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mRNA to the rescue?

I'm writing this editorial in early December 2021. Australia has fully vaccinated about 88% of its 16+ population against COVID-19, and we've been gearing up for restrictions to ease further in time for Christmas. So apparently that means we're just about due for a new variant of concern to throw all our plans into disarray — enter Omicron.

If there's a silver lining to be found from this and other coronavirus variants we've faced over the course of the pandemic, it's that their presence has promoted innovation and acceleration from Australia's scientists — who recently created the country's first mRNA COVID-19 vaccine candidate (and first ever mRNA drug product, period) in just five months. The work was led by mRNA Victoria in partnership with the Monash Institute of Pharmaceutical Sciences (MIPS), The Peter Doherty Institute for Infection and Immunity and IDT Australia, in what has been described as a landmark collaboration between Victoria's medical research and manufacturing sectors.

Professor Colin Pouton, who led the MIPS team that developed the vaccine, said it has the ability to rapidly adjust its composition in response to emerging virus mutations such as Omicron. 450 doses of the vaccine candidate have since been produced by IDT, in preparation for 150 people to take part in Phase 1 clinical trials to be run in early 2022 by the Doherty Institute.

Heading north to NSW, Premier Dominic Perrottet has announced that his government will invest in a $96 million pilot facility to develop mRNA and RNA drugs and vaccines, in order to better combat disease and save lives. The facility, to be established in partnership with all NSW universities subject to the approval of a final business case, will include laboratories and preclinical trial spaces that will enable early-stage RNA-based drug development.

Perrottet said the state government's funding for the facility aims to attract commercial investment in mRNA and RNA production here in Australia. NSW Minister for Jobs, Investment, Tourism and Western Sydney and Minister for Trade and Industry Stuart Ayres added that the facility would bridge the gap between NSW's world-class RNA research and a viable commercial RNA industry.

"There is also the potential for this facility to be scaled up to significantly increase our sovereign capacity in vaccine production, strengthening the state's resilience against future pandemics," Ayres added.

Of course the pandemic hasn't just altered how scientists fight disease, but also how they conduct their work. In our lead story on page 10, we look at how artificial intelligence, machine learning and automation are now at the forefront of the future-ready laboratory. Meanwhile, our article on page 24 showcases a smart wearable sensor that can assess chronic wounds in real time, giving patients the freedom to monitor their wounds at home. And in their efforts to speed up detection of multidrug-resistant pathogens, German researchers have developed a platform that will provide a result in just one hour, using just a single DNA molecule (page 37).

While our hopes for a COVID-free Christmas may have been dashed — again — we can take comfort in the knowledge that Australia's scientists are continuing their work to protect us against this and future viruses, since it's become apparent that the current vaccines alone will not be sufficient forever. And as we enter a new year, the fight will go on.

Regards,
Lauren Davis
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Lauren Davis

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Imaging software instantly diagnoses, treats jaundice


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Engineers from the University of South Australia (UniSA) and Middle Technical University have designed imaging software that can diagnose jaundice in the blink of an eye, automatically turn on an LED light to counteract it and send the diagnosis via SMS to the carer. Their breakthrough has been published in the journal *Designs*.

Jaundice is a common condition in newborns, especially premature babies, where there is an overload of an orange-yellow pigment called bilirubin in the bloodstream. It normally resolves quickly when the baby's liver is mature enough to remove it from the body, but in severe cases can be treated by phototherapy, whereby fluorescent blue light is used to break down the bilirubin in the baby's skin.

UniSA remote sensing engineer Professor Javaan Chahl says jaundice is particularly prevalent in developing countries, where there often isn't the equipment or trained medical staff to effectively treat it; as a result, an estimated 75,000 children are currently living with brain dysfunction worldwide due to complications from jaundice. The newly developed imaging software is designed to counteract this.

"Using image processing techniques extracted from data captured by the camera, we can cheaply and accurately screen newborns for jaundice in a non-invasive way, before taking a blood test," Prof Chahl said.

"When the bilirubin levels reach a certain threshold, a microcontroller triggers blue LED phototherapy and sends details to a mobile phone.

"This can be done in one second, literally, which can make all the difference in severe cases, where brain damage and hearing loss can result if treatment is not administered quickly."

Researchers tested the system in an intensive care unit in Mosul, Iraq, on 20 newborns diagnosed with jaundice. A second dataset captured 16 images of newborns — five healthy and the remainder jaundiced. The system was also successfully tested on four other manikins with white and brown skin colours, with and without jaundice pigmentation.

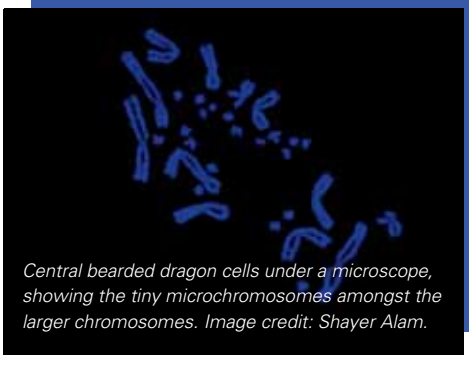
"Previous research using sensors to find a non-invasive way to detect jaundice has fallen short," said Prof Chahl. "Methods trialled have been unreliable, costly, inefficient and in some cases caused infections and allergies where sensors needed skin contact.

"Our system overcomes these obstacles by immediately detecting jaundice based on a novel digital representation of colour which allows high diagnostic accuracy at a relatively low cost. It could be widely used in hospitals worldwide and medical centres where laboratory facilities and trained medical staff are not available."

So-called 'dust specks' are actually genome building blocks

An international team of scientists has discovered that tiny 'microchromosomes' in birds and reptiles, initially thought to be specks of dust on the microscope slide, are linked to a spineless, fish-like ancestor that lived 684 million years ago. Indeed, they are believed to be the building blocks of all animal genomes, but underwent a significant rearrangement in mammals — including humans.

Led by Professor Jenny Graves from La Trobe University and Associate Professor Paul Waters from UNSW, the team made the discovery by lining up the DNA sequence of microchromosomes that huddle together in the cells of birds and reptiles. When these little microchromosomes were first seen under the microscope, scientists thought they were just specks of dust among the larger bird chromosomes, but they are actually proper chromosomes with many genes on them.


Central bearded dragon cells under a microscope, showing the tiny microchromosomes amongst the larger chromosomes. Image credit: Shayer Alam.

"We lined up these sequences from birds, turtles, snakes and lizards, platypus and humans and compared them," Prof Graves said.

"Astonishingly, the microchromosomes were the same across all bird and reptile species. Even more astonishingly, they were the same as the tiny chromosomes of amphioxus — a little fish-like animal with no backbone that last shared a common ancestor with vertebrates 684 million years ago."

Dr Waters added, "Not only are they the same in each species, but they crowd together in the centre of the nucleus where they physically interact with each other, suggesting functional coherence.

"This strange behaviour is not true of the large chromosomes in our genomes."

Prof Graves said in marsupial and placental mammals these ancient genetic remnants are split up into little patches on our big, supposedly normal, chromosomes. Dr Waters added that while we generally think of our own chromosomes as the normal state, mammal genomes have been "hammered" when compared to other vertebrates.

Prof Graves said the team's findings, published in the journal *PNAS*, highlight the need to rethink how we view the human genome.

"Rather than being 'normal', chromosomes of humans and other mammals were puffed up with lots of 'junk DNA' and scrambled in many different ways," she said.

"The new knowledge helps explain why there is such a large range of mammals with vastly different genomes inhabiting every corner of our planet."

Oral hookworm vaccine proves effective in mice

Researchers from The University of Queensland (UQ) and James Cook University have made a significant breakthrough in their development of an oral vaccine to prevent hookworm infection — a parasite which causes serious disease in tens of millions of people globally.

Hookworm lives within the human intestine, using the host's blood as its source of nourishment, digested through a special set of enzymes. It is often found in regions with poor water quality, sanitation and hygiene — greatly impacting on the physical and cognitive development of children and increasing the risk of mortality and miscarriage.

As explained by UQ's Dr Mariusz Skwarczynski, the new vaccine targets the hookworm's digestion enzyme (APR 1). "When the function of these enzymes is blocked, the parasite starves," Dr Skwarczynski said.

"Our vaccine produces antibodies against the hookworm enzymes responsible for the

digestion of blood — they simply stop being able to eat properly."

Professor Istvan Toth, also from UQ, said the ease with which the vaccine could be administered — via tablet, liquid or powder — would be a game changer for developing countries.

"Our vaccine candidate can be orally self-administered, bypassing the need for trained medical staff, and means there's no requirement for special storage, enabling it to reach large, isolated populations," Prof Toth said.

"Vaccination can be carried out at a significantly reduced cost, which not only improves the health of those affected and at high risk, but also helps improve economic growth in disease-endemic areas."

Trials of the vaccine candidate in mice indicate that it is more than twice as effective as existing alternatives, which only achieved a 30–50% reduction in the number of worms. These results, published in the journal *Vaccines*, thus mark a leap forward in the battle against the highly contagious parasite.

"The UQ-developed vaccine resulted in an impressive 94% worm reduction in mice," Prof Toth said.

"So not only is our new vaccine candidate easier to deliver, it triggers a staggeringly good immune response."

The researchers plan to continue working on and refining the vaccine candidate in preclinical development settings, to ensure its safety and efficacy, before beginning human clinical trials.

"We're very optimistic that … we will be able to deliver a successful vaccine that stops this parasite in its tracks," Dr Skwarczynski said.

Image courtesy of Chan et al under CC BY 4.0

Wearable injector can detect, reverse opioid overdose

Researchers at the University of Washington (UW) have developed a wearable device to detect and reverse an opioid overdose. The device, worn on the stomach like an insulin pump, senses when a person stops breathing and moving, and injects naloxone — a lifesaving antidote that can restore respiration.

In a multiyear collaboration, UW investigators worked on the prototype with West Pharmaceutical Services, which developed a wearable subcutaneous injector that safely administers medications. The team combined this injector system with sensors and developed an algorithm to detect the life-threatening pattern of respiration that occurs when people experience opioid toxicity.

The pilot device includes a pair of accelerometers that measure respiration and an onboard processor that detects the halt of motion associated with breathing. The wearable system, which has received regulatory approval in the United States, activates the injector in the presence of prolonged apnoeic events (ie, suspension of respiration). The device also can transmit data about breathing rates and apnoeic motion to a nearby smartphone via Bluetooth.

To test the device, a clinical study was conducted with 25 volunteers in a supervised injection facility and a parallel clinical trial was conducted in a hospital environment among 20 volunteers who manifested signs of apnoea by holding their breath. The injection facility deployment was crucial, the researchers said, to help develop algorithms involving real-world, opioid-induced breathing changes. The results were published in the journal *Scientific Reports*.

At the injection facility, the sensors were able to accurately track respiration rates among people with opioid-use disorder. Further, the device was able to detect non-medical, opioid-induced apnoea, which commonly precedes a potentially fatal overdose. The testing measured breathing patterns only to develop the respiratory algorithm and did not involve injection of naloxone, which was administered only in the second study.

In the second study, healthy participants simulated overdose events in a hospital setting by breathing normally, then performing a breath hold for 15 seconds to mimic an apnoeic event. When the wearable system detected that the subject had not moved for at least 15 seconds, it activated and injected naloxone into the participant. Following device actuation, blood draws taken from study participants confirmed that the system could deliver the antidote into the circulatory system, showing its potential to reverse opioid overdoses.

The researchers said further studies are needed to assess the comfort and discreteness of the device over longer time periods, particularly in unsupervised settings. Additional study of the device is needed to evaluate naloxone injection in people who use opioids for non-medical purposes.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Propelling the digital lab in the revolution of AI

Artificial intelligence (AI) and machine learning (ML) technologies are now at the forefront of the future-ready laboratory and have proven to optimise laboratory productivity like never before. Like all other revolutions that take off so fast, AI requires scrutiny from every angle if it is going to serve every facet of society.

Based on a recent podcast, this Q&A article — featuring three industry experts — explores the role of AI and ML applications in the digital lab, and takes a close look at the key learnings of AI and ML as we begin to enter a fully digitalised world.

A deep dive into the governance and ethical principles of AI and ML

Allison Gardner, PhD, Program Director, Data Science Degree Apprenticeship, Keele University, and co-founder of Women Leading in AI, educates us on the governance and ethical principles that need to be involved in AI and ML.

Q: On the frontier of health services, and in general, how thoroughly is AI already a part of our lives?

AG: AI is much more pervasive than people think it is in our lives. It is used in many sectors, from management systems in hospitals, to managing

flight paths in the aviation industry, and it even dictates the algorithms in our Netflix and social media. This is a response to big data and how we can utilise that information embedded in it to classify, predict and improve the efficiency of a system. My concern is that people think of it as a bit of cure-all, and only a system which will make life easier and augment human experience, but it is not as perfect as people think.

Q: Can you tell us more about your work with Women Leading in AI?

AG: I saw a significant gap between technologists, policymakers and lawyers in addressing the problems that we have been seeing with AI systems, particularly with regards to algorithmic bias and the discrimination that can result from that. For instance, these algorithms can misclassify black women at much greater rates than white men, meaning these women in high-risk situations could forego necessary health care and benefits.

Q: What was the reaction of the development community when you spoke to them about this?

AG: I noticed that there was a lot of deflection by technologists, who insisted that AI is 'a black box' that cannot be managed ethically. In response, I had a little bit of a tantrum because one of the key reasons for the deployment of biased algorithmic systems is the lack of diversity in the development teams for these products. Diverse development teams can identify the obvious mistakes that have been made, highlighting that the data is not diverse. With this in mind, I spoke with others who felt the same, and we decided to bridge this gap where we could bring leading thinkers in AI to leading thinkers in policy and government together, so we can fully understand these systems and actually start developing systems in an ethically aligned way.

Q: What would be the best advice for people developing AI, to avoid falling into the bias trap?

AG: Ensuring diverse input and the engagement of all stakeholders in the design of new systems is integral to using this technology in an unbiased way. Reaching out to impacted and diverse stakeholders so they can have a meaningful involvement in the design of the process is crucial.

For high-risk processes, there needs to be a point where if you have not had the application signed off from an independent auditor or an independent internal reviewer outside of the system confirming its suitability, then the system should not be deployed. I also advocate for a citizen-focus trust mark, not dissimilar for example to food labelling, fair trade, nutrition labelling, recycling labels and such, so informing the person on the receiving end, "An AI system has been involved in this process, go and see this further information."

Ultimately, we can educate people on these issues, but technology is developing so fast that we cannot educate people quick enough, so we can only inform and empower them to be AI-aware.

Transforming scientific research labs with advances in AI, data science and human–computer interaction

Paul Bonnington, PhD, Professor and Director of Monash eResearch Centre, Monash University, discusses the transformation of scientific research labs with advances in AI, data science and human–computer interaction.

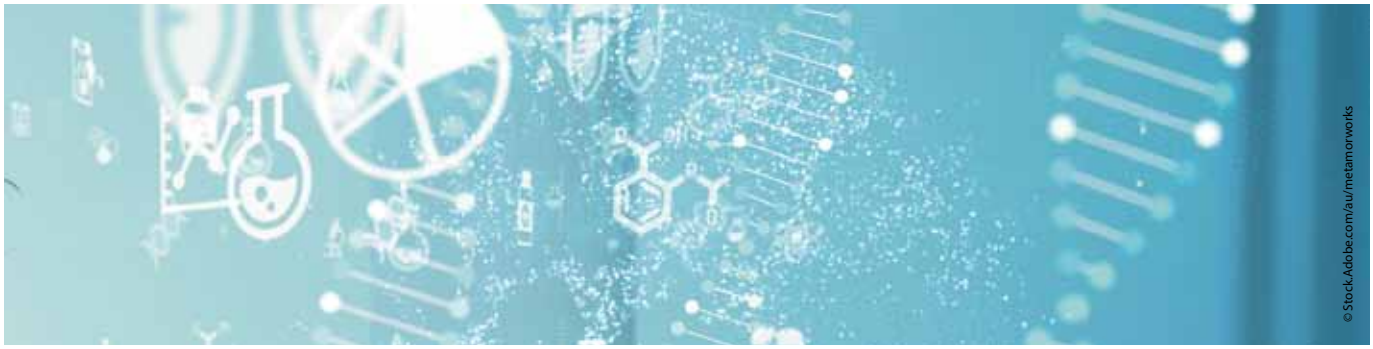
Q: Could you tell us more about how you define eResearch as a concept?

PB: eResearch is best thought of as digital research. All aspects of the research process are undergoing a transformation and it is being applied to all domains — from the humanities, arts and social sciences through to STEM disciplines such as engineering and medicine. These domains have all been fundamentally changed by digital technologies that are making their way into research, which is why the Monash eResearch Centre was established in the mid-2000s to help the university navigate this transformation, given that one of its core business areas is research.

Q: As AI is a big part of your work, what's your take on how it's best applied to medical research, or indeed generally?

PB: I believe that the way to apply artificial intelligence is always to make sure that the human is involved. We can see patterns and data that a computer is not going to necessarily be able to find unless we tell it to look for those patterns.

Personally, I find the most exciting application of AI is in computer vision and supported decision-making because it opens the potential for ordinary people to be able to apply decision-making AI tools



that have been trained to think like experts in the field and, more importantly, they're able to do that from almost anywhere. This AI is described as deep learning — essentially training computer models by throwing at the computer lots and lots of data which has been annotated by experts. After a while, the computer model begins to 'think' like those experts.

Q: You and your colleague Kimball Marriot were awarded the Agilent Thought Leader award recently for your work on the interface between AI and lab instrumentation. Can you tell us a little about that?

PB: Receiving the Agilent Thought Leader Award has enabled me to shift the focus in my own research. I started to see that there were applications of AI which were going to fundamentally change how people use scientific instruments. So I became much more interested in the use of deep learning capabilities and the use of computer vision to help solve problems.

Our team has been looking at the sample introduction area of an instrument which consists of tubes, spray chambers and nebulisers. There are a few challenges which could arise in the sample introduction area, but we've been collaborating on a project with Agilent where we're using computer vision to see these potential obstacles before the operator does. In doing so, we will be able to warn operators that the instrument might require attention, a component needs a reattachment or that the nebuliser needs to be clear.

Q: The potential benefits to efficiency and decision-making seem clear, but what are the challenges you face in this frontier of research?

PB: A big challenge of our own work is the fact that the people that benefit from our capabilities, techniques and infrastructure are actually generating more and more data. As a consequence, it is difficult to keep up with the growth that we are experiencing in the generation of new data. We therefore need to know if anything we generate will be useful at all, which is an equally complex problem because often data to any human is going to look like noise, but it might be that a hidden gem is in there somewhere. So, this is where AI can also help — it can provide algorithms and models to help pre-screen the data to give you a good indication of whether anything useful is likely to be found in it.

The digital lab: understanding the applications and tools for improving the future of science

John Sadler, Vice President and General Manager, Software and Informatics Division, Agilent Technologies, speaks about the digital lab and, more specifically, the understanding of applications and tools for improving the future of science.

Q: Could you explain your take on the benefit of digital innovation in the lab of the future?

JS: I like to think of it as the digital lab that we've needed for a long time now, as opposed to 'of the future'. Our customers, in general, need to do more with less every year. The customer value behind the digital lab really is about improving lab productivity by reducing labour intensity for analysts, through eliminating sample transcription errors and sample handling errors, and improving the scalability and IT friendliness of the data systems that run the lab.

Q: How has the COVID-19 pandemic changed the way in which day-to-day lab operations may function?

JS: The pandemic has really driven quite a radical change in the level of acceptance of remote deployment, maintenance, support, and the desire to be able to operate, conduct workflow review and other lab operations in a remote way. Vendors like us, who are developing lab systems, have been put in the hot seat to make sure that we do our part to provide secure systems that are still usable, and that provide the ability to do remote work. There has also been a growing recognition that we could use, with appropriately structured data, machine learning to take labour intensity out of lab operations and particularly to make analysts more productive. Overall, we have seen lots of opportunity for labour savings in day-to-day lab operations.

Q: And what are the advantages for labs who invest in these steps towards more automated or remote workflows?

JS: I think adopting more digitally advanced applications and tools typically accrues benefits for labs in a few different dimensions. The first is the reduction of rework and labour, and the improved quality of output. The secondary effect of adopting more digitally advanced techniques is the ability to have access to your data in a way that allows you to do more than just generate a report and sign off on it. Electronic records make it possible to start enabling secondary insights which ultimately improve the quality of lab operations.

Conclusion

Advances in AI and machine learning have certainly allowed for a fast-moving and exhilarating journey towards the digital lab, and one which we have the means to control and direct towards a better society. While there is always a flipside to every exciting innovation, particularly in technology, some of the wider challenges around biases in ML, which can lead to misclassification of subjects, are becoming better understood and therefore can be addressed ethically in the revolution of AI.

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The EchoLUTION protocols are up to three times faster than common silica-based methods, the company says; centrifugation steps are reduced from eight to a maximum of three, and protocol duration from several hours to 30 min. Since EchoLUTION-purified DNA is completely free of contaminants and enzyme inhibitors, it is suitable for all downstream applications. Particularly in experiments, where sensitivity is of high importance such as qPCR with limited sample material, EchoLUTION-purified DNA is said to outperform results obtained with silica technology-purified DNA.

BioEcho is also committed to encouraging ecological responsibility, reducing the number of plastic-based kit components that are consumed during the lab process. Due to the convenient single-step purification technology, 70% less plastics are wasted than with its silica counterparts, according to the company, and no hazardous liquids are required. BioEcho's kit and spin column packaging is completely free of plastics.

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Upright microscope

The Eclipse Ci-L plus biological microscope from Nikon has been ergonomically enhanced in order to improve long-term comfort.

Long-term microscope users know all too well the issues with back and neck strain, along with eye fatigue, associated with operating and observing specimens under a microscope every day. To reduce these common fatigue problems, Nikon has improved the design of the existing Eclipse Ci-L and released the Eclipse Ci-L plus with the intent of eliminating unnecessary operator movements while maintaining the high optical performance.

The light intensity management (LIM) function developed by Nikon automatically stores any changes to brightness settings. This helps avoid drastic changes in brightness when switching between different magnifications during observations, thereby helping to mitigate eye strain.

With the addition of a nosepiece spacer, the stage height can be lowered 20 mm from the standard position, reducing strain during frequent specimen change. The stage handle height can also be changed to enable a more comfortable hand position. The stage height can be locked using the refocusing knob, allowing quick refocusing after specimen changes.

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Label-free protein analysis system

When developing biotherapeutics, the ability to measure and characterise changes in the secondary structure of proteins is critical. Proteins in solution are prone to conformational change or instability as structural bonds are disrupted by thermal and chemical stresses in the local environment. Any structural change has the potential to compromise efficacy and trigger aggregation which can impact safety, and therefore must be understood and controlled.

Conventional techniques such as FTIR and circular dichroism do not possess the adequate feature set for researchers to accurately assess changes in their proteins within the required conditions. The need for high sensitivity, a wide dynamic range, a simplified and automated workflow, and high repeatability is therefore significant.

The AQS3pro provides label-free protein analysis with a novel IR technique called microfluidic modulation spectroscopy (MMS). The technique is purposely designed to directly address the limitations of current technologies and provide drift-free, background-subtracted, high-sensitivity measurements of the protein secondary structure. It is possible to measure protein similarity (fingerprinting), quantitation, higher order structure, protein stability and aggregation through thermal and chemical denaturation methods using a walkaway automated platform.

The product allows users to 'see change' in the secondary structure of proteins across a wide concentration range from 0.1 to over 200 mg/mL, and in the presence of excipients — the concentration range found across the full spectrum of drug development. Samples can be measured with minimal preparation and without dilution to generate data that is reliably representative of drug performance.

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Getinge's DPTE transfer system is designed to be a safe method for bidirectional transfer in aseptic or toxic working areas, without breaking containment or sterility.

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Once connected, the Alpha and Beta components join together to form a single unit. Tightness is secured by the lip seals of the assembly, which can be opened without breaking sterility or containment. This offers leak-tight transfer.

The DPTE transfer system is available with both fixed and flexible mountings. The patented system prevents loss of containment.

The operator cannot open the DPTE Alpha door when a DPTE Beta part is not properly connected, or when the DPTE Beta port is not equipped with the Beta part. The operator cannot disconnect the DPTE Beta part if the double door is not closed.

Users should match their DPTE Alpha port with the right Beta part from Getinge to protect their operators and production.

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Semi-automated pipetting system

The Eppendorf epMotion 96 is a semi-automated liquid handling system designed for fast and precise pipetting in 96- and 384-well plates. The device can pipette in the range of 0.5–300 *u*L using Eppendorf's classic air-cushion electronic pipetting technology and is designed to be 12 times faster than manual 8-channel pipettes.

Controlled by the epMotion 96 App (iOS devices only), the device can be easily programmed using the easy-to-use software, convenient touchscreen and pre-set application modes for common, repetitive pipetting tasks like aspiration, dilution, multi-dispensing and reverse pipetting. A new sequential dispense function enables users to aspirate in one step and dispense varying amounts in several steps using only one column of tips, while the additional pre-wetting mode means high-vapour liquids are completely dispensed from the tip for more accurate pipetting.

The lifting table can be easily adjusted to support a variety of SBS-formatted labware, and these can be positioned and locked into place using the stage scale and locking handle. Users can also position tips above any column of wells in a 96- or 384-well plate using the 4.5 mm grid, which has recently been added to the 2-position slider of the epMotion 96.

The system can fit under a laminar flow hood and be easily moved between labs, making it suitable for a wide range of applications including plate reformatting, bead-based clean-ups for nucleic acid purification, cell seeding, cell-based assays, ELISA, biochemical assays and more.

Eppendorf South Pacific Pty Ltd
www.eppendorf.com.au

Syringe pumps

The KD Scientific Legato 100 and 200 series syringe pumps are available in multiple models to provide the right pump for each user's application, including infuse only, infuse and withdraw, and push pull. Each of the pumps is available in a programmable version for maximum flexibility and capability. Each of the basic models works with one syringe or two and can be reconfigured in the field to use with multiple syringes.

The series offers ease of use through the high-resolution colour touchscreen user interface. The full touchscreen interface enables the user to quickly create configurations and recall them for easy use. The 4.3″ TFT colour display with touch pad interface presents all the pump operating parameters on one easy-to-view run screen. A protective cover over the display prevents leakage, and the resistive touch screen means using gloves is no problem.

The series is designed to optimise lab bench space, and can be placed on its side to reduce the footprint (8.9 x 27.77 cm) by four times. The display also tilts with the change to allow the user to operate the pump vertically.

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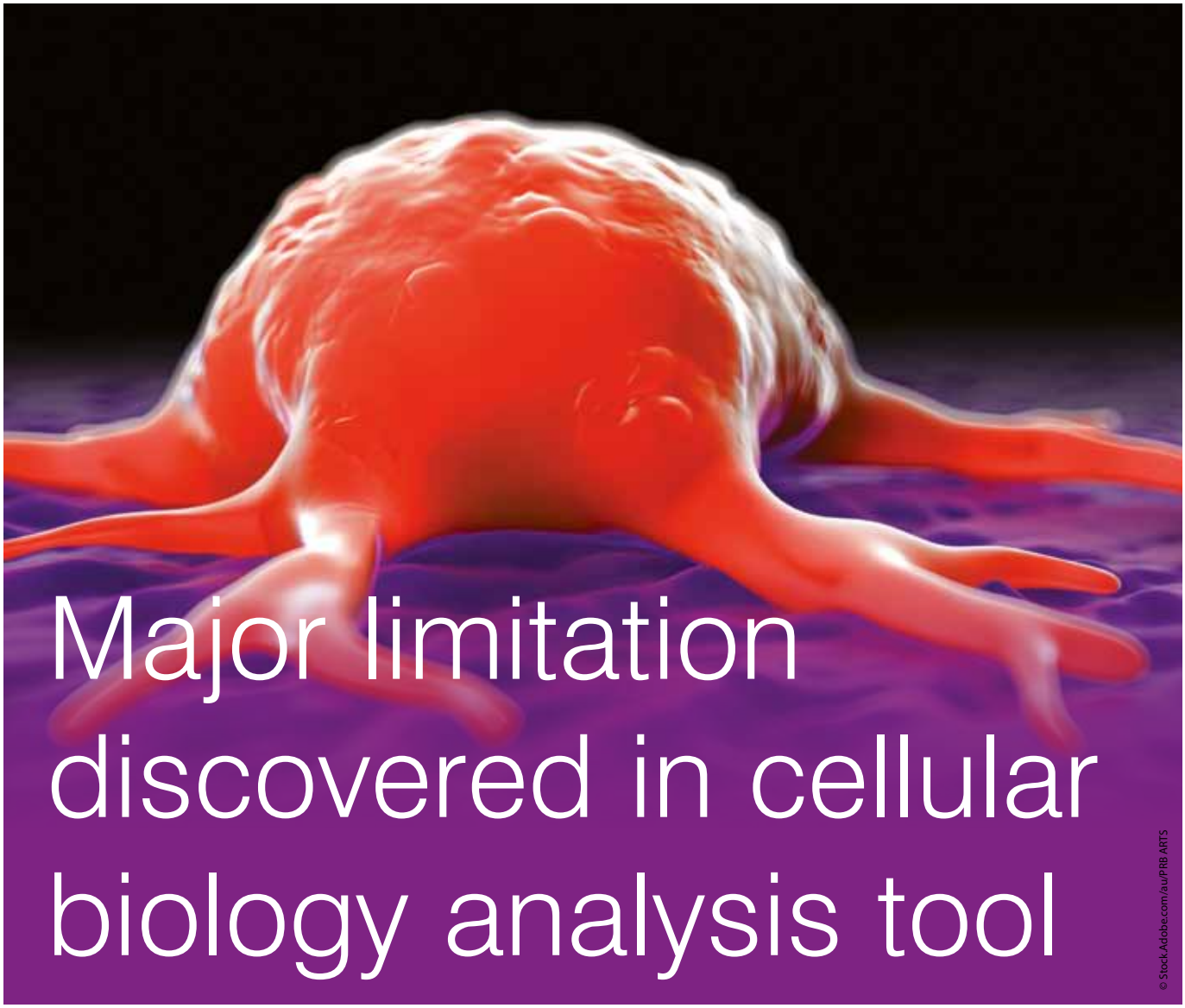

Major limitation discovered in cellular biology analysis tool

Australian researchers have revealed that specialised immune cells called macrophages are being fragmented during the extraction process to generate single-cell suspensions from bone marrow and other haematopoietic tissues.

Published in the journal *Cell Reports*, their discovery indicates that data collected using this scientific method are often skewed — which will force the reassessment of a large amount of already-published scientific literature to determine if the reported observations are accurate or incorrectly interpreted. It is also expected to change how researchers approach analysis of these tissues in the future.

Led by Mater Research, the scientists examined a specific subtype of macrophages, known as tissue-resident macrophages, that are present in each tissue of the body and adapt to where they are located to support the tissue's development, function, health, protection from infection and regeneration after injury. Previous research using single-cell preparations from hematopoietic tissues has often had unexplained, and often ignored, under-representation of tissue-resident macrophages in the generated datasets — even though these cells represent up to 15% of the tissue.

Lead investigator Professor Allison Pettit, Mater Research Director of Biomedical Research, said her team's examination of tissue-resident macrophages in bone marrow, spleen and lymph nodes discovered that all the macrophages were breaking up during the extraction process for single-cell preparation.

"It was a big shock as it has significant implications for the type of research we do, and it will likely cause controversy in the field, but the first priority of academic research is the integrity of the data, as this is integral to the reliability of translating knowledge gains into real-world impacts," Prof Pettit said.

Many biological fields rely on tissue disruption techniques to release individual cells for more detailed study. In the case of haematopoietic tissues, it is a simple procedure in which the whole organ is subjected to a gentle mechanical

disruption procedure to release the individual cells within the tissue.

"The most surprising aspect of our discovery is that during fragmentation, the macrophages leave remnants of themselves behind on other cells within the preparation, creating a 'Trojan horse' effect," Prof Pettit said.

"This means fragmentation of the macrophages during this procedure creates a great deal of complexity and confounding information in the analysis of the data.

"We have exposed that despite the use of state-of-the-art technical approaches, cells that were thought to be macrophages are actually other cells that had macrophage remnants stuck to them. Consequently, a lot of what we think we know about these cells from decades of research will include a lot of inaccuracies."

Prof Pettit said many studies that focused on other types of cells within these tissues have also been unknowingly co-detecting macrophage molecules, potentially creating misleading information about the cell types.

"Accurate knowledge relating to the cellular and molecular biology of these tissues is critical to understanding blood cell production and turnover and immune function, as well as informing discovery of causes and cures for leukaemia and other diseases," she said.

Dr Susan Millard, first author on the study, said the team discovered macrophage fragmentation and the problems it caused when they used imaging flow cytometry as part of their quality control assessment of tissue cell suspension analysis.

"We have been working with these tissues for decades and we always combine both intact whole tissue analysis with the tissue cells suspension analysis," Dr Millard said. "However, these separate analyses would often provide differing results and we weren't sure why.

"When the Translational Research Institute, where Mater Research is partly based, acquired the capability to perform imaging flow cytometry to visualise complex multidimensional molecular analysis, we were able to see our data in a whole new light that revealed the macrophage fragmentation issue.

"We know that tissue-resident macrophages in these tissues play incredibly important roles in many aspects of red and white blood cell production, education of effector immune cells to fight off disease, regeneration of these tissues after injury and adaption of these tissues in response to stress. We've had a poor track record of harnessing these functions to improve human health and fight disease — and this has likely been contributed to by the flawed analysis methods we uncovered.

"Our study exposes an opportunity for a renewed frontier of discovery empowered by precision knowledge."

The researchers intend to expand their work to investigate if tissue-resident macrophage fragmentation also occurs when other tissues are similarly studied using single-cell suspension strategies. They are also working to develop new ways to create single-cell suspension that preserves the macrophages.

Mass spectrometer

The Thermo Scientific Orbitrap Exploris MX mass detector allows biopharmaceutical laboratories to easily implement multi-attribute method (MAM) and to perform intact analysis of monoclonal antibodies (mAbs), oligonucleotide mass determination and peptide mapping, making it suitable for biopharma process confirmation. Accelerated drug characterisation processes in QC and productivity improvements are enabled by fully integrating the spectrometer into Thermo Fisher Scientific's MAM 2.0 workflow, thereby replacing multiple assays with one information-rich mass spectrometric assay.

To simplify the transition of biotherapeutics from development to manufacturing, the system enables QC customers to use the same method established earlier in a molecule's journey to commercialisation, accelerating the biopharmaceutical pipeline. Robust and flexible, the product is designed with everything required for biopharmaceuticals characterisation.

Laboratories can benefit from reduced downtime and maintenance, as well as seamless method transfers. The system offers good data quality and therefore high-confidence results, even for users with limited mass spectrometric experience. It offers easy adoption for contract research, development and manufacturing organisations enabled by rapid calibration procedures, built-in methods and stable performance; Orbitrap technology, which provides high resolution, mass accuracy and sensitivity; and simplified implementation of MAM into QC.

Thermo Fisher Scientific
thermofisher.com

Thermal mass flow meter for methane measurement

Engineers responsible for methane-fuelled electric power co-generation systems, pollution control, and oil/gas production and storage will find the ST80 Series Thermal Mass Flow Meter from Fluid Components International (FCI) useful for measuring methane and providing emissions data to meet emerging government environmental regulations and reporting requirements.

The thermal mass flow meter has a robust, open, cleanable, no-moving-parts sensor design, providing a suitable methane gas application solution for demanding industrial processes. It has international approvals for Div 1/Zone 1, for safe installation in hazardous gas processing areas.

The flow meter features FCI's Adaptive Sensor Technology (AST) — a hybrid sensor drive that combines the industry's constant power (CP) and constant temperature (CT) thermal dispersion sensing technologies in the same instrument. Complementing this measurement drive technique are a choice of four different precision flow sensor element designs for optimum installed performance, including FCI's latest wet gas solution. The Wet Gas MASSter sensor optimises the sensor head design and installation to prevent condensation droplets, entrained moisture or rain from contacting the thermowells, for steady measurement.

The flow meters are suitable for pipe diameters from 25 to 2500 mm and air/gas temperatures up to 454°C. They feature accuracy of ±1% of reading, ±0.5% of full scale and repeatability of ±0.5% of reading with flow rates as low as 0.07 to 305 NMPS and 100:1 turndown.

The meter's outputs and user interface choices are extensive to interface with virtually any control system and/or set-up or configuration devices. Standard outputs include dual, NAMUR NE43 compliant 4-20 mA analog outputs, HART (version 7), Modbus 485 and a USB port. Foundation Fieldbus or PROFIBUS PA or DP can be optionally added. The optional backlit LCD display provides digital and bar graph readouts of the flow rate and temperature, totalised flow, alarms, diagnostics feedback and even a user-defined label/tag field.

The ST80 Series transmitter enclosure is NEMA 4X/IP67 rated, selectable for NPT or metric conduit port threading and is available in both aluminium and stainless steel and may be remotely located up to 305 m apart from the flow element. The instrument also carries SIL compliance.

AMS Instrumentation & Calibration Pty Ltd
www.ams-ic.com.au

Vapour pressure osmometer

ELITechGroup's VAPRO Vapor Pressure Osmometer is designed to bring simplicity, convenience and precision to the routine determination of osmolality to help meet the demands of today's clinical and research laboratory.

Auto-calibration, a self-cleaning thermocouple, self-diagnostics, statistical analysis and a computer interface with printout capabilities make the osmometer suitable for any busy laboratory. With a small sample requirement of 10 µL (2, 20 and 60 µL sample holders also available), users can assay hard-to-get or expensive samples using the vapour pressure method.

ELITech Australia & New Zealand
www.elitechgroup.com

Genetic risk factors identified for spine osteoarthritis

Scientists from The University of Hong Kong (HKU) have identified the first genetic risk factors to be implicated in spine osteoarthritis (OA) — a breakdown of the cartilage of the joints and a major cause of pain and disability in older people. Their discovery thus represents a major advance, paving the way for further research to find new and more effective treatments for sufferers.

The research was conducted as part of the Genetics of Osteoarthritis (GO) consortium — an international study that analysed 826,690 individuals from nine populations and found 100 genetic risk variants for OA, of which 52 were new. The HKU team helped identify that the SOX5 gene, which is known to be essential for the development of the intervertebral discs, is implicated in spine OA. The study results were published in the journal *Cell*.

"This study demonstrates the power of genetics to uncover biological mechanisms and identify new treatment targets for complex human diseases, when researchers are willing to share data collected from different countries," said HKU Professor Sham Pak-chung, who led the spine OA genetic analyses.

The study also showed that spine OA was genetically correlated to OA at other joints including hip, knee, finger and thumb. Interestingly, it was found that the CHST3 gene was among the top three genes most confidently linked to hip OA. CHST3 was previously found by the Hong Kong team to be associated with intervertebral disc degeneration, which causes back pain.

These findings suggest a strong link between degeneration of the intervertebral discs, OA and back pain. Furthermore, spine OA was genetically correlated not only with back pain, but also with knee, hip and neck/shoulder pain. The study also showed that body weight rather than fat mass was genetically correlated with OA, and that weight-bearing and non-weight-bearing joints differed in genetic influences.

The putative OA genes identified in the study have diverse biological functions, including key molecules in the formation and development of the skeleton, and pathways that control how cells respond to stress. These biological processes are modifiable and represent potential treatment targets. Encouragingly, the study showed that some of the putative OA genes could be targeted by existing drugs or small molecules.

"The association of spine degeneration with hip and knee joint degeneration is of particular significance, implying that treatments that help the hip and knee joint may be useful for the spine and vice versa," noted HKU Professor Kenneth Cheung Man-chee. "It opens up the field to kinds of possibilities to the benefit of both groups of patients."

"I am sure that a treatment can be developed to relieve some of the back pain arising from OA that will have enormous impact on millions of people," added HKU Professor Kathryn Cheah Song Eng, coordinator of the study.

Since SOX5 is a master regulator of many genes, the study provides the foundation for the identification of downstream genetic factors that impact the development of spine OA. The genes identified for OA of other joints that are validated as therapeutic targets may also be relevant to spine OA as well as intervertebral disc degeneration.

"Patients suffering from back pain constitute a substantial portion of musculoskeletal disorders," said HKU Professor John Leong Chi-yan. "Of the two major causes — disc degeneration and OA — the former can be identified by MRI, whereas OA is difficult to pinpoint. Thus, only symptomatic treatment is possible by using anti-inflammatory drugs and various modalities of physiotherapy. The clarification of the genes responsible for OA spine is a major step forward towards the possibility of more specific treatment, such as new drugs."

"OA is a complex disease involving many factors," concluded HKU Professor Danny Chan. "This collaborative effort illustrates the benefit and power of international sharing of large-scale data from cohort studies, and thinking outside the box in extracting additional information so that far-reaching goals can be achieved for the development of treatments that will benefit patients."

Dye for flow cytometry

Bio-Rad Laboratories has launched StarBright UltraViolet 400 Dye, the first in a range of fluorescent nanoparticles designed for use with a UV laser in flow cytometry applications. The dye offers high brightness with narrow excitation and emission profiles, making it suitable for use in multicolour flow cytometry panels.

Bio-Rad's StarBright dyes are conjugated to highly validated flow antibodies and are compatible with most flow cytometers and experimental protocols. They are resistant to photobleaching and highly stable, with minimal lot-to-lot variation. They offer good Förster resonance energy transfer (FRET) for reproducible data and are designed to ensure no loss of signal in fixation.

The latest dye offers a high-performance alternative to existing dyes excitable by the 355 nm UV laser, without the need for special buffers. It works with common staining buffers, including special polymer dye staining buffers, for easy integration into multicolour panels. Its properties are designed to provide researchers with greater choice and flexibility when designing flow cytometry experiments.

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

sCMOS camera

The pco.edge 10 bi CLHS is described by PCO as a next-level sCMOS camera, with imaging performance features that make it suitable for applications in microscopy, life science and physical science.

Due to its back-illuminated image sensor, the camera has a quantum efficiency of up to 85% with broad spectrum out to NIR. The sensor incorporates microlenses and full pixel height deep trench isolation for crosstalk suppression, resulting in good MTF. Further, the camera provides a large image circle by using a high-resolution 10.5 MP image sensor with a square pixel size of 4.6 μm.

A low dark current and readout noise of 0.8 electrons are achieved by thermal stabilisation and active cooling of the sensor. Moreover, the sensor technology enables reduction of the noise peak and tail in addition, which makes it comparable to the noise behaviour of CCD sensors. Together with a high full well capacity, this leads to a dynamic range of 25,000:1. The camera offers high frame rates of up to 120 fps and transmission via a fibre-optic link.

SciTech Pty Ltd
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Single-cell analysis

Biological resolution at the level of individual cells is powering the next phase of precision health. The HIVE scRNAseq Solution integrates sample storage and single-cell profiling into a complete workflow, solving the issues that limit single-cell RNA analysis. It enables the generation of biologically complete and high-quality data from samples that require storage prior to processing for single-cell RNA libraries.

The workflow design enables multi-site and multi-timepoint sample collection without the need for specialised instrumentation. Cells can be collected anytime, anywhere and then be easily processed where they are collected or stored and shipped to a central facility for processing. By allowing safe sample storage, samples can be batched to improve lab efficiency.

The quality and biological complexity of single-cell RNA-seq data generated using the solution with integrated storage at -20°C are comparable to data generated from freshly processed samples. Additionally, the product can recover cells which are difficult to detect with other platforms because of their fragility. These include granulocytes, neutrophils, eosinophils and basophils.

The end-to-end workflow enables gentle capture, robust storage and easy processing for the analysis of single-cell samples.

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Semi-custom recombinant proteins

Many scientists are in need of small-scale recombinant proteins that are customised with the tag and expression system that will accelerate their research, but lack the time and resources to make it themselves. Aviva Systems Biology provides a solution with the Protein on Demand semi-custom recombinant proteins.

With a catalogue of over 300,000 protein targets across a wide variety of species, Protein on Demand allows users to semi-customise the tag and expression system used to produce their protein and order quantities as small as 50 μg. Whether proteins are needed for protein:protein interaction studies, western blotting, ELISAs or protein arrays, the company should be able to provide whatever recombinant protein is required.

Sapphire Bioscience
www.sapphirebioscience.com

Smart bandage
enables onsite chronic wound monitoring

Researchers from the National University of Singapore's (NUS) Department of Biomedical Engineering and Institute for Health Innovation & Technology (iHealthtech) have developed a smart wearable sensor that can conduct real-time, point-of-care assessment of chronic wounds wirelessly via an app.

Claimed to be a world first, the novel sensor technology can detect temperature, pH, bacteria type and inflammatory factors specific to chronic wounds within 15 minutes, hence enabling fast and accurate wound assessment. It has been described in the journal *Science Advances*.

It has been estimated that about 2% of the world's population suffer from chronic wounds, with healthcare providers now seeing more patients suffering from non-healing wounds such as diabetic foot and chronic venous leg ulcers. Timely care and proper treatment of chronic wounds are needed to speed up wound recovery; however, this requires multiple clinical visits for lengthy wound assessment and treatment, which adds to the healthcare cost.

Furthermore, current clinical assessments of wounds rely on visual inspection, or collecting and sending wound fluid to a centralised lab to detect and analyse specific biomarkers. The whole process usually takes about one to two days and may impede proper, timely and precise medical interventions. Although there are recent developments in flexible sensors designed for wound care, they can only probe a limited set of markers — such as acidity, temperature, oxygen, uric acid and impedance — to diagnose wound inflammation.

In response to these limitations, NUS researchers developed VeCare — a point-of-care wound assessment platform consisting of an innovative wound sensing bandage, an electronic chip and a mobile app. The bandage comprises a wound contact layer, a breathable outer barrier, a microfluidic wound fluid collector and a flexible immunosensor.

Professor Lim Chwee Teck and Dr Gao Yuji were the lead researchers of the NUS team that developed the VeCare platform to monitor chronic wounds.

VeCare is believed to be the first wound assessment platform that can detect bacteria type and probe inflammatory factors, in addition to measuring acidity and temperature, within a single 15-minute test. The immunosensing

The VeCare platform comprises (clockwise from bottom left) a chip, wound sensor, bandage and app for real-time, point-of-care chronic wound monitoring.

bandage enables rapid assessment of wound microenvironment, inflammation and infection state by detecting multiple chronic wound-specific biomarkers from wound fluid using an electrochemical system. The microfluidic wound fluid collector attached to the sensor directs and boosts wound fluid delivery to the sensor by up to 180%.

The design is said to ensure reliable sensing performance regardless of the ulcer shape or size. In addition, a chip integrated with flexible electronics is connected to the sensor to transmit data wirelessly to an app for convenient, real-time wound assessment and analysis onsite. The chip component, powered with a rechargeable battery, can be reused for subsequent applications.

The VeCare platform and mobile app enable doctors to monitor the condition of patients' chronic wounds remotely, reducing the hassle for patients to travel to a clinic. The bandage complements the patient's existing medical treatment while facilitating timely medical intervention for wound healing processes.

"Point-of-care devices coupled with telehealth or digital health capability can play a significant role in transforming the healthcare industry and our society, which is catalysed by the COVID-19 pandemic requirements for safe distancing," said study co-leader Professor Lim Chwee Teck, who is Director of iHealthtech at NUS. "Our smart bandage technology is the first of its kind designed for chronic wound management to give patients the freedom to perform the test and monitor their wound conditions at home."

In collaboration with the Singapore General Hospital, a small clinical test of VeCare was conducted on patients with chronic venous leg ulcers. They successfully demonstrated that the platform is effective in the assessment of chronic wounds and enabling monitoring of the progress of wound healing with timely medical intervention.

"The VeCare platform is easily scalable and customisable to accommodate different panels of biomarkers to monitor various types of wounds," Prof Lim said. "The aim is to have an effective and easy-to-use diagnostic and prognostic tool for precise and data-driven clinical management of patients."

The next step for the research team is to further develop VeCare to meet safety, regulatory and mass production considerations. The team will explore the incorporation of other appropriate biomarkers suitable for other wound types and utilise data in existing clinical workflows to improve diagnosis and treatment. They hope to test the technology on a larger prospective randomised clinical trial with different types of non-healing chronic ulcers, such as diabetic foot and pressure ulcers.

Sequel IIe platforms at the Earlham Institute. Image credit: Earlham Institute (EI).

BioGenome Project to decode the genomes of all life on Earth

The Earlham Institute (EI) has boosted its capability in high-fidelity long-read sequencing with a twin set of the cutting-edge Pacific Biosciences Sequel IIe platforms to support the Earth BioGenome Project (EBP), providing the UK bioscience community with critical technologies for biodiversity genomics.

As the EBP is gaining momentum to sequence, catalogue and characterise the genomes of all eukaryotic biodiversity on Earth within the next 10 years, global efforts are under way to deploy the technology and infrastructure capable of rapidly delivering large numbers of high-quality genome sequences. The Sequel IIe platform is designed to empower scientists to take genomic analysis to a higher level of accuracy by producing high-fidelity long reads (hi-fi) to resolve genomes and transcriptomes.

"The Sequel IIe platforms allow us to scale up our existing infrastructure in our contribution to BioGenome sequencing," said Dr Karim Gharbi, Head of Genomics Pipelines at the Earlham Institute. "Demand from the UK bioscience community for higher-quality genome references is growing rapidly, with requests to access hi-fi sequence data at an all-time high.

"Feedback from early adopters of the Sequel IIe across the genomics community has been extremely positive with hi-fi genomes, outperforming existing resources by at least one order of magnitude. The additional platform will immediately double our genome sequence capability, enabling continued, cost-effective access to hi-fi reads for EI researchers and UK bioscientists."

In the past few years, the Earlham Institute has made strategic investments in genome-enabling technologies, setting the path for a new era in biology where high-quality, richly annotated genome sequences are no longer the exception but increasingly the norm. These sequencing technologies support several national and international initiatives with the Earlham Institute as a core research partner — including the Vertebrate Genomes Project, Darwin Tree of Life (DTOL) Project and European Reference Genome Atlas (ERGA) — delivering key sequencing data and analyses for a wide range of organisms, and underpinning an ambitious program to catalogue the biodiversity of single-cell eukaryotes (protists).

"The Earth BioGenome Project initiatives are highly collaborative but the technology and infrastructure capable of producing high-quality genomes at scale need to be ensured," said Professor Neil Hall, Director of the Earlham Institute. "The additional hi-fi capacity at the Earlham Institute for the analysis of protist genomes strengthens our position in the global initiative as a leader in genome sequencing."

According to Dr Gharbi, key to EI's investment was the early adoption of Pacific Biosciences' Sequel II hi-fi sequencing platform in 2019, before the institute permanently acquired the instrument with support from the UK Biotechnology and Biological Sciences Research Council (BBSRC).

"This technology allowed the institute's researchers to secure early success in delivering high-quality genome references for key target species and establish EI as a leading centre in BioGenome research," he concluded.

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Benchtop confocal microscope

Andor Technology, an Oxford Instruments company, has added the BC43 benchtop confocal system to its microscopy portfolio.

A high-speed confocal microscope with a small footprint, BC43 is purposefully easy to use, allowing researchers to save time while capturing high-quality 3D images. Every component has been designed from the bottom up with performance and accessibility in mind.

Typically, microscopes capturing in 3D are expensive, complex to use and located in specialised darkroom facilities. This is especially true for confocal technology, which delivers high-quality 3D images, particularly in thick and more clinically relevant specimens.

Andor set out to change this with BC43, delivering 2D confocal images in milliseconds and generating 3D views in real time for immediate scrutiny. The compact design means it can sit on a bench in a regular lab, saving space and time. The system also offers a comprehensive imaging experience, handling scales from subcellular detail at single cell level right through to large model organisms and huge tissue samples, and does so in samples thicker than many microscopes are capable of handling.

Suitable for early-stage researchers and experienced microscopists alike, BC43 is simple enough to allow users to capture images within an hour of first using the device, yet sophisticated enough to address complex imaging needs for both live and fixed specimens. The result, the company says, is that researchers are empowered to capture quality images as part of their regular workflow and many times faster than other confocal microscopes.

Coherent Scientific Pty Ltd
www.coherent.com.au

Fully automatic benchtop autoclave

Designed to save space on the laboratory workbench, the Tattnauer 2840EL-D is a front-loading benchtop autoclave with a 28 L chamber. It provides high-quality, repeatable performance and accountability for a wide range of applications used in modern laboratories.

Created with the processing needs of most labs and research centres in mind, the 2840EL-D is made with high-quality stainless steel (316L or 316Ti) and has an advanced multicolour control panel to indicate cycle stage. Internal printing and other optional value-added features can be configured for each model to give fast cooling, efficient drying, biohazard and waste sterilisation, F_0 control and more.

The product provides peace of mind with multi-level password protection and features a safe automatic pressure locking system, meaning the door will not open when the chamber is over-pressured. It can be easily connected to local networks, giving users the ability to store up to 200 cycles and access data easily via USB, Ethernet or printer. Optional RPCR software allows users to generate PDF reports with graphs and tables and will also allow for remote monitoring of up to eight autoclaves.

Thermo Fisher Scientific
thermofisher.com

Single-cell analysis system

BD Biosciences flow cytometry instruments have enabled researchers to conduct flow cytometry analysis for over 45 years. The BD Rhapsody System extends this capability and facilitates the analysis of thousands of genes and proteins simultaneously at the single-cell level. It can be used to access the vast wealth of information that exists at multiple levels in a cell to better understand biological networks that underlie phenotypic responses.

The system includes the BD Rhapsody Scanner and the BD Rhapsody Express Single-Cell Analysis System and allows high-throughput capture of multiomic information from single cells using a simple cartridge workflow and a multi-tier barcoding system. The resulting captured information can be used to generate various types of next-generation sequencing (NGS) libraries. NGS libraries are sequenced and analysed to provide high-dimensional resolution of single cells.

The BD Rhapsody Scanner is recommended when quality control is important, for users new to single-cell workflows, for the development of single-cell protocols and when working with novel cell types or complex cell systems. Scanner metrics can confirm quality of input cell sample and success of each step of the cartridge workflow; assess viability of cells until cells are lysed; and provide an estimate of the number of cells retrieved by sequencing. This information gives users the power to change course and troubleshoot experiments, if necessary, before expensive downstream sequencing.

BD Life Science
www.bd.com

System for quantifying protein interactions

Quantitative understanding of the underlying mechanisms via which drugs and drug candidates interact with their intended targets is key for successful drug development. But conventional technologies including SPR (surface plasmon resonance) and BLI (biolayer interferometry) often struggle when characterising challenging interactions such as the formation of multi-protein complexes. These technologies rely on attaching one of the binding partners to a surface, which can interfere with the measurements and make it more difficult to distinguish whether a drug or drug candidate binds to a monomeric protein, a misfolded protein or a multi-protein complex.

Another problem with most surface-based technologies is that these methods rely on measuring binding kinetics to determine binding affinity. For heterogeneous protein targets such as complexes composed of several proteins, the binding kinetics can become increasingly complicated, which makes it challenging to extract any meaningful quantitative information about the binding reaction and its stoichiometry, specifically without any additional information on complex composition or size.

The Fluidity One-M system overcomes these challenges to quantify and characterise protein interactions in solution, using microfluidic diffusional sizing (MDS) technology — claimed to be a fundamentally new way of determining affinity (KD), size, concentration and stoichiometric information when proteins interact with DNA, lipids or other proteins. The product uses MDS technology to measure changes in molecular size (hydrodynamic radius) as binding events occur.

The system enables development of customised protocols to study a wide range of interactions, with a typical runtime of 35 min for 24 data points to determine KD. It eliminates the risk of binding artefacts or other surface constraints, as measurement directly in solution means there is no surface immobilisation. It also helps to minimise consumption of precious samples, requiring just 3.5 μL per data point (application dependent) or 50–80 μL to determine KD.

ATA Scientific Pty Ltd
www.atascientific.com.au

Outsourcing single-use technologies to accelerate speed to market

To fast-track time to market and gain a competitive edge, pharmaceutical development companies are increasingly implementing single-use technologies (SUT).

Single-use technologies are built using an array of components, including sampling bottles, tubing, filters, clamps, check valves, sterile connectors, Luer locks and fittings, seals and gaskets, and dispensing tips/nozzles. The technology can be as simple as a single assembly or an entire system made up of multiple complex assemblies that are utilised across the entire manufacturing process, including formulation, upstream/downstream processing and final product filling. SUTs offer many benefits compared to traditional stainless steel systems, such as the elimination of clean-in-place or steam-in-place (CIP/SIP) requirements, faster changeovers between batches resulting in reduced production time, more flexible infrastructure and a decreased risk of cross-contamination.

Although standard, off-the-shelf SUT assemblies are currently available, most are narrowly focused on upstream processes using kit components like bottles, tubing, connectors and filters likely supporting research applications. There are, however, a few companies leading the innovation of single-use systems for fill/finish. In addition, novel biologics and synthetic compounds often have unique manufacturing processes that require custom assemblies that are more advanced than standard off-the-shelf options.

Given the increasing adoption of single-use technology for both small- and large-molecule drug development, one area of emphasis to speed time to market is outsourcing the design, development, production and validation of the SUT assemblies and systems.

Invest upfront and focus on the science

By outsourcing, companies can keep the scientists and engineers focused solely on new product development. As product development progresses, scientists should not be spending their time designing and putting together bottles, caps and tubing systems, but instead maintain focus on the product. Unfortunately, off-the-shelf components may not meet this requirement; single-use systems comprising various components can quickly become a complex system that requires expertise in choice of materials, biocompatibility, connection strength and integrity.

"Research into the development of single-use systems can be a major distraction to the product

development process. With a qualified supplier that can integrate phase appropriate manufacturing solutions, companies can focus on the science and new product development," said Meghan Elizabeth, Manufacturing Operations Manager at Intellitech — a manufacturer of single-use process components and assemblies, cell transfer bottles and manifolds for the pharmaceutical, life sciences and specialty chemical industries.

Develop SUT in parallel with drug product

As a product moves out of R&D into clinical trials and then into commercial manufacturing, the requirements become more stringent and the SUT development should build concurrently. This type of approach focuses on specific requirements at each phase rather than a one-size-fits-all approach.

"Phase-appropriate implementation of SUT into the manufacturing process can be integral to accelerating the speed to market," Elizabeth said. "When small batches of product are being manufactured at the bench, the focus is on consistency and repeatability to increase the likelihood of successful scale-up."

As a product progresses from the bench into clinical trials, the next phase of SUT development is to conduct validation studies and provide documentation that can support the customer's Investigational New Drug (IND) Application and Good Manufacturing Practices (GMP) required by the US FDA. GMPs assure proper design, monitoring and control of manufacturing processes and facilities. This includes establishing quality management systems, obtaining appropriate quality raw materials, detecting product quality deviations and collaborating with third-party, accredited testing laboratories for method feasibility and validation studies.

"Instead of investing the time required for the design and management of validation studies, a company can partner with a SUT supplier that can aid in risk-based solutions and manage the project directly with the lab," Elizabeth said. She added that because SUT assemblies are typically custom designs with unique components, the validation process is considerably more complex than in the past.

As a result of this complexity, many pharmaceutical and specialty chemical developers and manufacturers are finding their unique requirements better served by outsourcing to a qualified and experienced SUT supplier that can partner with them to provide phase-appropriate solutions along with the necessary validation and documentation to navigate each product development phase from R&D through to commercial manufacturing.

Partner with an experienced SUT design firm

To facilitate the transition from R&D to commercial manufacturing and increase speed to market, an experienced SUT supplier has:

- an established supply chain of research and GMP-compliant components;
- a design library of proven, leak-proof connection;
- validated manufacturing, assembly, testing and packaging processes, and a registered quality management system.

If a component is not commercially available, the supplier can design and print 3D parts that are compliant with the customer quality and regulatory requirements such as biocompatibility and non-animal origin. An experienced SUT supplier collaborates with a customer's technical team to design and develop phase-appropriate SUT solutions based on the specific application and phase of development.

"A knowledgeable supplier tailors the SUT design and development to align and grow with the customer's product development based on phase-appropriate requirements, manufacturing strategy and risk assessment," Elizabeth explained.

As a qualified supplier to top pharmaceutical manufacturers, Elizabeth said Intellitech works with customers to validate processes and define acceptable operating ranges, critical quality attributes and acceptance criteria of the intended system. The company also partners with accredited labs for testing seal strength, integrity, bioburden, sterility and shelf life, and additionally creates, approves, releases and maintains the required documentation to support GMP requirements.

Intellitech
https://intellitech-inc.com/

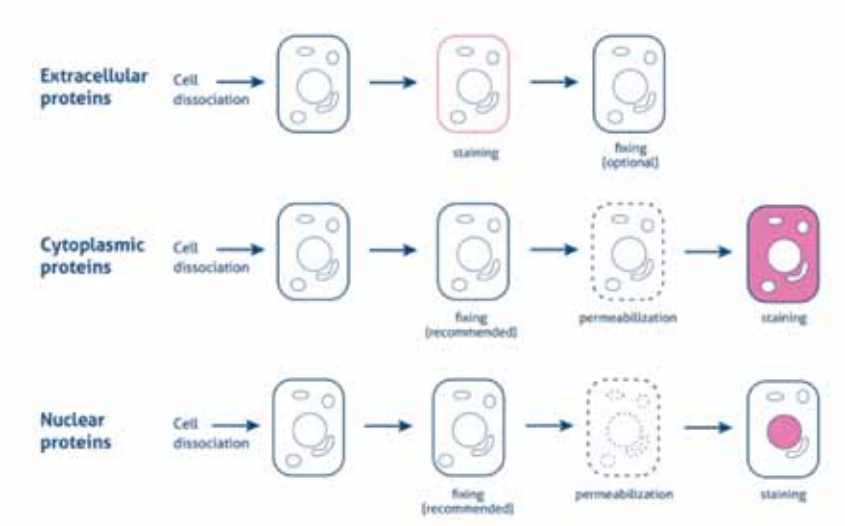
Pipette service and calibration

Pipettes are high-precision instruments that require regular checks to stay in peak performance. Maintenance, calibration and adjustment services by Eppendorf help to maintain the precision and accuracy of pipettes and dispensers so that they continue to generate reproducible results. Eppendorf offers a range of service options, from an economic calibration to a fully certified calibration service, in its NATA-accredited laboratory located in Sydney. The company adheres to the latest local and international quality standards to provide peace of mind for qualification and regulatory audit processes.

The clearly designed calibration services thoroughly check pipettes inside and out, and replace wearable parts like O-rings in a timely manner. The company's calibration technicians are fully trained and equipped to service single- and multi-channel Eppendorf and non-Eppendorf branded pipettes with a fast turnaround time. Booklets of calibration vouchers can also be purchased for economy and convenience. For any pipettes that can no longer be serviced, Eppendorf offers a Trade-In program.

For a wide range of services available, onsite pipette maintenance service and onsite pipette pick-up options, consumers should contact their local Eppendorf Sales specialist or Service Centre.

Eppendorf South Pacific Pty Ltd
www.eppendorf.com.au



Antibodies for intracellular flow cytometry

Measure intracellular cytokines with Proteintech's range of flow cytometry antibodies.

Unlike ELISA or WB, intracellular flow techniques can pinpoint the cellular source of a particular cytokine within a larger, heterogenous population when combined with traditional surface labelling. Through fixation and permeabilisation, antibodies are able to penetrate the cell and nuclear membranes to stain target proteins within the cell.

Proteintech's selection of conjugated antibodies for both intracellular cytokines and surface markers can help streamline the user's protocol and provide additional insights. Foxp3/Transcription Factor Fix and perm reagents, along with flow buffers and lysis buffer, are also available.

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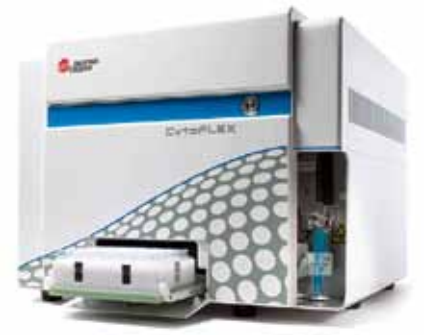
www.unitedbioresearch.com.au



Flow cytometry platform

Beckman Coulter's CytoFLEX Platform is a flow cytometry system that is designed to present optimal excitation and emission, minimising light loss and maximising sensitivity. Since its initial unveiling, the compact system with innovative technology borrowed from the telecommunications industry has garnered attention from the flow cytometry community. Since that time, Beckman Coulter has continued to expand the platform, creating even more choices for researchers.

The product features 80 nm sensitivity, enabling nanoparticle analysis including extracellular vesicles, viruses and more. It offers an extensive set of repositionable bandpass filters and the flexibility to upgrade by adding additional parameters. It also has intuitive software to facilitate multi-colour analysis.

The CytoFLEX Platform is divided into several series across three models. A series is defined by the lasers it includes. Each series is offered in a number of present configurations, determined by the number of activated channels from each laser. Choose the configuration and number of parameters needed immediately and activate additional parameters as the needs of the laboratory change in the future.

Each instrument includes the full complement of repositionable bandpass filters. Move filters to the activated channels based on the wavelengths to be detected. Additional non-standard bandpass filters are available for even more assay flexibility.

Beckman Coulter Australia
www.beckman.com.au

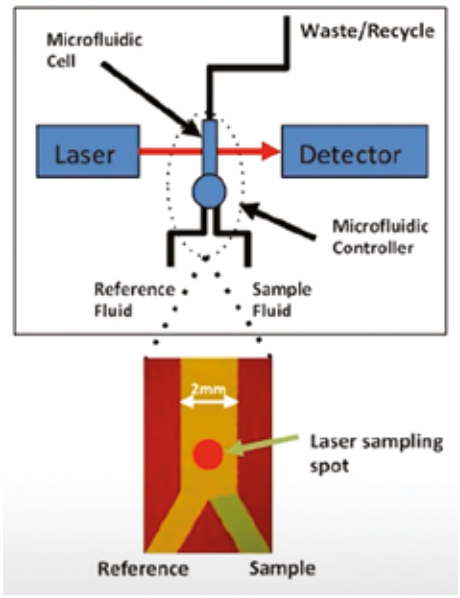
SPONSORED CONTENT

Measure previously undetectable structural changes in biomolecules with RedShiftBio AQS³pro

During biopharmaceutical manufacturing, proteins can undergo conformational changes that can alter their secondary structure and lead to aggregation, which ultimately affects their efficacy and specificity.

Proteins are complex, labile molecules that present considerable challenges during drug development. Conventional analytical techniques like Fourier-transform infrared (FTIR) spectroscopy and far-ultraviolet circular dichroism (far-UV CD) have considerable utility for measuring secondary structure but inherently possess several practical limitations. The need for high sensitivity, a wide dynamic range, a simplified and automated workflow, and high repeatability is significant and, until now, has not been adequately provided. The solution for today's researcher is Microfluidic Modulation spectroscopy (MMS).

RedShiftBio's AQS³pro, powered by MMS, exploits the inherent utility of IR spectroscopy to elucidate results for Aggregation, Quantitation, Stability, Similarity and Structure in a single analysis. Sensitivity is improved up to 30x that of conventional FTIR instrumentation with a desirable concentration range of 0.1 mg/mL to over 200 mg/mL with protein analytics that is equally enviable to the operator and the researcher. The time saving for sample testing can be more than 80% thanks to the fully automated multi-sample capability.



Often the buffers used in a formulation are not compatible for the analytical method, as seen with spectopolarimetry. The AQS³pro experiences no interference from excipients in the buffer. This is a game changer, to measure at concentration, and in the final drug conditions, removing the guesswork from formulation, de-risking many steps.

What is the magic behind the AQS³pro system?

There are 3 key components in the AQS³pro that separate it from all others: 1) A mid IR tuneable quantum cascade laser, 2) a thermal, electrically cooled detector, and 3) a Y-shaped microfluidic transmission cell.

The tuneable laser provides an optical signal almost 100x brighter than the conventional light source used in FTIR, allowing the use of a simple thermal electrically cooled detector without the need for liquid nitrogen cooling. Given the intensity of the laser, the system is amenable to low concentration samples as low 0.1 mg/mL. The sample and reference stream are injected alternately through the Y-shaped microfluidic cell passing through the observation zone. Alternating at a rate of 1–5 Hz, the absorbance of the reference and sample are measured almost simultaneously, allowing the reference absorbance to be subtracted from the sample absorbance in real time, resulting in the collection of reference corrected absorbance spectra. Real-time buffer subtraction and auto-referencing greatly enhances the sensitivity method and produces an almost drift-free signal. The speed of the AQS³pro impresses; where it may take 30 min per sample for the FTIR the MMS clocks in at 1.5 min. The AQS³delta analytics package is refreshingly simple and intuitive, applying advanced analytical tools enabling its use in a vast range of applications across the industry.

What does the AQS³pro actually measure?

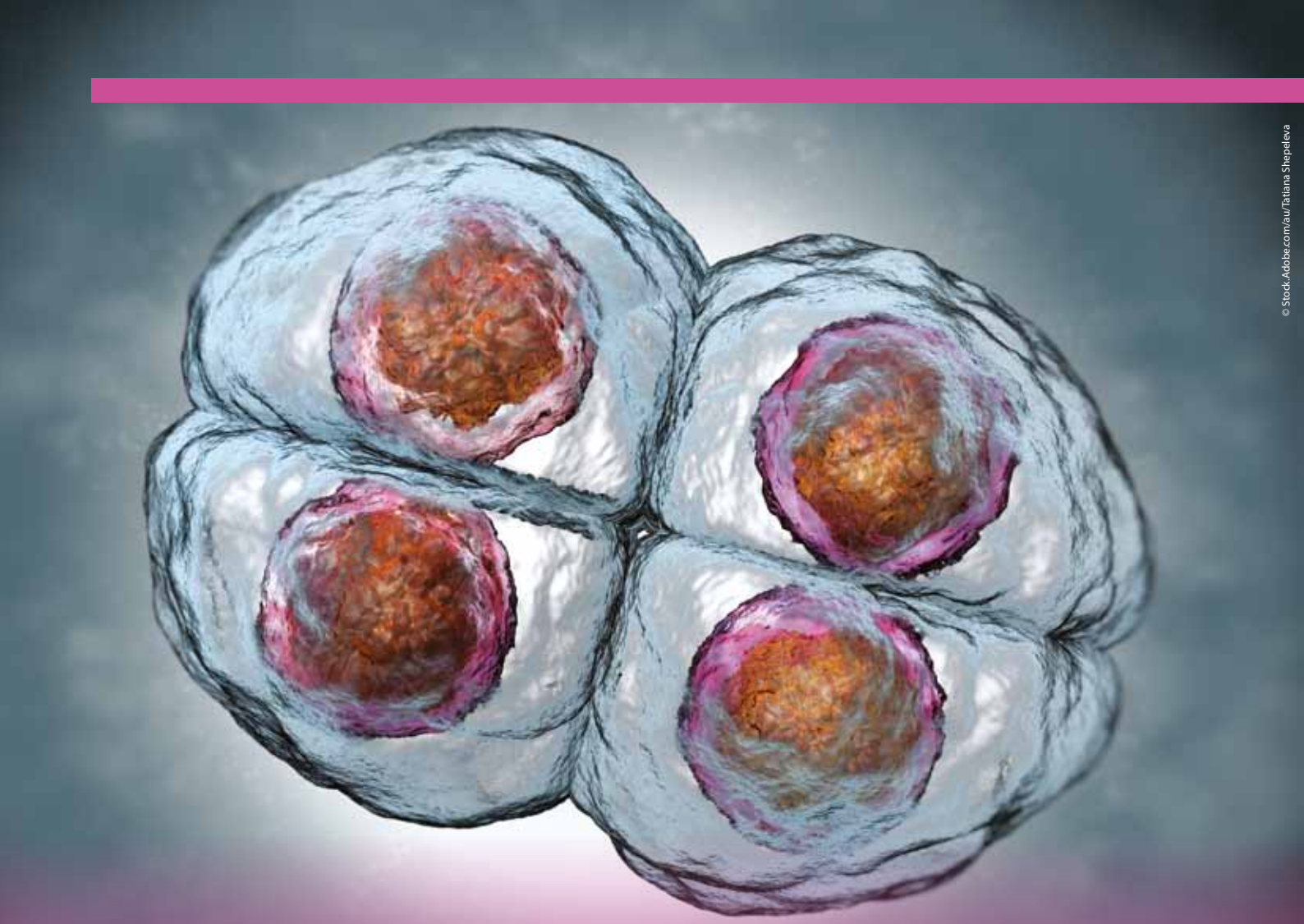
This is an infrared system that measures the Amide 1 band of a protein, in the wavenumber range of about 1580–1720. Alternating between buffer and sample produces a differential absorbance plot which is interpolated into a spectrum and in turn converted to a second derivative affording fine detail changes from spectrum to spectrum to be elucidated. Flipping the spectra shows the baselines and area of overlap plot, enabling you to look at similarity and trends between spectra. This can then be deconvoluted using a normal Gaussian deconvolution, giving rise to secondary structure motifs, the percentage of the components such as α-Helix, β-Sheet, and Anti-parallel β-Sheet Higher Order Structures (HOS).

De-risk drug development

MMS's sensitive, accurate measurements coupled with a robust data analysis package provide simple, accessible, and reliable results to de-risk and accelerate drug development workflows. The AQS³pro can identify at-risk candidates far earlier than traditional methods, clearly saving time and resources.

ATA Scientific are proud to have the RedShiftBio AQS³pro within our suite of instrumentation. Should you require further information or a demo, please contact us.

ATA Scientific Pty Ltd
www.atascientific.com.au



Early embryonic development stage finally mapped in humans

Scientists have shed light on an important stage of early embryonic development that has never been fully mapped out in humans before — a milestone that should contribute to the improvement of experimental stem cell models.

Due to more readily available samples, studies so far have focused on the first week after conception and at later stages beyond a month into pregnancy, during which organs form and mature. However, there is currently very little understanding of events that take place in the intervening days, which includes the crucial gastrulation stage that occurs shortly after the embryo implants in the womb. Analysis of a unique sample by researchers from the University of Oxford and Helmholtz Zentrum München, published in the journal *Nature*, helps fill this gap in our knowledge of early human embryogenesis.

Taking place roughly between days 14 and 21 after fertilisation, gastrulation is one of the most critical steps of development, in which a single-layered embryo is transformed into a multilayered structure known as the gastrula. During this stage, the three main cell layers that will later give rise to the human body's tissues, organs and systems are formed.

"Our body is made up of hundreds of types of cells," said Oxford Professor Shankar Srinivas, principal investigator on the new study. "It is at this stage that the foundation is laid for generating the huge variety of cells in our body — it's like an explosion of diversity of cell types."

The acquisition of ethically obtained human samples at these early stages is exceptionally rare, but the research team managed to obtain a sample through the Human Developmental Biology Resource, from an anonymous donor who generously provided informed consent for the research use of embryonic material arising from the termination of her pregnancy. The sample is estimated to be from around 16–19 days after fertilisation.

"This is such an early stage of development that many people would not have known they were pregnant," said lead researcher Dr Richard Tyser, also from Oxford. "It is the first time an embryo at this stage of development has been characterised in such detail using modern technology."

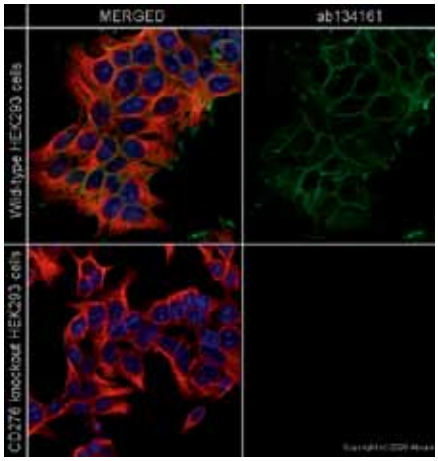
Researchers can only legally culture human embryos up to the equivalent of 14 days of development, which is just before the start of gastrulation, so it is not currently possible to study this stage in cultured human embryos. Consequently, our knowledge of events beyond 14 days after fertilisation is largely based on studies in animal models such as mouse and chicken. The study thus offers a unique glimpse into a central but typically inaccessible stage of our development.

"Our new sample is the bridge that links the very early stage of development with the later stages when organs begin to form," Dr Tyser said. "This link in the human had previously been a black box, so we had to rely on other model organisms such as the mouse. Reassuringly, we have now been able to show that the mouse does model how a human develops at the molecular level. Such models were already providing valuable insights, but now this research can be further enriched by the fact we're able to cast light into that black box and more closely see how it works in humans."

Using single-cell sequencing to closely profile the embryo's individual cells, researchers were able to identify 11 distinct cell types. While most of these cells were still immature, they discovered the presence of both blood cells and the primordial germ cells that give rise to gametes (ovum and sperm cells). Notably, the team did not find any evidence of mature neuronal cells or other cell types associated with the central nervous system.

As part of the University of Oxford's commitment to open research, the team made the raw data available to researchers around the world prior to publication. Prof Srinivas noted, "Many people have already requested our molecular data and used it in their own analyses. The images of the embryo are also really valuable and have attracted a lot of interest because they are amongst the clearest images of this particular stage of development."

To further make this valuable information accessible, the team created an interactive website — www.human-gastrula.net — for both the science community and general public. Dr Tyser said, "We've made it very easy for people to access this data, so anybody can go and look at a gene of interest and see where it's expressed in the human embryo at this stage."



Ready-made knockout cell lines, lysates and pellets

Abcam's knockout (KO) catalogue range and custom service makes it easy for scientists to get the gene-edited cell lines they need. The expertly engineered CRISPR-Cas9 KO cell lines allow users to confidently interrogate the relationship between genotype and phenotype without having to establish their gene-edited cell line.

The company's KO cell lines have over 400 gene targets available, with multiple parental cell lines, supplied frozen as 1x 10^6 cells/vial in 1 mL. They are suitable for cell-based assays, with a wild type cell line available at no cost.

The company's KO cell lysates have over 2600 gene targets available, with parental cell lines including HeLa, HEK293T, A549, HCT116, Hep G2 and MCF7 derived from single-cell clones. Supplied lyophilised as 1x 100 μg, they are suitable for WB with parental wild-type lysates available.

The company's KO cell pellets provide access to native proteins, without the need to culture cells. Prepared from single-gene KO cell lines and snap-frozen, they are suitable for extraction with alternative lysis buffers or for preparation of lysates from subcellular fractions. They can be used for a variety of applications, including PCR, gene expression profiling and DNA library preparation.

Abcam Australia Pty Ltd
www.abcam.com

Cell analyser

BD (Becton, Dickinson and Company) has announced the BD FACSymphony A1 Cell Analyzer, a compact design fluorescence-activated cell analyser that brings sophisticated flow cytometry capabilities to laboratories of all sizes.

The analyser features BD FACSymphony Instrument technology with the flexibility to meet a broad spectrum of research needs from small particle research to 16-colour immunophenotyping, along with the BD FACSDiva Software for streamlined workflows from system set-up to data acquisition and analysis. Researchers can perform independent detection of both large and small particles, such as extracellular vesicles on a single instrument using the optional BD Small Particle Detector.

The BD FACSymphony A1 Cell Analyzer is scaled to fit on the benchtop and also enables larger laboratories to perform exploratory experiments without engaging free-standing cell analysers needed for more complex and longer lead-time experiments. It joins the extended family of BD FACSymphony Cell Analyzers and Sorters and is an important addition to a comprehensive line-up of flow cytometers designed to make powerful flow cytometry capabilities more accessible to researchers.

BD Life Science
www.bd.com

Freezing point osmometer

ELITechGroup's FreezePoint Freezing Point Osmometer is designed for routine medical, research and industry measurements that determine the total osmolality of aqueous solutions.

The product is easily controlled via a touch screen display and step-by-step user guidance. Using the instrument and a sample size as small as 15 μL, users can receive rapid results in 60 s (Models 6000/6000S).

The osmometer is easy to handle and maintain, with a robust design. It features automatic two- or three-point calibration for correct results.

ELITech Australia & New Zealand
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Rapid pathogen detection from a single DNA molecule

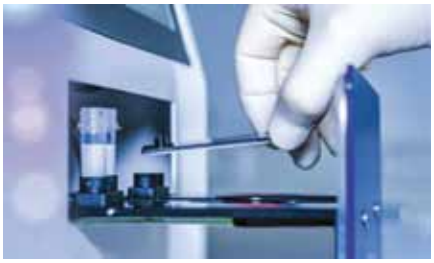
With resistance to antibiotics on the rise worldwide, German researchers have developed a process for rapidly detecting multidrug-resistant pathogens. The standout feature of their platform? Just a single molecule of DNA is sufficient for pathogen detection.

Choosing the correct antibiotic to treat bacterial infections is a deciding factor when it comes to the success of a treatment — and it is particularly difficult to do so in cases where a disease is caused by multidrug-resistant pathogens, which are unaffected by many antibiotics. Furthermore, searching for the most effective antibiotic often requires information about the bacteria's genome — information which is not readily available at medical practices and can only be obtained through a laboratory diagnosis.

To accelerate and simplify the process, researchers from the Fraunhofer Institute for Physical Measurement Techniques IPM collaborated with the Ludwig Maximilian University of Munich to develop a new platform for detecting pathogens on the basis of single molecules on a microfluidic chip. The focus of the SiBoF (signal boosters for fluorescence assays in molecular diagnostics) project, funded by the German Federal Ministry of Education and Research (BMBF), lies on an easy-to-use point-of-care (POC) detection method.

The portable, compact test platform is equipped with an automated fluidic system; all necessary reagents are stored within the system. The injection-moulded microfluidic chip is incorporated in a drawer in the test system, where it is supplied with the reagents through the fluidics system before the optical analysis takes place.

"We detect part of the pathogen's DNA strand," said Fraunhofer IPM's Dr Benedikt Hauer, who serves as project manager. "Using our new process, even a single molecule of DNA that binds to a specific site on the microfluidic chip is sufficient to do this. Fluidic channels are integrated into the chip, the surfaces of which are primed with binding sites for specific pathogens."



The compact device for detecting multidrug-resistant pathogens performs all stages of the reaction automatically and provides a result within one hour. Image ©Fraunhofer IPM.

Typically, target DNA molecules are detected by means of specific fluorescence markers. A unique feature of the new method is that researchers are utilising antennas with nanometre-sized beads, which amplify the optical signals of these markers. Because of this, chemical amplification via polymerase chain reaction (PCR) is not required.

"The optical antennas consist of nanometre-sized metal particles that concentrate light in a tiny region and also help to emit the light — much as macroscopic antennas do with radio waves," Dr Hauer said. "These metal particles are chemically bound to the surface of the chip."

A structure of DNA molecules, known as 'DNA origami' and designed by the Ludwig Maximilian University of Munich, holds both of the gold nanoparticles in place. Between these nanoparticles, the structure provides a binding site for the respective target molecule and a fluorescence marker. This patented design provides the basis for the novel assay technology.

"The particles, which are 100 nm in size, serve as antennas,' Dr Hauer said. "Field enhancement, caused by plasmonic effects, takes place in the hotspot between the two gold particles. If a fluorescent dye is placed there, the detectable long-wave fluorescence radiation is enhanced multiple times. Using this method, a single molecule can be detected using a small, compact optical device." Low concentrations of pathogens can thus be detected.

The result is available after one hour and is displayed on the monitor. This is true not only for multidrug-resistant pathogens, but for any type of DNA molecule. In principle, the single molecule assay can be adapted to molecules beyond DNA, such as RNA, antibodies, antigens or enzymes. Numerous tests have successfully confirmed the functionality of the process.

At the heart of the POC device is a miniaturised high-resolution fluorescence microscope, developed by Fraunhofer IPM. Specifically developed image analysis software identifies single molecules and by doing so enables the captured target molecules to be counted, providing a quantitative result. The fluorescence is stimulated using LEDs, which are affixed underneath the cartridge containing the fluidic channels.

The POC system was presented at the MEDICA 2021 trade fair in Düsseldorf from 15–18 November. In future, the platform could be introduced as part of POC diagnostics on hospital wards or in medical practices — either as an alternative to the established PCR analyses or in combination with other diagnostic methods.

Australasian Society of Diagnostic Genomics 2022 Interim Scientific Meeting

March 25–27, Sydney
This event will be the third independent meeting of the ASDG, a special interest group of the Human Genetics Society of Australasia (HGSA). The biannual conference is typically well attended by a significant number of genomic scientists from Australia, New Zealand and Southeast Asia.
With the theme of 'HomeGrown: Our Scientists take the stage' the meeting will showcase current experts and emerging leaders of diagnostic genomics in Australasia. The program will run over three days, with the Friday being a hybrid day providing both onsite and virtual attendance. Social events include a welcome reception on the Friday evening in the trade display area and a dinner on the Saturday night.
https://aacb.eventsair.com/asdgconference2022/

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February 3–6, Lorne and online
https://www.lorneproteomics.org/

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February 6–10, Lorne and online
https://www.lorneproteins.org/

Lorne Cancer 2022
February 10–12, Lorne and online
https://www.lornecancer.org/

Lorne Genome 2022
February 13–16, Lorne and online
https://www.lornegenome.org/

Lorne Infection & Immunity 2022
February 16–18, Lorne and online
https://www.lorneinfectionimmunity.org/

Acoustics 2021 Wollongong
February 21–23, Wollongong
https://www.acoustics.org.au/Acoustics2021/Home/Acoustics2021/Home.aspx

Science meets Parliament 2022
February 28–March 4, Canberra and online
https://scienceandtechnologyaustralia.org.au/what-we-do/science-meets-parliament/

Cutting-edge Symposium on Integrated Systems Biology: Challenges and Future Perspectives
March 1–3, Brisbane and online
https://wp.csiro.au/sisb/

Pathology Update 2022
March 4–6, Sydney and online
https://www.rcpa.edu.au/Events/Pathology-Update

ARPS 2021 Conference
March 7–10, Canberra
https://arpsconference.com.au/

World Science Festival Brisbane
March 9–13, Brisbane
https://www.worldsciencefestival.com.au/

TSANZSRS 2022
March 31–April 2, online
https://www.tsanzsrsasm.com/

Energy Oceania 2022
April 4–6, Melbourne
https://www.energyconferenceaustralia.com/

ACS 49th Annual Scientific & Business Meeting
April 29–May 3, Glenelg
https://www.cytology.com.au/49th-annual-scientific-business-meeting

ASM 2022
July 11–14, Sydney and online
https://www.theasmmeeting.org.au/

Human Genetics Society of Australasia Annual Scientific Meeting
August 6–9, Perth
https://aacb.eventsair.com/hgsa-45th-annual-scientific-meeting

National Science Week
August 13–21, Australia-wide
https://www.scienceweek.net.au/

ComBio2022
September 27–30, Melbourne
https://www.combio.org.au/combio2022/

AACB 59th Annual Scientific Conference
October 18–20, Perth
https://www.aacb.asn.au/professionaldevelopment/annual-scientific-conference

32nd International Congress of Antimicrobial Chemotherapy
November 27–30, Perth
http://32icc.org/

Australian Institute of Physics (AIP) Congress
December 11–16, Adelaide
https://aip.org.au/congress/

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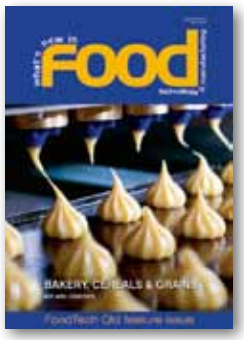

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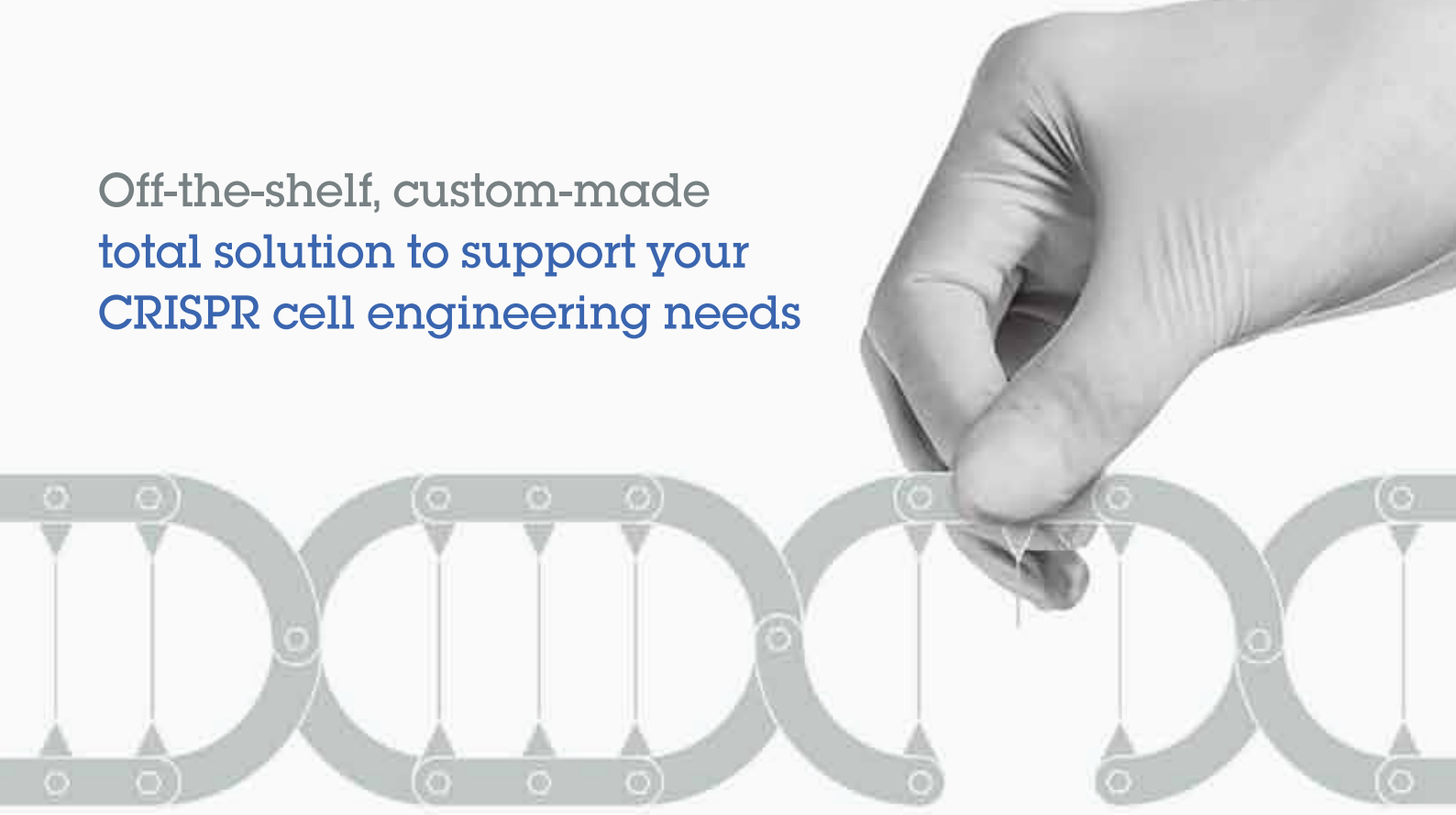

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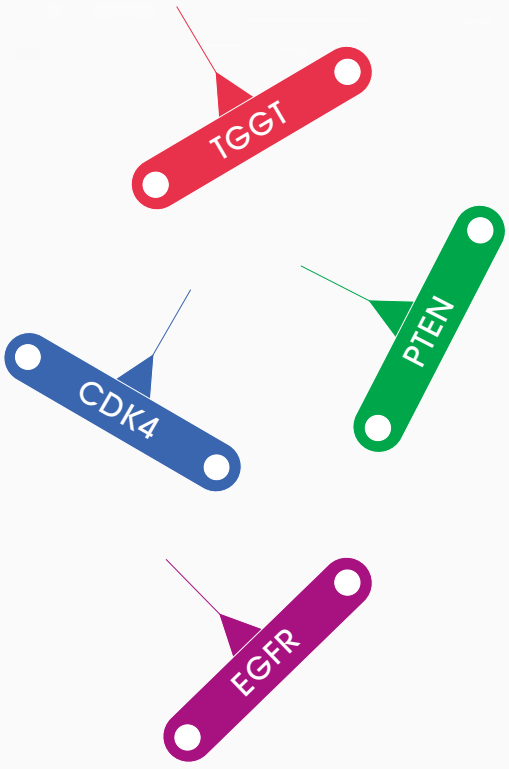

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