Walker said.

"This issue comes up every year in this survey. The casualisation of the STEM workforce and the short-term funding cycle in scientific research compounds that sense of instability."

Two-thirds of Australia's STEM professionals reported that their organisation is suffering in the face of cost-cutting and one third reported a decline in the number of scientists being promoted to decision-maker roles in their organisation.

"As a nation we've invested in building a strong and enviable workforce of scientific and technological researchers — they are our nation's solution-seekers and future-builders," Walker said.

"But this survey shows through gender inequity and short-termism we are squandering this resource.

"Australia must take direct action to implement a strategic, stable, long-term approach to supporting all scientific researchers to keep defining challenges and articulating solutions for our health, wealth and wellbeing," Walker said.

Reducing genomic testing time for critically ill babies

In a move to reduce the turnaround time of genomic testing from months to days, the Murdoch Children's Research Institute's (MCRI) Victorian Clinical Genetics Services (VCGS) has installed a DRAGEN Bio-IT Platform from Edico Genome.

VCGS is a specialist in childhood and adult genetics services, offering a comprehensive range of genetic testing and clinical support services to thousands of individuals and families throughout Australia. Together, VCGS and MCRI are said to have the largest collective genetics expertise in the Southern Hemisphere, offering fully integrated research, diagnostics and clinical genetics services.

"We are a collective of scientists, doctors, genetic counsellors, technicians, researchers and other health practitioners jointly dedicated to delivering world-class clinical genetics services and testing throughout Australia," said Dr Sebastian Lunke, head of the Translational Genomics Unit at VCGS.

VCGS installed the Bio-IT platform in January, following a six-month-long validation period, as part of the Acute Care Genomics project, which is analysing genomic data from 250 babies and children in neonatal intensive care units (NICUs) and paediatric intensive care units (PICUs) across Australia. Leveraging field-programmable gate array (FPGA) technology, DRAGEN rapidly accelerates analysis of next-generation sequencing (NGS) data, completing analysis in as little as 20 minutes.

"Diagnosing children and newborns in the NICU and PICU is a race against the clock," said Pieter van Rooyen, president and CEO at Edico Genome. "While NGS is known to be a rich diagnostic tool, lengthy turnaround times have prevented its use in this setting.

"Shrinking NGS analysis times enables potentially life-altering results and corresponding treatments to be received as quickly as possible while increasing labs' capacity, enabling more patients to benefit from NGS. VCGS is truly changing the landscape of NGS at the point of care in Australia, and we look forward to working together on this important endeavour."

The platform is highly reconfigurable, enabling users to run DRAGEN's complete suite of pipelines, including Germline, Somatic, RNA and more, all from the same platform. Edico Genome's dedicated staff of bioinformaticians, computer scientists and engineers continuously develop new algorithms and features for pipelines designed to increase accuracy, speed and scalability. DRAGEN is available on-site, in the cloud and through a blended hybrid-cloud solution.

"With the integration of DRAGEN, we are now able to drastically reduce the turnaround time for genetic tests," said Dr Lunke. "As a result, we can not only provide potential life-altering results faster, but also sequence more patient data and help to save more newborn babies' lives."

Listeria monocytogenes detection kit

Key Diagnostics is expanding its RapidChek testing solutions portfolio to include a system that detects ***Listeria monocytogenes***, a serious foodborne pathogen often associated with contamination from food production processes.

The FSANZ maintains a zero-tolerance policy for ***L. monocytogenes*** pathogen in ready-to-eat (RTE) meat and poultry products, with national and state regulatory bodies recommending and enforcing hygienic measures that call for frequent testing of surfaces in the environment that come into contact with food ingredients as well as finished products. RapidChek ***Listeria monocytogenes*** is designed to meet this diagnostic need.

The product is claimed to provide results days faster than other standard methods, combining a sensitive immunodetection strip with a single proprietary enrichment media. After enrichment, the highly sensitive and specific strips indicate the presence of ***L. monocytogenes*** in only 10 min, with minimal processing.

The RapidChek Listeria NextDay PUR-Blue DUO sampler combines a convenient sample collection device and enrichment media for the growth of ***Listeria*** species, all in one unit. One part of the unit contains a polyurethane tip swab hydrated in Hi-Cap neutralising broth. The other tube contains pre-made RapidChek Listeria NextDay media for resuscitation and growth to detectable concentrations of ***Listeria*** species in 24 h, with no extra handling steps and no media preparation step. Users can couple the sampler with the RapidChek ***Listeria*** immunodetection strip for fast and sensitive detection of ***Listeria*** species from the environment.

The system has several benefits, including unlimited scalability; ease of use with a one-step enrichment process; the need for minimal training; and a long shelf life at room temperature. It is AOAC certified for use on environmental surfaces and for various ready-to-eat foods.

Key Diagnostics Pty Ltd
www.keydiagnostics.com.au

Parallel bioreactor system

Sartorius Stedim Biotech (SSB) has announced the ambr 250 high throughput (ht) perfusion, an automated parallel bioreactor system. It has been specially designed for rapid cell culture perfusion process development to optimise production of therapeutic antibodies.

Developed in collaboration with major biopharma companies, the ambr 250ht perfusion system combines 12 or 24 single-use perfusion mini bioreactors (100–250 mL working volume) with associated single-use perfusion components, all controlled by one automated workstation. The combination of this multiparallel processing capacity and fully single-use perfusion vessel enables scientists to perform more perfusion culture experiments in a fraction of the time of traditional perfusion-enabled benchtop bioreactors, according to the company. The product supports a range of hollow fibre perfusion applications, enabling design of experiments (DoE) studies for high cell density process development in a quality by design (QbD) approach.

Central to the system is the perfusion bioreactor assembly, which is based on the established ambr 250 bioreactor design. Intensified cell culture processing is enabled via components such as high-efficiency spargers, perfusion pump chambers and a hollow fibre for cell retention filter. The geometrical similarity of the mini perfusion bioreactor design to BIOSTAT STR pilot and manufacturing scale bioreactors enables rapid scale-up of optimised perfusion processes, as well as short development timelines.

The perfusion system is simple to set up and use, due to the fully assembled and irradiated perfusion bioreactors which include all the essential components. This includes single-use sensors to continuously monitor pressure at the culture fluid inlet and permeate outlet, enabling online monitoring of transmembrane pressure, as well as parameters such as pH and DO.

Sartorius Australia Pty Ltd
www.sartorius.com

VIS-SWIR imaging in HD

Raptor Photonics, a global leader in the design and manufacture of high-performance digital cameras, has launched an additional member of its family of visible SWIR cameras with the Ninox 1280, offering HD resolution for high-end scientific and astronomy applications.

Using a 1280 x 1024 InGaAs sensor, cooled to -15°C, the camera offers visible extension from 0.4 to 1.7 μm to enable high-sensitivity imaging. The 10 x 10 μm pixel pitch enables high-resolution imaging. It offers less than 40 electrons readout noise combined with one of the lowest dark current readings on the market, according to the company. The camera offers an ultrahigh intrascene dynamic range of 69 dB, enabling simultaneous capture of bright and dark portions of a scene.

Available with a 12-bit CameraLink output, the camera will run up to 60 Hz. It features onboard automated gain control (AGC), which is said to enable the best contrast image from low light to bright, as well as an onboard intelligent 3-point non-uniform correction (NUC) algorithm providing high-quality images. The camera comes with a range of analysis software, including XCAP and Micromanager, and a standard CameraLink frame grabber (EPIX).

Lastek Pty Ltd
www.lastek.com.au

Lauren Davis

CRISPR gene-editing tool targets RNA, tackles dementia

Scientists at the Salk Institute have used CRISPR gene-editing technology to target RNA — as opposed to DNA — and in the process corrected a protein imbalance in cells from a dementia patient.

Called CasRx, the tool opens up the vast potential of RNA and proteins to genetic engineering, giving researchers a powerful way to develop new gene therapies as well as investigate fundamental biological functions. It has been described in the journal *Cell*.

Based on the immune system of bacteria, CRISPR-Cas9 gene editing technology can be described as the use of targeted 'molecular scissors' to cut and replace disease-causing genes with healthy ones. The cutting is performed by the Cas9 protein, while other parts of the system act as guides that instruct where Cas9 should cut the DNA.

Scientists have been harnessing Cas9 molecular scissors for a few years now in combination with artificial guides to modify genes in bacteria, plants and animals. But while these scissors typically cut DNA, the Salk team decided to search bacterial genomes for new CRISPR enzymes that could instead target RNA — a working copy of DNA that is translated into proteins. As faulty RNA is the cause of many genetic diseases, the team's hope was that they could engineer CRISPR enzymes to address problems with RNA and the resulting proteins.

"The DNA in your cells are largely the same, whereas the RNA product is really what's changing, and mediates dynamic processes like inflammation or behaviour," said Patrick Hsu, senior author of the study. "And in fact, many genetic diseases are actually caused by defects directly at the RNA level. And so by targeting RNA we can start to try to manipulate these processes."

For example, a given RNA message can be expressed at varying levels and its balance relative to other RNAs is critical for healthy function. Furthermore, RNA can be 'spliced' in various ways to make different proteins, but problems with splicing can lead to diseases such as spinal muscular atrophy, atypical cystic fibrosis and frontotemporal dementia (FTD).

"What splicing does is, it basically modifies the RNA message to turn into two different kinds of proteins, for example," said Salk Research Associate Silvana Konermann, the paper's first author. "And this balance of these two different types of proteins is dysregulated in certain diseases, like neurodegeneration."

So how did the researchers manage to target RNA? As explained by Konermann, "We began the project with the hypothesis that different CRISPR systems may have been specialised throughout an evolutionary arms race between bacteria and their viruses, potentially giving them the ability to target viral RNA."

The team developed a computational program to search bacterial DNA databases for the telltale signatures of CRISPR systems: patterns of particular repeating DNA sequences. In doing so, they discovered a family of CRISPR enzymes that targets RNA, and called it Cas13d.

The team realised that, just like the Cas9 family, Cas13d enzymes originating from different bacterial species would vary in their activity, so they ran a screen to identify the best version for use in human cells. That version turned out to be from the gut bacterium *Ruminococcus flavefaciens* XPD3002, which led them to name their tool CasRx.

"Once we engineered CasRx to work well in human cells, we really wanted to put it through its paces," said Konermann. Deciding to focus on a disease-related condition, the researchers engineered CasRx to tackle FTD — a type of dementia in which the ratio of two versions of the Tau protein (also implicated in Alzheimer's disease) is out of balance in neurons.

"The Tau transcript can be translated into two different types of Tau protein," explained Konermann. "And in a healthy cell, there's a very finely controlled balance between those two different types of Tau proteins. In the diseased cell,

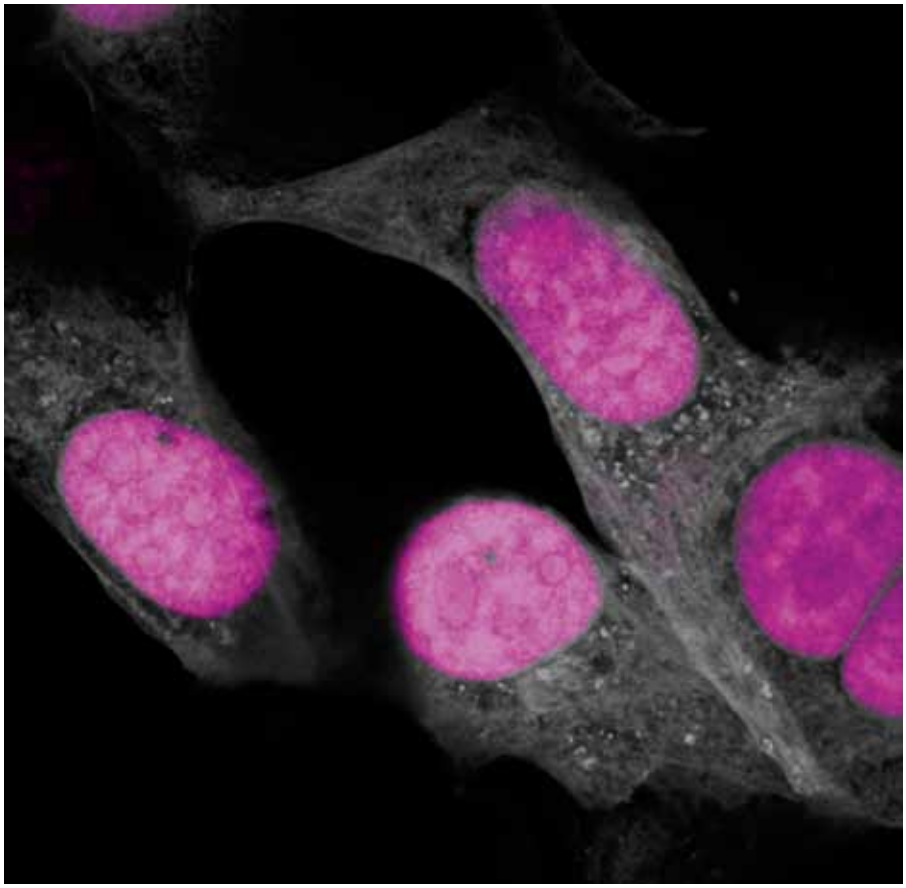
one type of protein now is dominating, and more than it should be."

The team genetically engineered CasRx to target RNA sequences for the version of the Tau protein that is overabundant. They did this by packaging CasRx into a virus and delivering it to neurons grown from an FTD patient's stem cells.

According to the researchers, CasRx was 80% effective in rebalancing the levels of Tau protein to healthy levels. Konermann stated, "By using our RNA-targeting CRISPR protein to target specific elements inside the RNA message, we're able to reset the balance between these two kinds of Tau proteins."

The Salk team is not the first to develop molecular scissors to target RNA. Earlier this year, German scientists showed that the Cas9 protein of the foodborne pathogen *Campylobacter jejuni* is capable of cutting RNA — a revelation that came soon after two other research groups reported similar findings with Cas9s from two other bacteria.

The Salk team does, however, believe CasRx has certain advantages compared to other RNA-targeting technologies, citing its small size (making it easier to package into therapeutically relevant viral vectors), its high degree of effectiveness and the fact that it created no discernible off-target effects compared to RNA interference. The researchers are excited about the possibilities their tool opens up for exploring new biological questions about RNA and protein function, as well as therapies to tackle RNA and protein-based diseases.



CasRx (magenta) targeting RNA in the nucleus of human cells (grey). Image credit: Salk Institute.

"I think we're really only scratching the surface of what we can do with these genetic engineering tools," said Hsu. "And by targeting RNA, the hope is we can develop new types of intelligent therapies that can respond to the state of a cell, and not just the genome that encodes it."

what's new

Made-to-order gas mixtures

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The high-precision mixtures will support key sectors including life sciences, universities, biotechnology, lung function testing, pathology, IVF applications, emissions reduction, LNG exports and many more. BOC will tailor mixtures to meet customers' needs, whether this means measuring NO_x and SO_x levels in the chemical and power sectors or supporting Australian universities in research. The company offers more than 8000 Australian-made specialty gas mixtures.

BOC Limited
www.boc.com.au

Fume hood

UniFlow SE AireStream Fume Hoods are constructed entirely of chemical-resistant, flame-retardant, non-metallic composite resin materials. The high-performance fume hood is said to maximise user protection and energy savings.

The product features a 'unitised' construction that does not require screws, bolts, rivets or metallic hardware for assembly. The fume chamber is moulded seamlessly in one piece, with all corners coved for easy cleaning and light reflectivity.

The hood is equipped with a 0.91 m high extended view height; a vector-slotted rear VaraFlow baffle system; an aerodynamic sash lift with a perforated air-sweep feature; and a moulded-in belled outlet collar for reduced airflow resistance. The lighting is a vapour-proof LED strip fixture with a central switch, pre-wired to a single point junction box 115 V/60 Hz.

The fume hood series is UL 1805 certified and offered in 1.22, 1.52, 1.83 and 2.44 m widths in either constant air volume or restricted bypass models. The hood is shipped completely assembled and can include a wide selection of accessories that can be factory installed to meet the user's specific needs. Work surfaces in a variety of materials and a choice of base cabinets, including acid or flammable storage, are optional as required.

HEMCO Corporation
www.hemcocorp.com

Modular hearing aids

A Melbourne researcher has helped design what is claimed to be the world's first modular hearing aid — a breakthrough that took 130 prototypes to get right.

The design process for the new hearing aid, Facett, saw RMIT University lecturer Leah Heiss spend 37 weeks embedded with the company behind the device, Blamey Saunders Hears. Her role during this time was to always keep good design at front of mind.

"There is often a disjunct between design and technology development," explained Heiss.

"When a concept design is handed over to engineering, a whole lot of technical decisions are made, and by the time the designer returns the technology has a form that can't easily be modified.

"Because I was there for almost nine months, I was at the table with the engineers and the audiologists. I could keep human-centred design principles in focus.

"As a core part of the team, I could say, 'This change will have an adverse impact on how users feel about this technology, let's keep thinking.'"

The result of this collaboration is a product that is not only incredibly functional — modular, rechargeable and snapping together with magnets so anyone with dexterity issues can use it with ease — but also aesthetically beautiful.

"With medical technologies, there is often very little consideration of the emotional impact," said Heiss. "The focus is on clinical efficacy and making sure something works, then basic maintenance — is it cleanable, is it wipeable? Just make it skintone, it will be fine.

"Whereas we're all actually thinking, feeling human beings. We have aesthetic wants and needs."

This is especially important for the millions of people around the world who have untreated hearing loss, and don't want to suffer from the perceived stigma of wearing a hearing aid.

"The stigma is closely connected with ageing and all the feelings people have about that, growing more frail or dependent, wanting to avoid giving away signals your body is 'letting you down'," Heiss said.

"This is about helping people get over the line to take up a technology that could dramatically improve their health and wellbeing — to get them past that emotional barrier through great design."

Inspired by the natural forms of crystals, Heiss spent days with the Melbourne Museum's mineralogy collection, constantly thinking about colour, texture and form. All 130 iterative models are currently on display at a special exhibition at the museum, recognising their significance for Victoria.

About half of the prototypes were 3D printed at RMIT's Advanced Manufacturing Precinct, with the evolving models tested by a cross-disciplinary team involving mechanical engineering, electronic engineering, audiology and design. The team would take each new model and test it on a special mannequin, examining issues like how it sat on the ear and what effect that had on the microphones inside.

"Actually creating the 3D-printed models and having something physical to work with was an essential part of this process," said Heiss.

"Rather than just a concept on paper, we had something tangible that helped draw these varied fields of expertise together around some really complex problems."

For Dr Elaine Saunders, co-founder of Blamey Saunders Hears, the collaborative development process was essential to fulfilling the company's philosophy of creating health solutions in partnership with its clients.

"One of the challenges in creating a revolution via product innovation is that most people can't detail exactly what they want to see in a product until it starts to take form," Saunders said.

"By embedding a designer throughout our process we have been able to really connect with clients right from the start, and then iteratively evolve our solution based on what works from a human-centred design perspective.

"It's this clinical, design and engineering collaboration over time that has enabled such a strong solution that we can see people connect with in a deeply personal way."

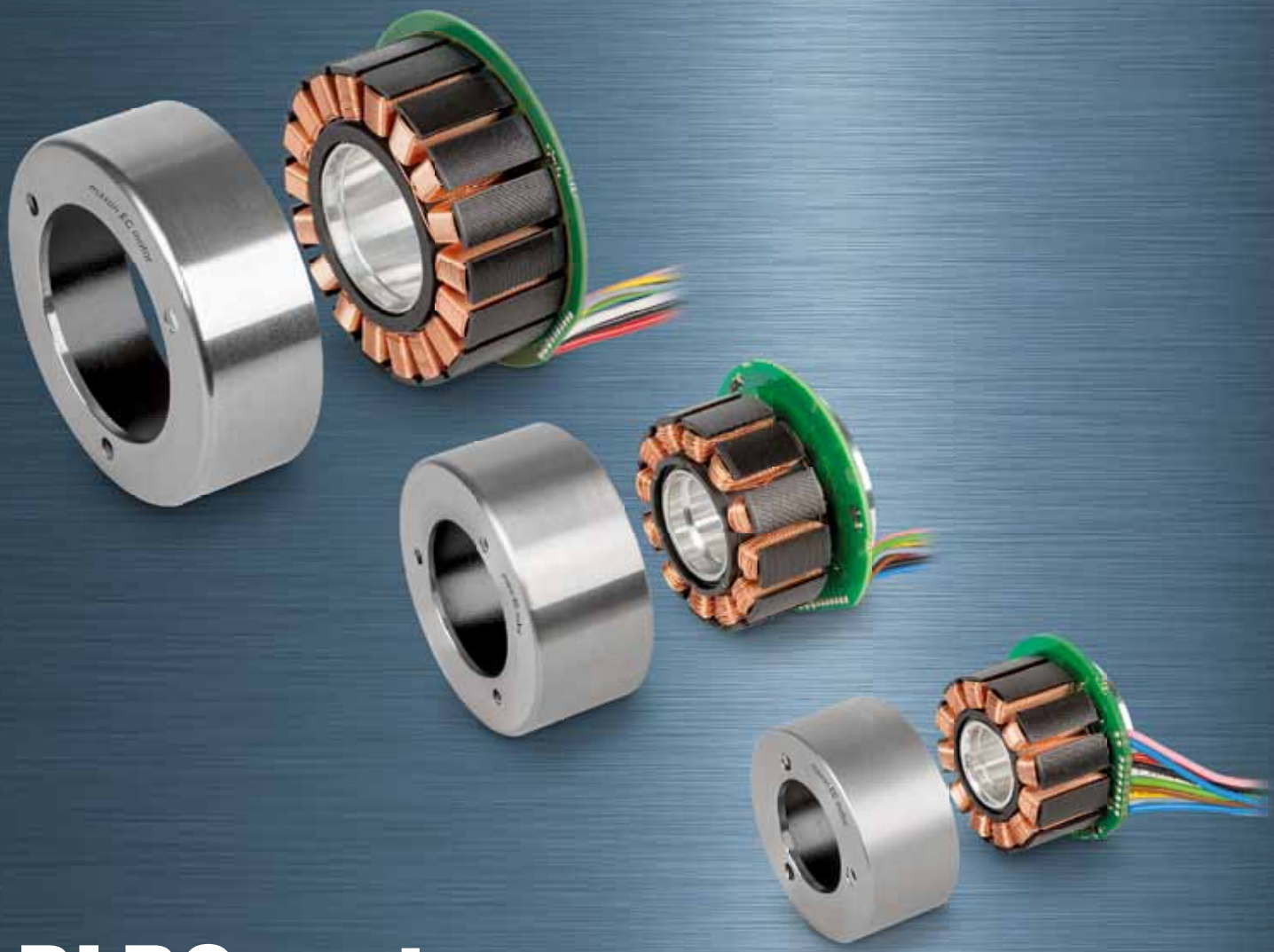
Saunders said universities are in a unique position to support technology innovation by providing 'thinkers' who can come into a team and represent a clear, often challenging view, backed by a wealth of knowledge.

"It's this convergence of commercial strategic development and specialist university-supported global thinking that creates a cutting-edge view, with a real passion for delivery motivated by different drivers.

"Indeed, this could present strong possibilities for both industry and universities in delivering innovations through collaboration."

As for Heiss, she continues to be driven by design to improve life; to humanise health technologies and engage with people's emotional experience.

"By working to understand, through empathy, the shame and embarrassment people feel when they have to deal with these medical apparatuses, we can develop things that people really want to wear — and that can be life-changing."



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The annual conference of the Cooperative Research Centres Association (CRCA) provides an opportunity for researchers, educators and industry to network with CRCA members while gaining valuable insights regarding the nature of cooperative research ventures.
This year's conference will explore the importance of business and industry working with researchers to create innovation, and how to foster these relationships.

AusMedtech 2018
May 1–2, Adelaide
https://www.ausmedtech.com.au/

Science on the Swan 2018
May 1–3, Fremantle
http://scienceontheswan.com.au/

Australasian Society For Infectious Diseases Annual Scientific Meeting 2018
May 10–12, Gold Coast
https://www.asid.net.au/meetings/asid-annual-scientific-meeting-2018

Collaborate | Innovate | 2018
May 14–16, Sydney
https://collaborateinnovate.com.au/

5th Asian and Oceanic Congress on Radiation Protection
May 20–23, Melbourne
http://www.aocrp-5.org

Science at the Shine Dome
May 22–24, Canberra
www.science.org.au/news-and-events/events/science-shine-dome

64th Annual Scientific Meeting for the Australian Mammal Society
July 1–5, Brisbane
http://australianmammals.org.au/events/20_64th_annual_scientific_meeting

Australian Society for Microbiology 2018 Meeting
July 1–5, Brisbane
http://asmmeeting.theasm.org.au/

MACRO2018 — World Polymer Congress
July 1–5, Cairns
http://www.macro18.org/

1st World Congress on Nutrition & Food Sciences
July 09–10, Sydney
http://www.nutritionalconference.com/

8th World Congress on Plant Science & Genomics
July 09–10, Sydney
http://plantgenomics.plantscienceconferences.com/

International Conference on Chemistry Education 2018
July 10–14, Sydney
http://www.icce2018.org/

15th Asia-Pacific Pharma Congress
July 16–18, Melbourne
http://asiapacificpharmaconference.blogspot.com.au/

International Symposium on Relations between Homogeneous and Heterogeneous Catalysis
July 22–25, Sydney
http://www.ishhc18.com/

National Science Week
August 11–19, Australia-wide
www.scienceweek.net.au/

9th Vacuum and Surface Science Conference of Asia and Australia
August 13–16, Sydney
http://www.ansto.gov.au/Events/9thVacuumandSurfaceScienceConferenceofAsiaandAustralia/index.htm

2018 ARCS Annual Conference
August 21–23, Sydney
https://www.arcs.com.au/events/event/ARCS-Conference

International Society for Clinical Biostatistics and Australian Statistical Conference 2018
August 26–30, Melbourne
http://iscbasc2018.com/

SAFETYconnect 2018
August 29–30, Brisbane
www.safety-connect.com.au/

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