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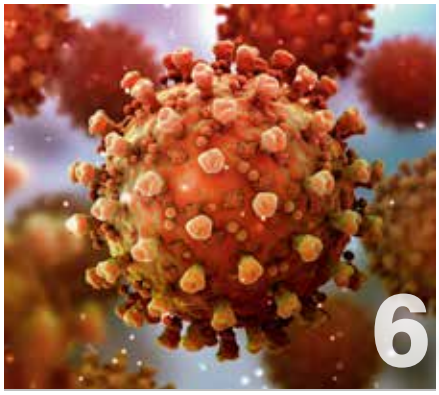
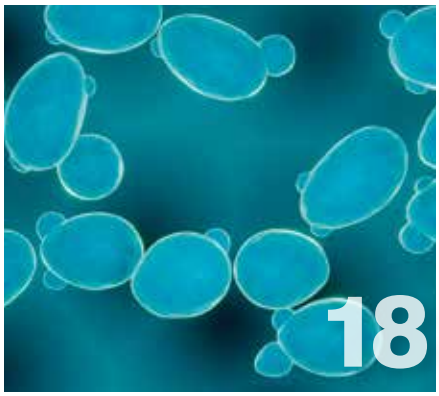
Contents





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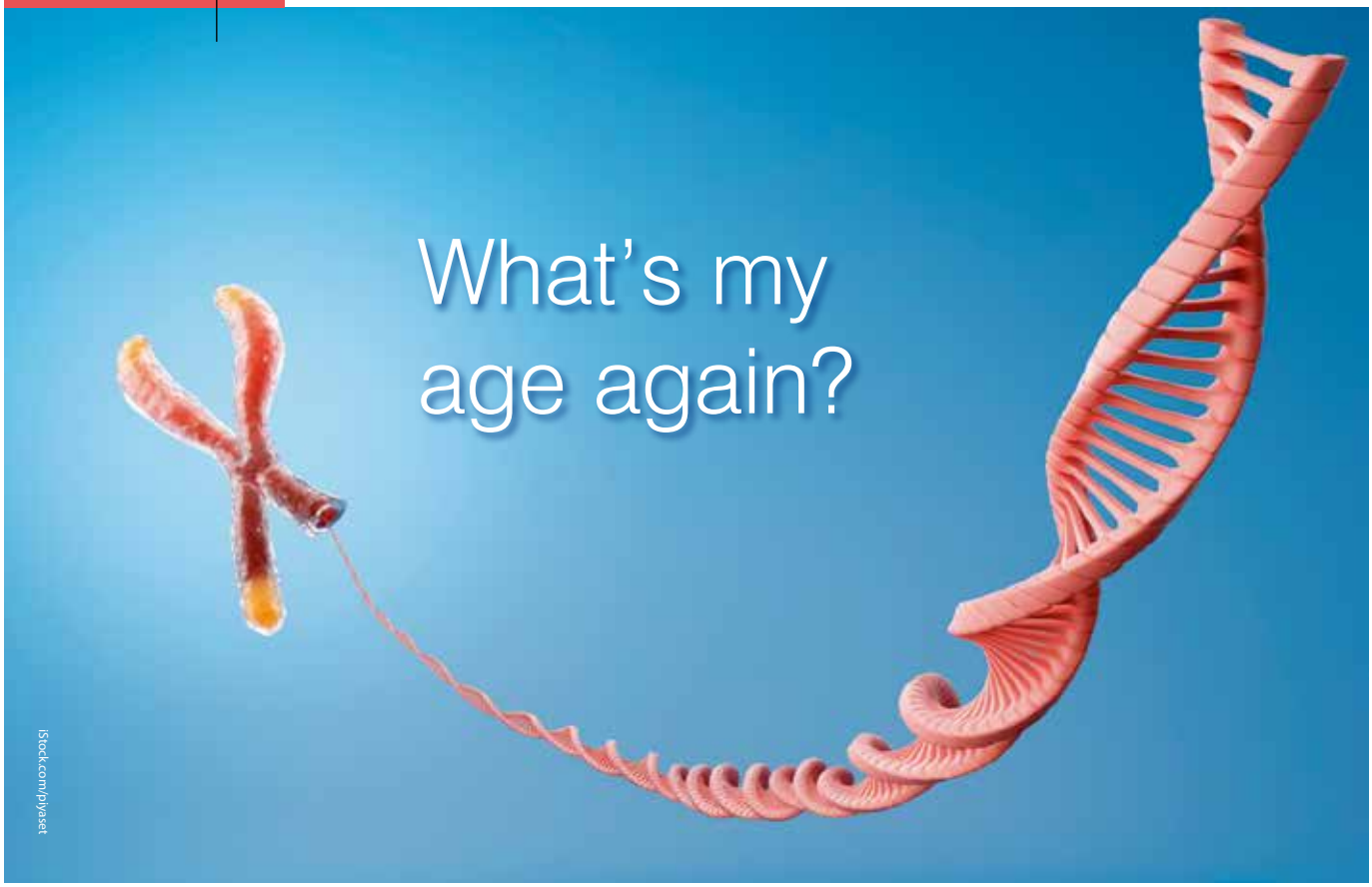

What's my age again?

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It may not surprise you to learn that a recent study by Chinese researchers has confirmed that smoking causes us to age faster, with this deadly habit found to significantly shorten the end fragments of chromosomes in the white blood cells of our immune systems. These end fragments, called telomeres, are like the sheaths at the end of shoelaces which prevent them from fraying — and their length is an indicator of our cells' ability to repair and regenerate.

But what you may not know is that renting your home has also been found to have a stronger link to faster biological aging compared to unemployment or even being a former smoker. And in the midst of a national housing crisis, that's quite a big issue.

Numerous aspects of housing are associated with physical and mental health, including cold, mould, crowding, injury hazards, stress and stigma. In order to explore how these aspects might exert their effects, researchers from The University of Adelaide and the University of Essex drew on epigenetic information alongside social survey data and signs of biological aging, captured through evidence of DNA methylation (a chemical modification of DNA that can alter gene expression) in blood samples.

The results showed that living in a privately rented home was associated with faster biological aging — ie, the cumulative damage to the body's tissues and cells — even taking into account factors such as socioeconomic status, diet, cumulative stress, financial hardship, urban environment, BMI and smoking status. What's more, the impact of renting in the private sector, as opposed to outright ownership (with no mortgage), was almost double that of being out of work rather than being employed. It was also 50% greater than having been a former smoker as opposed to never having smoked. Interestingly, living in social housing, with its lower cost and greater security of tenure, was no different to outright ownership in terms of its association with biological aging once additional housing variables were included.

The researchers acknowledged several limitations to their findings, including the fact that there were no contemporary measures of housing quality and that the DNA methylation data came only from white, European respondents. Nevertheless, they said their findings are likely to be relevant to housing and health elsewhere, particularly to countries with similar housing policies, and so suggested that policies to reduce the stress and uncertainty associated with private renting — such as ending no-fault evictions, limiting rent increases and improving conditions — may go some way to reducing the negative impacts of private renting.

Assuming your home has the capacity to accommodate visitors, I hope you have the chance to catch up with family and friends over the Christmas period, and that your festive gatherings are not too badly affected by COVID-19, which has once again reared its head for a new wave. In our lead story this issue, we hear from three pre-eminent vaccinologists on the challenges faced and lessons learnt from vaccine development during the early days of COVID-19, which will be key to preparing for the pandemics of the future; you can also turn to page 32 to discover how gene editing may be used to protect chickens from their own problematic respiratory condition. And with 2023 marking a significant upturn in the use of AI, the article on page 29 offers a timely round-up of the potential use cases of AI in medical diagnostics and health care (as well as some of the concerns).

Regards,
Lauren Davis
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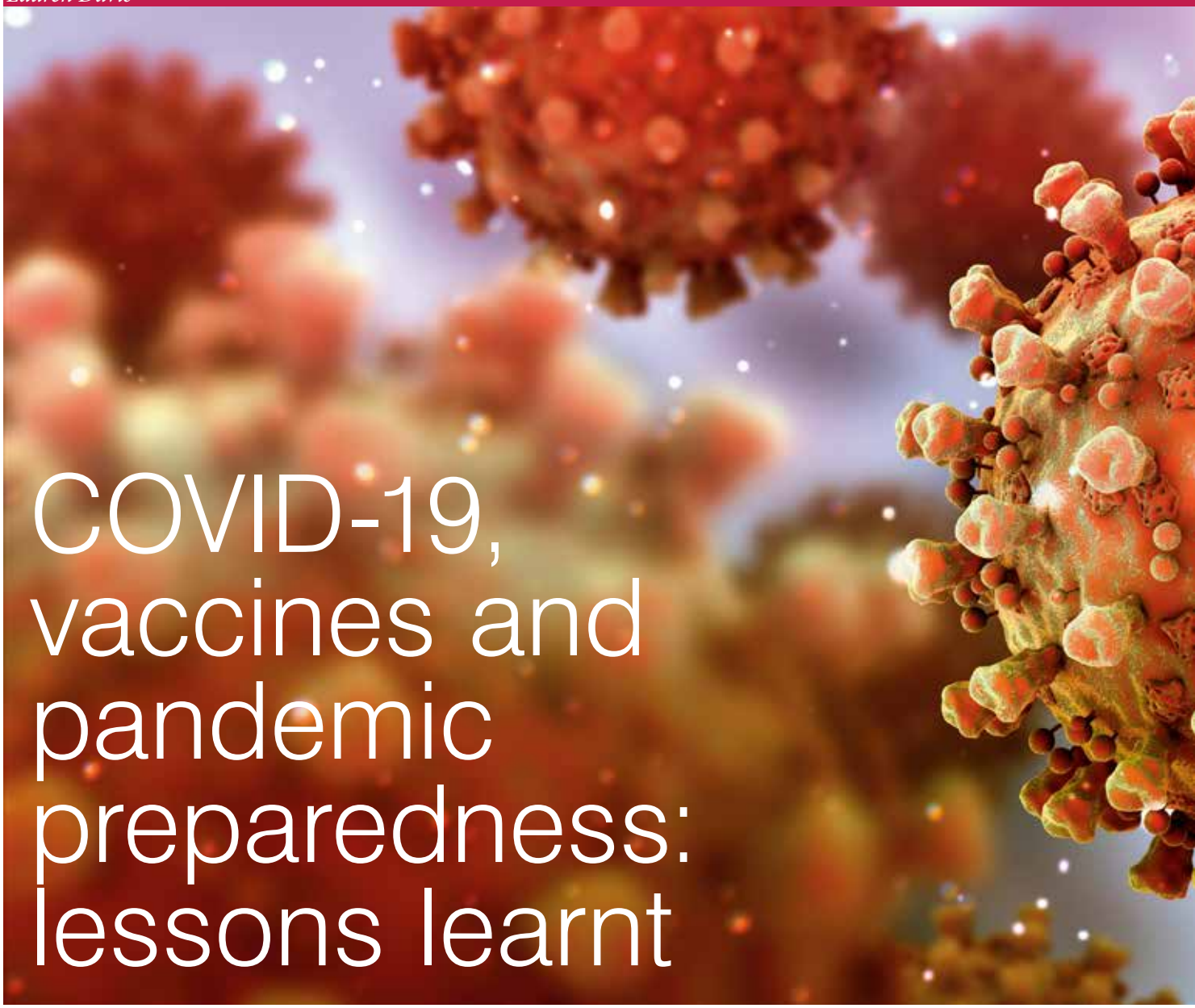
Lauren Davis



COVID-19, vaccines and pandemic preparedness: lessons learnt

With Australia officially in its eighth wave of COVID-19 at the time of writing, the time is ripe to look back at the challenges faced and lessons learnt from vaccine development during the early days of the pandemic. The Peter Doherty Institute for Infection and Immunity recently covered this very topic in a discussion with three pre-eminent vaccinologists.

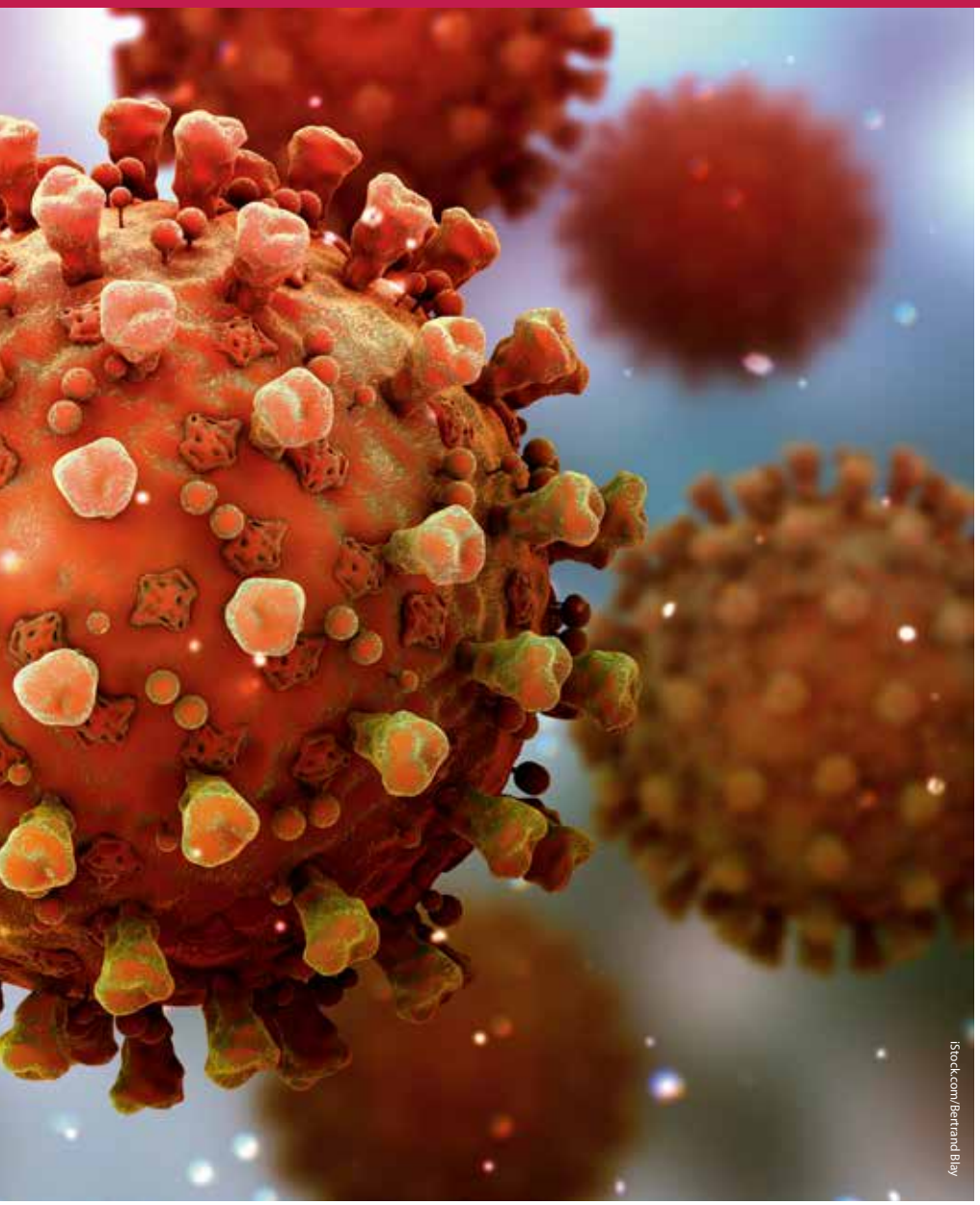
Professor Sarah Gilbert was made a Dame Commander of the British Empire in 2021, in recognition of her work initiating and leading the production and development of the Oxford–AstraZeneca vaccine (trade name Vaxzevria). The first Vaxzevria vaccine was administered less than a year after the pandemic was officially declared, on 4 January 2021 — so how did Gilbert's team at the University of Oxford manage to develop it so rapidly?

"With outbreak pathogens, we'd been following the usual academic funding model of doing a little bit of work and then publishing results and then trying to get money for the next stage," Gilbert said. "It was very, very slow. So in 2019 I'd started thinking how would we do all this if we needed to do it quickly; how would we move from the idea through to actually having a vaccine in clinical trials in a really short space of time?

"I wasn't successful in getting that project funded, but at least it had meant that we'd done a lot of thinking about what would we need to do to respond fast if there was an outbreak of an unknown virus, and that's then what happened at the beginning of 2020.

"We'd done 12 clinical trials with ChAdOx1 [adenoviral] vector vaccines prior to April 2020 when we started the COVID vaccine trials; so we had all the teams in place, we had the expertise, we had the experience of working with the regulatory and ethical authorities, we'd done all of this before in terms of at least getting to a phase 1 trial.

"It was a question of doing what the team knew how to do but working out the fastest way we could do it, what had to be done before the next thing could be done, looking many steps ahead, and just getting everything off the ground as quickly as possible."



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The big challenge, Gilbert said, was actually not to do with speed but funding — she said she had "a little bit of research funding" available to kickstart the process in the lab, but she was unsure how she would be able to afford to manufacture the vaccine for clinical trials. Luckily, this issue was soon resolved.

"We got to the point, later on in April, where the UK Vaccines Taskforce was formed, and that was set up to assess all the different technologies that were being used to create vaccines and to test them, and to provide whatever funding was necessary for multiple different technologies owned by different people, with the aim of getting at least one of them through to licensure in the shortest possible time," she said.

Following that first clinical trial, AstraZeneca agreed to take on the manufacture of the vaccine for full clinical development and then for commercial supply. Gilbert explained, "What they did was set up a fantastic manufacturing network, they took our vaccine technology, they understood how to make it, they then transferred it to 25 different manufacturing sites worldwide — one of them in Australia, CSL — and got all of these manufacturing sites up and running and making essentially the same product, so that the regulators would recognise it as the same product.

"They also ran some clinical trials themselves … and they really were a great partner to work with in this crisis situation where we had to get things moving really quickly. They not only used their own expertise, but they allowed us to use our expertise, which is really important in a partnership."

Meanwhile, here in Australia, Professor Paul Young's team at The University of Queensland (UQ) were developing their own vaccine based on so-called 'molecular clamp' technology, which works by 'locking' viral proteins involved with infection and cell entry into a shape that allows for an optimal immune response. Young explained that the team had already been working on the technology for about eight years, but in 2019 they received a grant from the Coalition for Epidemic Preparedness Innovations (CEPI) to develop the platform, and spent a year targeting MERS before CEPI asked them to pivot to COVID-19.

"We'd had significant funding to do it, and that meant we were also able to reach out and support a wider team, and that included people at the Doherty and other academic organisations, and also into some NGOs, and ultimately CSL agreed to partner with us early in 2020," Young said.

"That was probably the biggest component of 2020 that I took out of the experience, and that was the power of partnerships. That broader national perspective — everybody keen to be working with each other with a single directive was really empowering."

Clinical testing of UQ's vaccine candidate was underway by July 2020, which provided positive safety and immunogenicity data. But disaster struck when the scientists discovered that a constituent of the vaccine candidate resulted in diagnostic interference with some HIV tests, leading to false positive HIV results in study volunteers.

The team revealed in December 2020 that they would not progress the COVID-19 vaccine candidate into phase 2/3 clinical trials, with Young saying at the time that re-engineering the vaccine would set development back by around 12 months. CEPI did however support the team to resolve the diagnostic interference issue, and announced in November 2022 that it would help fund phase 1 testing for potential use in the global response to future disease outbreaks.

"It was a big call to say we're just going to pick ourselves off the floor and re-engineer and move forward, but that's exactly what we did," Young said. "I think we took a week off after [working] 24/7 for a full year… and came back and redesigned, and we were back fairly quickly.

"The structural motif that we use that underlies the platform is seen across a wide array of different proteins, and we were able to choose one from many that works really well. And we were able to take that COVID vaccine back into clinical trial just earlier this year, and that was with CEPI-funded support."

That trial compared the second-generation clamp (Clamp2) vaccine head-to-head with the TGA-approved Novavax vaccine, finding that the two produced highly comparable results; indeed, while there have been no new COVID infections recorded among the Clamp2 volunteers, there have been three such cases detected among the Novavax recipients. UQ's commercialisation company, UniQuest, has since licensed the molecular clamp

technology to startup company Vicebio, which is looking to progress its use against respiratory pathogens such as respiratory syncytial virus, human metapneumovirus and parainfluenza viruses.

Young said his team has been able to sort out a number of the issues that they faced during 2020, such as with downstream processing and manufacturing, but he has also become aware of significant gaps in the translational development pipeline here in Australia — one of the biggest being the ability to get a product into phase 1 clinical trials in the first place.

"It's an extraordinarily complex process; you need a lot of expertise around the regulatory environment, the GMP manufacturing of products and so on, but you also need to be able to make that product in the early stages, and that's a very expensive prospect, and often too big a hurdle to cross," he said. "So I think what we could be doing in Australia is really focusing to some degree on developing that early-phase, small-scale manufacture that can go into phase 1 clinical trials."

Young is not the only one who's been trialling a new COVID vaccine, with Professor Terry Nolan last year leading a phase 1 trial of two different vaccines — one made by the Doherty Institute and one by the Monash Institute of Pharmaceutical Sciences (MIPS).

"In fact we started early in 2020 in preparing one of those two vaccines … a recombinant protein vaccine based on not the whole of the spike protein but on the tip of the spike, which is called the receptor binding domain of the spike protein," Nolan said.

"At that time we didn't know whether any vaccine was going to work … [and] that pipeline was being filled with potential candidates, and some proceeded very, very rapidly, including the AstraZeneca vaccine.

"The mRNA candidate, which was the second of the two vaccines, from our Monash colleagues, was also similarly targeted at just the tip of the spike protein, and we had planned from the very beginning to actually have a head-to-head comparison of these two quite different candidates. Again, at the time this all started no one knew that an mRNA vaccine was actually going to work for sure, and certainly whether it would be better or different to a more conventional approach … So that was the set-up for doing this, and we actually started enrolling last year and finished the follow-up of those enrolled subjects for our phase 1 study in April of this year."

The phase 1 study of 76 subjects confirmed that the two vaccines were safe, with no evidence of any issues in terms of reaction to the vaccines. Both candidates were also found to work very well against the target receptor binding domain of the variant that was studied, as well as a high level of cross-protection against Omicron and subvariants of Omicron that have subsequently evolved.

Professor Dame Sarah Gilbert.

Professor Terry Nolan.

Professor Paul Young.

"To start with a candidate early in 2020 and get it to phase 1 now completed itself is a remarkable feat — nothing of course in comparison to what Sarah was able to achieve in Oxford," Nolan said. He said his team is now seeking the support of a major manufacturer to help take the vaccines into phase 2/3 studies, and is currently floating the idea of the recombinant protein candidate going into a combination vaccine that would protect against multiple respiratory viruses.

So with all they have learnt from COVID-19, how do the scientists think we can prepare for the next pandemic? Young noted that many scientists are focusing on respiratory pathogens, since they tend to spread out in a pandemic environment, and that many countries are looking to develop a local manufacturing capacity.

"We're getting more and broader engagement by industry in focus on potential pandemic-type agents, and the development of both vaccines and therapeutics to combat those — as a toolkit or even as a stockpile for future potential emergent — but also locally developing in each country the infrastructure that will be able to move swiftly in developing some of those," he said.

Nolan said that influenza remains one of the most likely pandemics to arise in the future, with the last such flu pandemic occurring back in 2009, and that groups such as Gilbert's are now trying to develop a type of vaccine that could be adapted very quickly to an unexpected virus that might come from a group of similar or related viruses.

"So rather than having to start from scratch, [to] very quickly adapt as Sarah did with her coronavirus, because they were already studying a different type of coronavirus; this MERS one that Paul also had mentioned, that was readily adaptable to the platform and also it was the same family of viruses," he said. "So that so-called pandemic preparedness, and having those sort of platforms available, is really the most important insurance that we can do in the research sector to be prepared for whatever might unexpectedly turn up in the future."

"The more that we can do before a new pandemic starts, the better placed we are," Gilbert agreed. "So we shouldn't just be thinking about getting ready to move quickly from a standing start. We should be thinking about how much of the work can be done in advance of a new outbreak starting, or a new pandemic starting, because then we actually have a much better chance of achieving it. And there's many, many different factors to that.

"It's not just about the vaccines — it's about diagnostics, about therapeutics, it's about the non-pharmaceutical interventions, and it's about the social science studies of how people respond to these interventions, because I think people have maybe changed their views since the pandemic as to what they will be prepared to do another time.

"We've learnt a lot in the last pandemic, but unfortunately this has probably moved out of the public eye, but we need to keep it there, because there's a lot more that we need to do to keep countries protected for the future."

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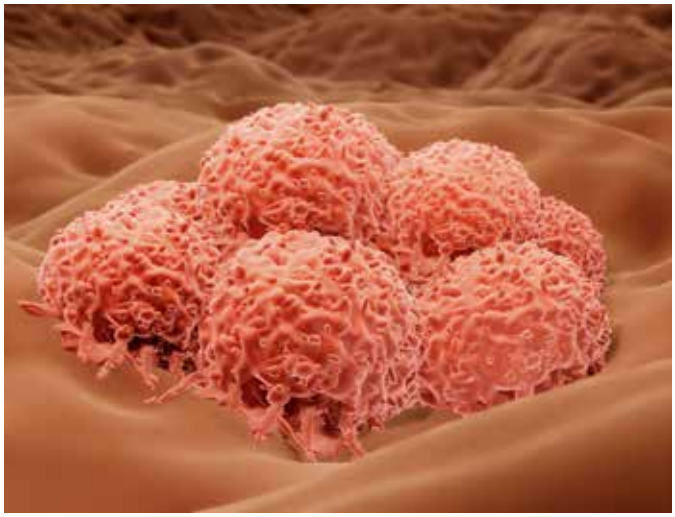

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Screening platform identifies drugs to halt cancer spread

Research led by the Centenary Institute has given rise to a tool called Invasion-Block that can identify drugs capable of halting the spread of cancer cells. An automated high-content screening platform, Invasion-Block is designed to measure the invasive capacity of cancer cells, enabling scientists to assess how well various drugs and compounds can prevent the spread of cancer.

In a recent study published in the journal *PNAS*, Invasion-Block was employed to investigate the invasive behaviour of melanoma cells, particularly their ability to infiltrate other parts of the body. It was used in conjunction with a custom-designed image analysis program called S-MARVEL to screen thousands of compounds, including drugs that are already approved for use in people.

"Melanoma is a tough opponent, often spreading rapidly and making it difficult to treat," noted Dr Shweta Tikoo, a senior study researcher affiliated with the Centenary Institute and the Medical University of Vienna. "The key to finding better treatments lies in drug discovery and this is where the Invasion-Block tool plays a pivotal role."

Excitingly for the researchers, Invasion Block revealed that drugs that blocked a class of enzymes — known as Abl/Src, PKC, PI3K and ATM kinases — made melanoma cells much less able to invade other tissues. As noted by first author Dr Dajiang Guo, currently a postdoctoral researcher at Weill Cornell Medicine, "This suggests these enzymes may hold the key to finding treatments that can help curb the spread of melanoma."

The researchers went on to use CRISPR technology to 'turn off' the gene responsible for expressing ATM kinase in melanoma cells. In doing so, they observed that the melanoma cells became less invasive in laboratory tests and didn't spread as much to the lymph nodes when tested in mice.

"We believe that ATM may serve as a potent therapeutic target for treating the spread of melanoma in patients," Tikoo said.

The researchers say the study is a significant step in the fight against melanoma, offering fresh hope to patients while laying the groundwork for further studies and the development of new and better treatments. Tikoo concluded, "The combination of Invasion-Block and S-MARVEL is opening new avenues in the search for drugs that can arrest the spread of cancer."

Orthopaedic implant coating helps to ward off infection

Better knee and hip replacements are one step closer, with Australian and Chinese researchers having developed a new orthopaedic implant coating that has the strong ability to ward off infection as well as to stimulate bone growth. Their patented technology, which has been described in the journal *Advanced Functional Materials*, consists of novel silver–gallium (Ag–Ga) nano-amalgamated particles that can be easily applied to medical device surfaces.

Infections after orthopaedic implant surgery are a global health issue, with rates ranging from 2–10% in developed countries and up to 15% in developing regions. About 6% of orthopaedic implant infections lead to intensive care, with a mortality rate up to 4.6%; the cost of treating such infections can exceed US$100,000 per case.

"The antibacterial capabilities of compounds derived from silver have been extensively researched," said corresponding author Dr Vi-Khanh Truong, from the Biomedical Nanoengineering Laboratory (BNL) at Flinders University. "However, the cytotoxicity of silver ions currently poses a significant obstacle for the utilisation of silver ions in medical materials.

"Our new formula involving Ag–Ga nano-amalgamation ensures the sustained release of silver and gallium ions in a very controlled manner to eliminate these issues."

Gallium liquid metal (GaLM) was used to facilitate the galvanic deposition of silver nanocrystals on an oxide layer. The GaLM not only serves as a carrier for silver through the galvanic replacement process but also provides a controlled-release mechanism for silver.

The Ag–Ga nano-amalgamated particles were found to exhibit potent antimicrobial properties against a broad spectrum of bacterial strains in animal models. Senior author Matthew Flinders Professor Krasimir Vasilev, Director of the BNL, said the breakthrough provides an urgently needed solution to medical device-associated infections.

"The new material could be easily and controllably applied by spray-casting on many medical devices to protect them against infection, and also provide anti-inflammatory effect and stimulate bone growth," he said.

"Our latest testing indicates this combination of antibacterial protection and tissue integration properties can benefit many devices in the orthopaedic, trauma and also dental areas."

Truong added that the discovery has the potential to apply to various implantable devices, catheters and other access devices, and even wound dressings where infections are also problematic. "Commercialisation opportunities could make this solution available to clinicians and patients in the near future — at a time when growing antibiotic resistance is yet another problem in global health care," he said.

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Chimeric monkey created from embryonic stem cell lines

Researchers from the Chinese Academy of Sciences have reported the live birth of a 'chimeric' monkey composed of cells that originate from two genetically distinct embryos of the same species of monkey. This has previously been demonstrated in rats and mice but, until now, has not been possible in other species. The breakthrough was described in the journal *Cell*.

The monkeys used in the study were cynomolgus monkeys, also known as crab-eating or long-tailed macaques. The investigators established nine stem cell lines using cells removed from seven-day-old blastocyst embryos, which were placed in culture to give them enhanced ability to differentiate into different cell types.

Images show the green fluorescence signals in different body parts of the live-birth chimeric monkey at the age of three days. Images courtesy of Cell/Cao et al under CC BY-SA 4.0.

The team performed tests on the cells to confirm that they were pluripotent — having the ability to differentiate into all the cell types needed to create a live animal. The stem cells were also labelled with green fluorescent protein so the researchers would be able to determine which tissues had grown out of the stem cells in any animals that developed and survived.

The team selected a particular subset of stem cells to inject into early monkey morula embryos (embryos that are 4–5 days old). The embryos were implanted into female macaques, resulting in 12 pregnancies and six live births.

One monkey that was born alive and one foetus that was miscarried were substantially chimeric, containing cells that grew out of the stem cells throughout their bodies. The investigators used the green fluorescent protein label to determine which tissues contained cells derived from the injected stem cells. They also used gene sequencing and other tests to confirm the presence of stem-cell-derived tissue across several organs.

In the live monkey, the contribution of the stem cells in the different tissue types ranged from 21% to 92%, with an average of 67% across the 26 different types of tissue that were tested; the numbers were lower in the monkey foetus. In both animals, the team confirmed the presence of stem-cell-derived cells in the testes and in cells that eventually develop into sperm cells.

"This research not only has implications for understanding naive pluripotency in other primates, including humans, but it also has relevant practical implications for genetic engineering and species conservation," said senior author Zhen Liu. In the future, the researchers will try to increase the efficiency of their method by optimising the culture conditions for the stem cells, the cultures for the blastocysts where the stem cells are inserted, or both.

COVID-19 causes epigenetic scars in the lung

Spanish researchers have determined that COVID-19 causes profound epigenetic changes in the lungs of patients who have died from the disease. Such alterations particularly affected genes related to hyperinflammation and fibrosis, leading to lung damage, respiratory failure and, eventually, death.

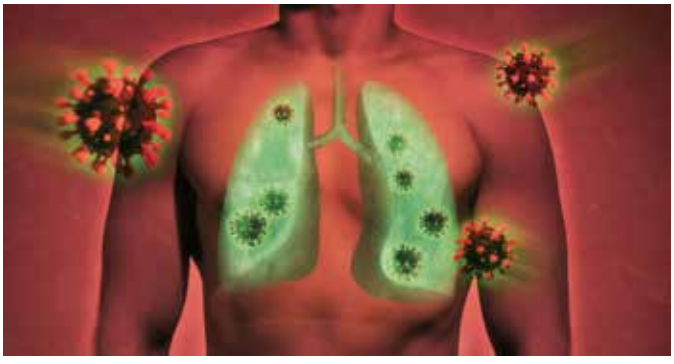
To date, more than 770 million people have suffered from COVID-19 and nearly 7 million have lost their lives. The most common cause of death in the studied group is lung involvement with consequent respiratory failure. However, the targets of the virus in the lung and the mechanisms by which lung tissue can cease to be functional in the disease are largely unknown.

Dr Manel Esteller, Director of the Josep Carreras Leukaemia Research Institute, led a group of researchers in analysing an extensive collection of lung autopsy samples from patients who died from COVID-19 and compared them with healthy lungs from people who died from other unrelated diseases. Comparison of the DNA between both groups showed epigenetic differences in more than 2000 regulation points of the genetic material; analysis revealed that these were genetic sequences mainly associated with promoting a state of hyperinflammation, such as the overproduction of interferons and chemokines — chemical signals used by the immune system to promote inflammation.

Epigenetics is the control layer a cell uses to finely tune whether a gene will be active or not, without modifying its genetic information. Alterations in the epigenetic program of a cell can make it behave far differently than expected, with organic consequences like the ones seen in the study.

"Knowing the mechanisms associated with death from COVID-19 due to lung involvement can [help] pinpoint targets for drugs and medical interventions to avoid lethal outcomes in fragile patients, and may also serve to prevent the progression of other viral diseases that affect the lungs," Esteller said. Indeed, the findings — published in the journal *CHEST* — may help doctors predict the progression of the disease more confidently and allow for a more efficient treatment of patients in the clinic.

"Two consequences of this study to be evaluated are, first, the use of epigenetic drugs to prevent the progression of this and other viral diseases in patients susceptible to worsening; and second, it opens the possibility that the molecular lesions found in these lungs may also be related to the so-called long-term COVID-19, in which these alterations have not 'healed' correctly, but without reaching the extremes of lethal COVID-19," Esteller said.



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FFPE DNA analysis

New England Biolabs has released the NEBNext UltraShear FFPE DNA Library Prep Kit (NEB #E6655), a solution for working with challenging formalin-fixed paraffin-embedded (FFPE) samples in molecular labs. FFPE DNA has long posed difficulties due to its low input amounts, non-uniform ends and DNA damage caused by fixation and embedding. However, the NEBNext UltraShear FFPE DNA Library Prep Kit offers a streamlined, user-friendly workflow that minimises hands-on time and addresses these challenges.

The kit incorporates the NEBNext FFPE DNA Repair Mix v2, designed to selectively target damaged DNA bases and enhance data accuracy while improving library conversion rates. It effectively rectifies issues like nicks, gaps and overhangs, resulting in good library quality.

Additionally, the NEBNext UltraShear FFPE DNA Library Prep Kit prevents over-fragmentation and retains intact DNA by filling in single-stranded overhangs that are free from damage, enabling optimal sequencing coverage. Importantly, the kit preserves true mutations while removing damaged bases, preventing false-positive results in mutation analysis.

The kit offers a sample-quality-agnostic workflow with a broad input range, making it suitable for high-throughput settings such as clinical labs. Enzymatic fragmentation is automation-friendly and less dependent on sample quality, providing consistent results.

With the NEBNext UltraShear FFPE DNA Library Prep Kit, researchers can unlock valuable genetic insights from FFPE samples — regardless of their quality or quantity — putting an end to compromised library preparation and sequencing results and resulting in efficient and consistent FFPE DNA analysis.

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Widefield and spinning disk confocal system

The latest spinning disk confocal microscope system from CrestOptics is the CICERO. The confocal microscope offers an all-in-one solution for widefield and confocal imaging and it allows users to simply switch between modes as their imaging requirements evolve. It can be integrated into any imaging set-up, transforming it into a user-friendly confocal system.

Widefield mode supports informative data collection from samples, such as cell monolayers and tissue sections, whereas the confocal mode allows higher-quality analysis of larger 3D structures, including organoids or whole organisms. Additionally, CICERO's speed and light efficiency provide the capability for prolonged live imaging and the capture of fast cellular events, such as chromosome segregations and organelle trafficking.

CICERO makes high-end fluorescence imaging accessible to every laboratory, enabling a variety of applications. Life sciences, metrology and material sciences are among the disciplines relying increasingly on high-resolution 3D imaging. Both entry-level and challenging applications can be addressed by using LED (3 mm LLG) or multimode laser (SMA fibre) as illumination sources.

With its small footprint and weighing only 7.65 kg, the system delivers fast image acquisition speed (15K rpm) and sensitivity, easily enabling live cell imaging and large-scale 3D object imaging. Due to its large field of view (up to 22 mm FOV), the CICERO offers a minimal scanning process and can capture large samples in a single frame. With an excitation range of 390–750 nm and emission range of 430–850 nm, the device offers a wide wavelength coverage.

The product has been designed to fit upright and inverted microscope frames with a C-mount camera port to attach an imaging camera, providing maximum configuration flexibility. CICERO allows seamless integration with all major microscopy systems and offers an easy user experience. The disk is hosted in a sealed compartment, securing a dust-free environment.

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Platform helps accelerate synthetic and metabolic workflows

Biosyntia is an industrial biotech company, focusing especially on developing more natural and sustainable processes for producing active ingredients used in beauty and nutrition such as vitamins and antioxidants. Investing in the right technology is key to helping the company achieve its goals — and by integrating Sphere Fluidics' Pico-Mine platform, Biosyntia is now exploring genetic diversity faster than ever before.

Ultrahigh-throughput, droplet-based screening had long been on Biosyntia's radar for its immense potential in cell factory development and Biosyntia's synergistic expertise in biosensor development. Having explored various companies over several years to help bring this technology in-house, a partnership was born with Sphere Fluidics and its groundbreaking Pico-Mine platform. Designed to support earlier-stage research using picodroplet technology, Pico-Mine is designed to provide:

- semi-automated platform capabilities;
- flexibility for workflows and assays to help find valuable and rare biological variants among large cell populations;
- radically increased throughput; and
- reduced cost across a wide range of applications helping save on resources.

One of Biosyntia's technologies for developing state-of-the-art cell factories for precision fermentation is the use of genetically encoded biosensors. However, uses of traditional tools, such as flow cytometry, are based on sensing internal product concentrations only. Pico-Mine droplet-based screening allows miniaturisation of a fermentation process to the nanolitre scale with direct sensing of extracellular product concentrations, and easy single-cell isolation of improved producing strains.

Within the first months of using Pico-Mine with Biosyntia's proprietary B7 biosensor, the company has already been able to identify improved genetic variants of its B7 production strain, which are currently in the process of being upscaled for precision fermentation of sustainable and natural B7 vitamin (Bio-B7). It is able to explore genetic diversity faster than ever before, identifying the one-in-a-million cells from large mutant libraries that show improved production phenotypes.

"Droplet screening is a game changer, and with Pico-Mine from Sphere Fluidics in our lab we are now able to test 1000-fold more strains within the same timeframe and with a fraction of the resources," said David Lennox-Hvenekilde, senior scientist and droplet screening lead at Biosyntia. "We are already seeing super-exciting results and expect many more to come."

Pico-Mine offers droplet microfluidic technology in an easy-to-use platform, allowing researchers with no experience in microfluidics to run experiments in just a matter of weeks and therefore making it possible for scientists to quickly integrate the platform into their workflows and projects. In addition to its ease of use, due to its semi-automated design, there are many different experiments researchers can do with the set-up to expand research capabilities and stay at the forefront of single-cell research and implement effectively.

Pico-Mine is allowing Biosyntia to develop novel industrially relevant cell factories, with next steps to scale this technology to a wide array of further molecules, not limited to B vitamins. Droplet-based ultrahigh-throughput screening will play a cornerstone role in Biosyntia's R&D strategy going forward to aid in reaching the company's goals of European bio-based production of greener and more sustainable nutritional ingredients.

"We are truly excited about having the droplet technology in-house to substantially accelerate the improvement of strains for precision fermentation of nutritional ingredients," said Hans Genee, CSO and co-founder of Biosyntia. "From what I have already seen, I expect to see significant impact across a wider portfolio of projects."

Flexible but simple, Pico-Mine lets users mix and match functions to build the workflow they need for every project, without requiring microfluidics expertise. The high-throughput, low-cost picodroplet technology allows both cell-by-cell assessment and rapid, low-stress processing of cells — all at tiny volumes — which should enable precise measurement of large libraries in hours. Pico-Mine biochips meanwhile allow a wide range of functions to be combined to execute even complex workflows, and Sphere Fluidics can provide custom biochips too if the user needs something slightly different.

Capella Science
www.capellascience.com.au

Orthocell adopts CryoSure solution for shipping advanced cell therapies

Shipping temperature-sensitive pharmaceutical products and biologic medical devices globally presents a unique set of challenges, driven by the necessity for maintaining product integrity and compliance with regulatory requirements, and ensuring patient safety. Finding the right packaging solution for your shipment can overcome these challenges — without compromising on your environmental impact.

Shipping temperature-sensitive healthcare products can be a complex process — regulatory requirements are understandably strict, and even a minor deviation from storage and transportation requirements can compromise the efficacy and safety of a product. Manufacturers must navigate these requirements to guarantee that their products reach their destinations safely and in perfect condition.

This case study explores how Orthocell worked with Envirotainer to understand the solutions available for shipping its treatments, and how the company was able to ensure the quality of its specialised biologic medical products as they reached their destination on the other side of the world.

Orthocell, based in Perth, Western Australia, is a pioneering company focused on the treatment of musculoskeletal disorders. The organisation is focused on its mission to introduce cutting-edge medical solutions for optimised patient outcomes. In pursuit of this commitment, Orthocell requires reliable and environmentally friendly shipping solutions and efficient cold chain logistics to ensure the safe and effective transportation of its products.

The problem

Orthocell's Autologous Chondrocyte Implantation (OrthoACI) offers treatment for symptomatic defects of the articulating cartilage of the joints, using the patient's own healthy cartilage cells to assist the regeneration of damaged cartilage. OrthoACI is a highly customised treatment — each procedure is tailored to the individual patient's requirements. Because of the personalised nature of this therapy, product safety and quality are paramount to ensure the successful treatment of the patient.

Orthocell faced several challenges with its existing packaging solution. The company relied on a traditional dry ice shipping solution, specifically polystyrene boxes, to transport its products. However, this method raised concerns regarding the quantity of dry ice required and how long it was able to maintain the required temperature of below -70°C.

Additionally, Orthocell was looking to adopt a more sustainable packaging solution, aligning with its commitment to environmental responsibility. Given the sensitive nature of the product, temperature monitoring was also desired to ensure product integrity throughout the shipment.

The solution

To address Orthocell's shipping challenges and to ensure its strict product requirements were met, the CryoSure X2 solution was proposed. The primary requirement was for a packaging solution that could maintain a stable temperature of below -70°C consistently throughout the shipment. The CryoSure X2 (1.6 L size) is validated to have a duration of >21 days — offering Orthocell above the required duration, whilst also allowing for additional contingency time should there be any delays, without risking product integrity.

The CryoSure solution would also support Orthocell's desire to have a reusable solution which decreases the company's carbon footprint. As a fully reusable cold chain shipping solution, CryoSure is designed to be volume efficient, have a low weight and require less dry ice than other traditional dry ice solutions — reducing both carbon emissions and transportation costs.

The real-time Live Monitoring service offered with CryoSure would also allow Orthocell to track the temperature and location of the shipment 24/7, providing visibility into its status, and prove the integrity of the valuable cargo inside when it reached its destination.

"As we began to work through the requirements, it soon became clear that we had the right solution to meet their needs," said Jonathon Haydn-Evans, Regional Senior Sales Manager, Envirotainer. He continued, "We presented the CryoSure solution and its performance data to the Orthocell team and they were impressed that it would be able to meet their requirements while still contributing to their sustainability goals."

As the discussion progressed, Haydn-Evans was able to provide in-depth validation documentation to ensure compliance with quality standards and regulatory requirements. This documentation provided Orthocell with the assurance that the proposed solution met all the necessary criteria for safe product transportation.

Results

Having shipped the OrthoACI product using the CryoSure X2 in July 2023, Envirotainer and Orthocell observed the following outcomes:

The temperature stability and dry ice duration of the shipment was a success, maintaining the required temperature of below -70°C throughout the entire journey. This achievement was crucial in preserving the efficacy of the product and ensuring product integrity.

The Live Monitoring service provided Orthocell with real-time visibility of the shipment all the way from its origin to its destination. This capability minimised the risk of product loss and would have allowed for prompt intervention if any issues had arisen during transit. The post-shipment Insight Report service has also given Orthocell further insights into the shipping processes for future process improvement.

By transitioning to the CryoSure solution, Orthocell has also been able to align its shipping practices with its sustainability values without compromising on quality.

In the words of Eda Daryal, Senior Supply Chain Manager from Orthocell: "The CryoSure solution mitigates most if not all risks currently faced when shipping biologic medical device products globally below -70°C as well as reducing our carbon footprint. Thank you, Envirotainer, for ensuring our life-changing products can be delivered safely anywhere in the world."

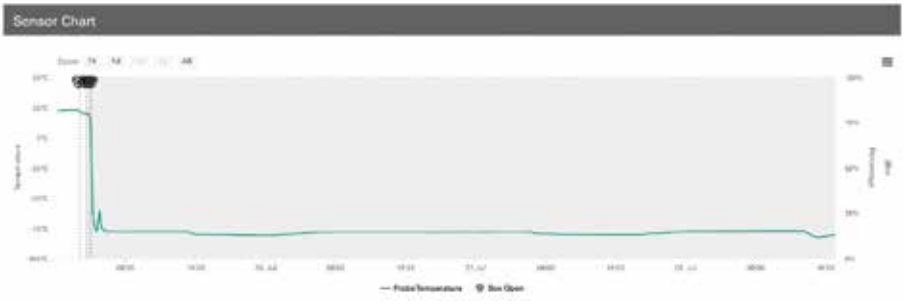
Conclusion

The CryoSure solution offered Orthocell the means to safely transport its product from Western Australia to the USA efficiently, while still maintaining a stable product temperature of below -70°C throughout the entire journey.

By working together to fully understand the product requirements and the wider goals of Orthocell's business, Envirotainer was able to find the best solution for the shipment — protecting the quality and integrity of the product while also supporting Orthocell's commitment to patient care and environmental responsibility.

About Orthocell: *Orthocell is a regenerative medicine and medical device company dedicated to the development of breakthrough products for the treatment of musculoskeletal disorders.*

About CryoSure: *The CryoSure dry ice -70°C shipping solution is designed to keep pharma products in good condition, eradicating deviations through a consistently reliable and secure shipment cycle. By combining groundbreaking innovation, technology and service backed by Envirotainer's 35-year industry experience and expertise, CryoSure sets a high standard in -70°C shipping, offering good performance, long duration and sustainability.*



Temperature sensor data throughout the live shipment.

All-in-one genomics liquid handling platform

SPT Labtech has announced updates to its firefly all-in-one genomics liquid handling platform, specifically targeted to address the bottlenecks of NGS library preparation in laboratory developed tests (LDTs).

The platform was designed to transform NGS library preparation for genomics researchers by bringing together capabilities for precise pipetting, non-contact reagent dispensing, shaking and incubating within a compact benchtop design. Automating repetitive and menial liquid handling tasks enables laboratories to overcome throughput challenges by increasing the quality and quantity of output data.

The platform is claimed to offer higher efficiency than competing automation solutions, with less reagent dead volume required for automating NGS library preparation due to the integrated positive displacement non-contact dispensing capability in a compact footprint with intuitive, easy-to-use software. Users not only benefit from fast and precise liquid handling, SPT Labtech claims, they also get access to the company's dedicated reliance service and support team to sustain high-throughput operations and aid in protocol development.

The latest enhancements recognise what is paramount for clinical laboratories offering LDTs when implementing any solution: rapid set-up, minimised downtime, versatility, robustness and user-friendly and consistent operation. These additional features, designed to optimise firefly for regulated environments, address the increasingly complex nature of LDTs and alleviate the increased operational burden they represent.

The unit's compact design maximises functionality by exploiting vertical space, meaning that labs don't need to sacrifice premium footprint. Its user access control provides individual accounts with set privileges, so there is no ambiguity in operations and maintaining up-to-date records. Easy-to-use protocols can be built using the intuitive and visual user interface, with no coding knowledge required, while open-access software offers compatibility with any computer.

Thermo Fisher Scientific
thermofisher.com

pH, EC and DO meter

In the world of precise measurements, Hanna Instruments' edge pH, EC and DO meter is a hybrid meter that can be used in portable, wall-mount and benchtop configurations for professionals from various industries. The lightweight and versatile device offers measurement of common laboratory parameters for pH, conductivity or dissolved oxygen.

Designed with simplicity in mind, the product offers user-friendly features such as light weight (250 g), a large LCD screen (5.5″) and a thin design (12 mm thick) that make it useful for applications including agriculture, brewing, aquarium, aquatic, food processing and more. The digital display has a wide viewing angle that provides easy-to-read results and can be clearly viewed from over 5 m away, eliminating guesswork.

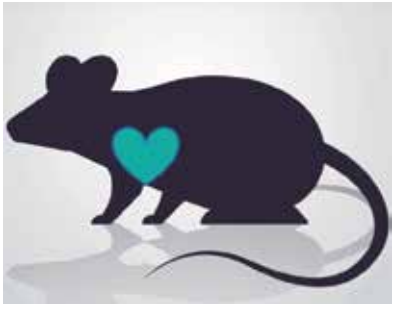
The product's light and compact design makes it portable and convenient, allowing the user to carry it wherever they go. It provides up to 8 h of battery life when used as a portable device and can be easily slipped into a backpack or messenger bag.

Other features include: two USB ports; clear, full text readout; data logging, allowing users to store up to 1000 log records of data; GLP; basic mode; CAL check; and a 3.5 mm probe input.

Hanna Instruments Pty Ltd
www.hannainst.com.au

ELISA kits for preclinical toxicology testing

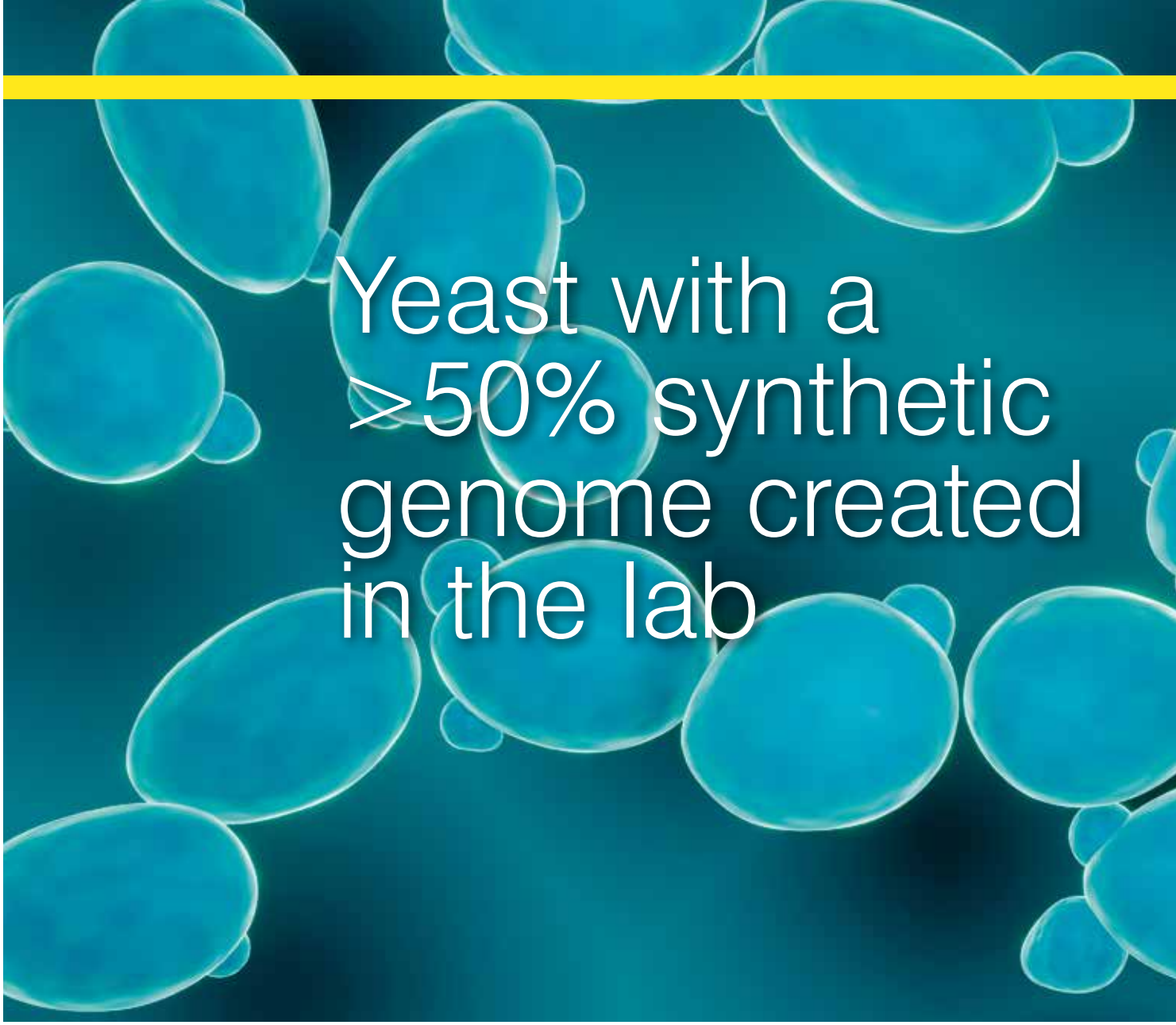
Cardiac toxicity is a leading cause of preclinical safety failures in drug development. The cardiac markers NT-proANP and NT-proBNP have proven to be useful in preclinical toxicology testing.



The BIOMEDICA NT-proBNP and NT-proANP ELISA kits are robust assays to quantify these cardiac hormones in rat samples. The NT-proANP ELISA kit is widely published for use in rat samples and has been independently validated for cardiovascular safety studies in rats.

Features of these quantitative ELISAs for translational research and drug discovery include: only 10 µL/well required, serum or plasma; kit control included; sample values provided; widely cited; suitable for use in human and non-human samples (high cross-reactivity between species).

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



Yeast with a >50% synthetic genome created in the lab

Researchers have combined over seven synthetic chromosomes that were made in the lab into a single yeast cell, resulting in a strain with more than 50% synthetic DNA that survives and replicates similarly to wild yeast strains.

The team presented the half-synthetic yeast in the journal *Cell*, as part of a collection of papers across *Cell*, *Molecular Cell* and *Cell Genomics* that showcase the Synthetic Yeast Genome Project (Sc2.0) — a global consortium of more than 250 researchers working to develop the first synthetic eukaryote genome from scratch. Now, after 15 years of work, the team has synthesised and debugged all 16 yeast chromosomes.

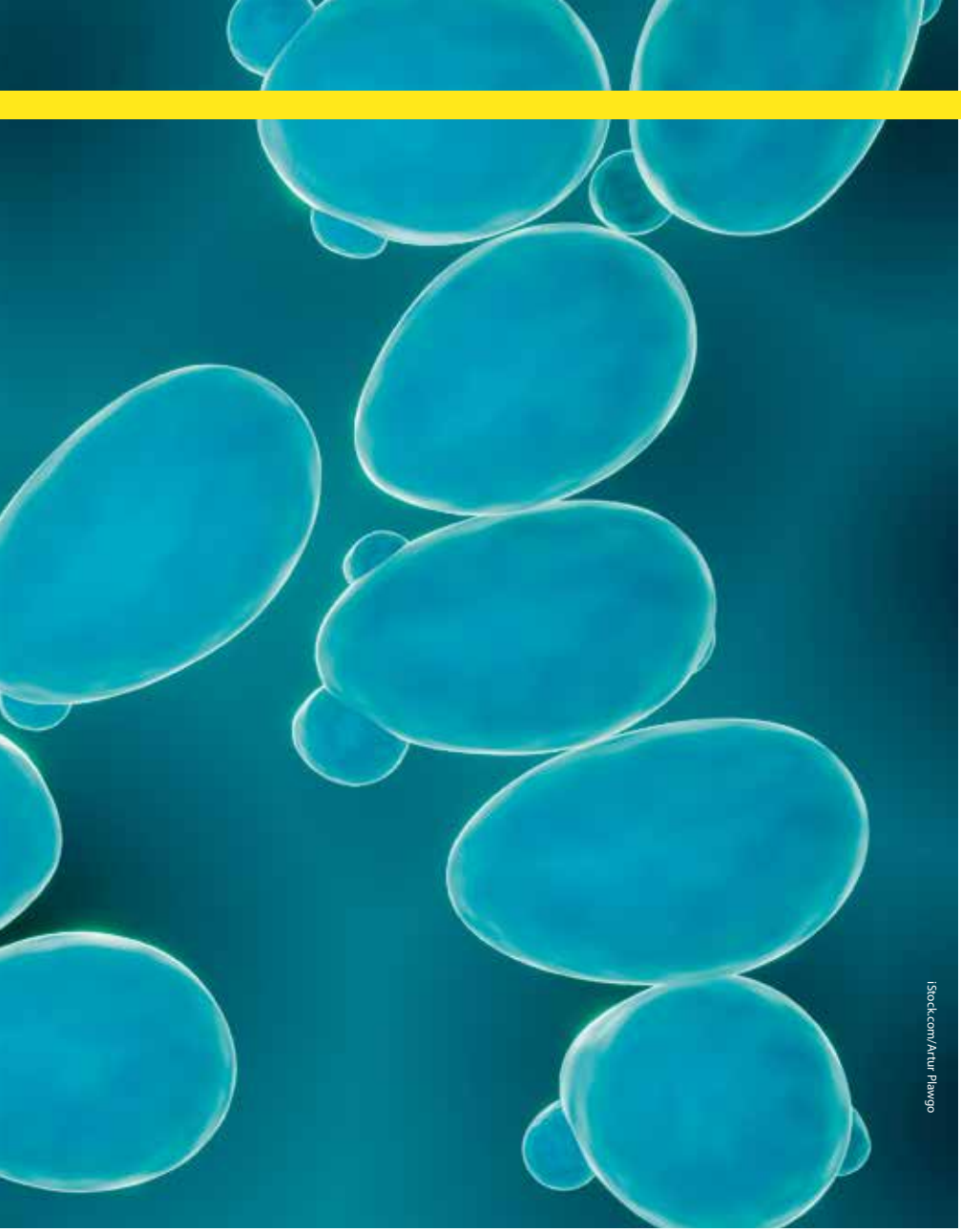
Yeasts are a common workhorse of industrial biotechnological processes as they allow valuable chemicals to be produced more efficiently, economically and sustainably. They are often used in the production of biofuels, pharmaceuticals, flavours and fragrances, as well as in the more well-known fermentation processes of bread-making and beer-brewing.

Being able to rewrite a yeast genome from scratch could create a strain that is stronger, works faster, is more tolerant to harsh conditions and has a higher yield. The process also sheds light on the traditionally problematic genome fundamentals, such as how genomes are organised and evolved.

"Our motivation is to understand the first principles of genome fundamentals by building synthetic genomes," said Professor Patrick Cai, Chair in Synthetic Genomics at The University of Manchester and international coordinator of Sc2.0 project. "The team has now rewritten the operating system of the budding yeast, which opens up a new era of engineering biology — moving from tinkering a handful of genes to de novo design and construction of entire genomes."

Though bacterial and viral genomes have been synthesised previously, this would be the first synthetic eukaryote genome, which introduces the complication of multiple chromosomes. The synthetic yeast is also a 'designer' genome that differs substantially from the natural Saccharomyces cerevisiae (brewer's or baker's yeast) genome on which it is based.

"We decided that it was important to produce something that was very heavily modified from



iStock.com/Artur Plawgo

nature's design," said senior author and Sc2.0 leader Jef Boeke, a synthetic biologist at NYU Langone Health. "Our overarching aim was to build a yeast that can teach us new biology."

To this end, the researchers removed chunks of non-coding DNA and repetitive elements that could be considered 'junk', added new snippets of DNA to help them more easily distinguish between synthesised and native genes, and introduced a built-in diversity generator called 'SCRaMbLE' that shuffles the order of genes within and between chromosomes.

Scanning electron micrograph of the syn6.5 strain of yeast, which has ~31% synthetic DNA and displays normal morphology and budding behaviour. Image courtesy of Cell/ Zhao et al under CC BY-SA 4.0

To increase genome stability, the team also removed many of the genes that encode transfer RNA (tRNA) and relocated them to an entirely new 'neochromosome' consisting only of tRNA genes. "The tRNA neochromosome is the world's first completely de novo synthetic chromosome," Cai said. "Nothing like this exists in nature."

Since the yeast genome is organised into 16 chromosomes, the researchers began by assembling each chromosome independently to create 16 partially synthetic yeast strains that each contained 15 natural chromosomes and one synthetic chromosome. The next challenge was to begin combining these synthetic chromosomes into a single yeast cell.

To do this, Boeke's team started by using a method reminiscent of Mendel's peas: essentially, the researchers interbred different partially synthetic yeast strains and then searched among their progeny for individuals carrying both synthetic chromosomes. Though effective, this method is very slow, but the team gradually consolidated all previously synthesised chromosomes — six full chromosomes and one chromosome arm — into a single cell. The resulting yeast strain was more than 31% synthetic, had normal morphology, and showed only slight growth defects compared to wild-type yeast.

To more efficiently transfer specific chromosomes between yeast strains, the researchers developed a new method called chromosome substitution that is separately discussed in the new collection. As a proof of concept, they used chromosome substitution to transfer a newly synthesised chromosome (chromosome IV, the largest of all the synthetic chromosomes), resulting in a yeast cell with 7.5 synthetic chromosomes that is more than 50% synthetic.

When the synthetic chromosomes were consolidated into a single yeast strain, the team detected several genetic defects or 'bugs' that were invisible in yeast strains that only carried one synthetic chromosome. "We knew in principle that this might happen — that we might have a huge number of things that had tiny little effects and that, when you put them all together, it might result in death by a thousand cuts," Boeke said.

Some of these bugs were simply due to the additive impact of having many tiny defects within the genome, while others involved genetic interactions between genes on the different synthetic chromosomes. The researchers were able to map and fix several of these bugs and increase the synthetic yeast's fitness by using a method based on CRISPR/Cas9.

"We've now shown that we can consolidate essentially half of the genome with good fitness, which suggests that this is not going to be a big problem," Boeke said. "And from debugging, we learn new twists on the rules of life."

The team's challenge now, after having assembled all 16 synthetic yeast chromosomes, is to consolidate them into a single living yeast strain, with Boeke saying, "Now we're just this far from the finish line of having all 16 chromosomes in a single cell.

"I like to call this the end of the beginning, not the beginning of the end, because that's when we're really going to be able to start shuffling that deck and producing yeast that can do things that we've never seen before," he said.

Vaporised hydrogen peroxide sensors

Vaisala's HPP270 series probes, which use PEROXCAP sensor technology to measure vaporised hydrogen peroxide in bio-decontamination applications, do not have a specified calibration interval. Although the typical calibration interval is one year, calibration intervals should be based on how the probe is used. This means that the key considerations are the duration and concentration of H_2O_2 exposure. Further, the requirements of the user's internal quality management system must be met.

A novel feature of the HPP270 series probes is the ability to evaluate the sensors' performance through the 'Sensor Vitality' value. This value is like a health check for the sensor. Accessed with Vaisala Insight software, sensor vitality is displayed as a percentage; Vaisala recommends replacing the probe when the value reaches ≤40%.

Vaisala's recent webinar, 'Vaporized hydrogen peroxide sensors: How to maintain measurement quality', answered several questions on sensor vitality, and a few on basic use of the HPP270 series probes.

Vaisala Pty Ltd
www.vaisala.com

Compressed air flow meters

The compact FS10i flow meter series is an easy-to-install solution to measure the flow rate of compressed air, air and natural gas. They are accurate to ±1.5% of reading and ±0.5% of full scale, with repeatability of ±0.5% of reading and a response time of 4 s (one time constant). Their go-anywhere small size, plug-in wiring and inline or insertion style threaded connection into plant piping enables quick and effective installation. In addition, they are SIL-2 rated for safety instrumented system (SIS) critical processes.

Providing precision direct mass flow measurement, the flow meters require no additional pressure or temperature sensors or other components to infer flow measurement. Their sealed and no-moving-parts sensor does not foul or clog and requires no routine maintenance, for years of trouble-free, continuous operation.

Utilising decades-long, applications-proven thermal dispersion flow-sensing technology, the FS10i Flow Meters provide a fluid-matched, calibrated and linearised 4–20 mA output of flow rate and a user-programmable high- or low-flow alarm/trip point with a 1 A SPDT relay output. For visual indication, the flow meters include a 10-segment LED array. This display illuminates proportionally to the flow rate and flashes if an alarm trip occurs.

The flow meters are available in both inline and insertion style configurations to support installation in line sizes from DN25 to DN500. They operate over a wide, 100:1 turndown from 1.6 to 122 NCMH depending on the fluid media and line size.

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

Disposable pipette tip washers

Grenova delivers innovative solutions for pipette tip washing for the life science community, offering a way to protect supplies, cut costs and control the lab's supply chain.

Since 2014, Grenova has provided the lab industry with patented and scientifically proven green technology capable of washing, sterilising and reusing pipette tips in large quantities. Over 100,000,000 pipette tips have been washed and reused by Grenova, proving the safety and effectiveness of the technology. The tip washers were developed and have been tested in CLIA- and CAP-approved labs on multiple assays without carryover. In addition, they are implemented by the NIH, NCI and CDC.

Labs that leverage Grenova technology have reportedly experienced the following results: pipette tip consumption reduced by 90%; significant cost savings; reduction in plastic waste impacting the environment; no supply shortages; improved lab efficiency; zero carryover effect; and improved sustainability rating. The current tip washers available are the TipNovusMini and TipNovus, each with cleaning and drying technology equipped to handle low or higher throughputs.

The company has also announced the release of the Purus for microwell plate cleaning. The Purus removes chemical and biological contaminants from microwell plates so they can be reused and can be configured to be 96- or 384-well compatible.

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

Filters for process safety

Camfil offers a complete range of ProSafe filters designed to comply with the strict demands on safety, traceability and control in the food and beverage or life science industries. Explicitly designed for process safety, all HEPA classified ProSafe filters are thoroughly tested before they leave the factory to eliminate potential leakage.

The quality of the raw material is tested and developed according to precise specifications with resistance tested to chemicals used for cleaning and decontamination processes in cleanrooms. Free of harmful chemical components such as formaldehyde, phthalates and Bisphenol-A, all ProSafe filters are packed individually in hygienic bags.

The Hi-Flo ProSafe is a pocket filter with high efficiency, used for air-conditioning applications and preparatory filtration in cleanrooms. It has an optimised pocket design for energy-efficient air distribution.

The Opakfil ProSafe ES has been designed to fulfil the strict safety requirements for preparatory filtration of air for cleanrooms in the most energy-efficient way.

The Hi-Cap ProSafe is suitable for preparatory filtration of air in cleanrooms. It features rigid self-supporting pockets designed to remove the largest particles.

For air-conditioning applications and filtration preparation of cleanrooms, the ProSafe range is designed for process safety, with food contact certificates for the materials used for frame parts, frame potting, gasket and filter media (according EC1935-2004) and antimicrobial growth certificates (according ISO846 and VDI6022).

Camfil Australia Pty Ltd
www.camfil.com.au

Pill-sized device monitors vital signs from the gut

The VM pill shown in a clear gel capsule for ease of visualisation of internal components. Image credit: Ben Pless.

US scientists have developed an ingestible device that can safely monitor vital signs like breathing and heart rate from inside of us, providing patients with easier access to health care without the need to go to hospital. The so-called vitals-monitoring pill, or VM pill, has been described in the journal ***Device***.

Unlike implantable devices such as pacemakers, ingestible devices are easy to use and do not require a surgical procedure. For example, doctors have in recent years been using pill-sized ingestible cameras to conduct colonoscopies, a procedure traditionally conducted in a hospital setting.

"The idea of using an ingestible device is that a physician can prescribe these capsules, and all the patient needs to do is to swallow it," said co-author Benjamin Pless, founder of the medical device developer Celero Systems. "People are accustomed to taking pills, and costs of using ingestible devices are much more affordable than performing traditional medical procedures."

The VM pill works by monitoring the small vibrations of the body associated with breathing and the beating heart. The pill can detect if a person stops breathing from the inside of the digestive tract.

To test out the VM pill, the team placed the device in the stomach of pigs, which were put under anaesthesia. Researchers then administered the pigs with a dose of fentanyl that caused the pig to stop breathing, which is what happens during fentanyl overdose in humans. The device measured the pig's breathing rate in real time and alerted the researchers, who were able to reverse the overdose.

The team also tested the device in humans for the first time by giving the VM pill to those being evaluated for sleep apnoea, a disorder in which breathing repeatedly stops and starts during sleep. Many people with the condition remain undiagnosed, in part because diagnosing the condition involves admitting people to a sleep laboratory where they are hooked up to external devices to monitor their vital signs during sleep.

"Given our interest in opioid safety, it came to our attention that sleep apnoea has a lot of the same symptoms as opioid-induced respiratory depression," Pless said.

Researchers gave the VM pill to 10 patients with sleep apnoea at West Virginia University (WVU). The device was able to detect when the participants' breathing stopped and to monitor respiration rate with an accuracy of 92.7%. Compared with external vital monitoring machines, the pill can monitor heart rate with an accuracy of at least 96%. The trial also showed the device is safe, and all participants excreted the device in the few days after the experiment.

"The accuracy and correlation of these recordings were excellent compared to the clinical gold standard studies we performed in our sleep laboratories," said co-author Ali Rezai, a neuroscientist at the WVU Rockefeller Neuroscience Institute. "The ability to remotely monitor critical vital signals from patients without wires, leads or need of medical technicians opens the door for monitoring patients in their natural environments versus the clinic or the hospital setting."

First author Giovanni Traverso, an associate professor at the Massachusetts Institute of Technology, said the current version of the VM pill passes through the body in about a day, but the device could be modified in the future to allow it to stay longer for long-term monitoring. The researchers also hope to upgrade the device so it can deliver drugs to reverse conditions like opioid overdose automatically once it detects symptoms.

News of the VM pill's development came just weeks after Breakthrough Victoria announced it was investing in medical technology company Atmo Biosciences, to support the commercialisation of an ingestible gas-sensing capsule that can help diagnose functional gastrointestinal disorders (FGIDs). Breakthrough Victoria is an independent investment company established in 2021 to manage the state government's $2 billion Breakthrough Victoria Fund, supporting breakthrough innovations that will improve people's lives and benefit the state of Victoria.

Atmo Biosciences has created a gas-sensing capsule the size of a vitamin pill which, when swallowed, can electronically report data about the human gastrointestinal system by detecting gases in real time from known locations within the gut. This data is then sent to Atmo's cloud platform for analysis.

Unlike existing approaches that may be invasive, inaccurate or rely on trial and error, the gas-sensing capsule provides insight into microbiome function, from direct measurement of the gases produced by the microbiota, while allowing patients to go about day-to-day activities. This is expected to facilitate more targeted treatment, earlier relief of symptoms and reduced healthcare costs for FGID patients.

"Gastrointestinal disorders are a big problem in Australia and around the world, with patients suffering debilitating symptoms such as nausea, vomiting, diarrhoea and abdominal pain," said Atmo Biosciences CEO Mal Hebblewhite. "Unfortunately, due to shortcomings with current diagnostic methods, and despite frequent visits to the doctor, it's estimated about 30% of sufferers remain undiagnosed or are misdiagnosed. Atmo is hoping to change that."

Atmo's first clinical application is a diagnostic tool for motility disorders (where food or waste doesn't move properly through the digestive system), with a pivotal clinical study taking place in Australia and the United States. The capsule is also in clinical trials for conditions including irritable bowel syndrome, inflammatory bowel disease and liver disease, with a possible future application as a diagnostic tool for small intestinal bacterial overgrowth.

The technology was first invented at RMIT University in 2011 before being spun out into startup company Atmo and developed with commercialisation support from healthtech innovation company Planet Innovation. Breakthrough Victoria is investing in Atmo via a share purchase from Planet Innovation.

"Atmo's gas-sensing capsule is a world-first innovation developed and manufactured in Victoria with the potential to help millions of people suffering gut disorders around the world," said Breakthrough Victoria CEO Grant Dooley.

"The company has enormous potential for growth at a global scale and we look forward to working with them to help achieve these goals."

Malvern OMNISEC Emerges as the Ultimate tool for Quantifying LNP Therapeutic Payloads

Lipid-based nanoparticles (LNPs) hold great promise for the treatment, cure, and prevention of a range of challenging medical conditions, from genetic diseases to cancers. Not only do LNPs enable the efficient delivery of therapeutic payloads such as RNA, but unlike viral vectors, they can also be manufactured using cell-free production processes with the potential for rapid scaling, as demonstrated by the Micropore Pathfinder advanced cross flow technology. Understanding the therapeutic payload, particularly how much of the payload has been incorporated into the LNP, is critical to ensuring patients receive the correct therapeutic dose.

Although RNA quantitation has traditionally been performed using fluorescence measurement with RiboGreen dye, the analytical method has several downsides.

The need for complex method development, where protocols are not easily transferable between different LNP formulations, in addition to the relative insensitivity of the assay and the presence of several commonly used salts, can compromise the accuracy of this popular assay.

Size exclusion chromatography (SEC) coupled to light scattering detectors

The Malvern Panalytical OMNISEC has emerged as a key approach to aid payload quantification when it comes to LNP-based therapies. SEC works by loading samples onto a column, which separates the sample

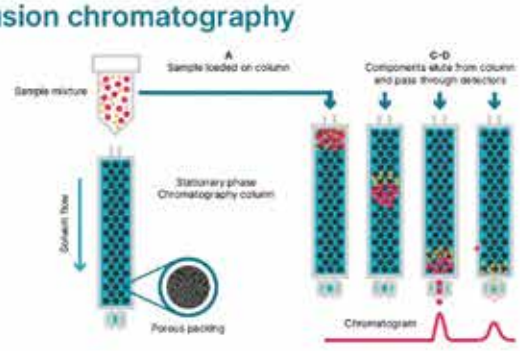


Figure 1: Schematic showing a typical SEC setup.

Malvern Panalytical OMNISEC: the most advanced multi-detector GPC/SEC system for higher resolution and faster sample analysis

components based on their hydrodynamic radius. Smaller components are retained in the column longer than larger molecules, meaning larger molecules elute from the column first. Unlike other SEC systems, the Malvern OMNISEC can be coupled to multiple advanced detectors, such as light scattering (right-angle and low-angle light scattering and multi-angle light scattering, RALS/LALS and MALS, respectively), UV/vis-PDA, and refractive index (RI) detectors and a differential viscometer enabling direct measurement of a range of parameters, several of which can be used to calculate payload information.

Compositional analysis: calculating the weight fraction of your LNP payload

The compositional analysis method uses output from both the RI and UV/Vis-PDA detectors to determine the concentration of two components within a single sample (in this case, LNPs and the genetic payload). By using the data from two concentration detectors, advanced SEC system software can set up two equations to solve for the two unknowns: the concentration of component A (C_A) and the concentration of component B (C_B). The RI increment (dn/dc), which is a representation of the difference between the RI of the sample and the solvent together with the specific absorption coefficient (dA/dc), can be used to calculate the concentration of each component.

$$\text{RI Signal} \propto C_A \bullet \frac{dn}{dc}_A + C_B \bullet \frac{dn}{dc}_B$$

$$\text{UV Signal} \propto C_A \bullet \frac{dA}{dc}_A + C_B \bullet \frac{dA}{dc}_B$$

By comparing the concentrations of the two components, you can then obtain the weight fraction (%) of the LNP payload.

The multi-detection Pyramid

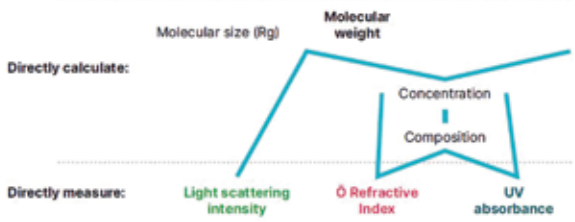


Figure 2: An overview of the multi-detection pyramid, displaying what each SEC-coupled detector can directly measure and calculate.

SEC-LS: advantages and key considerations

SEC coupled to light scattering detectors (SEC-LS) has several benefits for LNP developers. As well as being a helpful tool to support LNP payload quantification, SEC-LS can be used to measure a range of other important sample parameters including size, molecular weight, and aggregation profile. Being able to measure multiple parameters without resorting to several different techniques delivers significant throughput benefits.

The measurements from SEC-LS are also highly accurate and reliable, and the technique does not require the difficult-to-acquire dedicated reagents needed in traditional methods. When it comes to getting the most out of SEC-LS for compositional analysis of LNPs there are some key considerations. The first is to ensure that a suitable chromatography column is used and that the LNP sample is adequately eluting from it. To minimise the risk of the sample sticking in the column, users should check the surface charge or measure the zeta potential of any samples to optimise the running buffer. This can

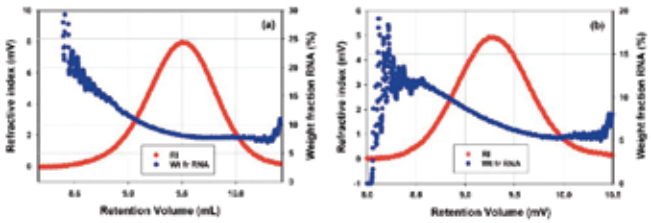


Figure 3: RI chromatograms of two mRNA-LNP samples, each overlayed with respective weight fractions of mRNA.

done using Electrophoretic Light Scattering (ELS) as employed by the Malvern Zetasizer. LNP therapies prepared in physiological buffer can pose challenges when measuring zeta potential as they are highly conductive and can aggregate. Malvern's diffusion barrier method protects the sample by keeping it away from the electrodes within the buffer while also reducing the amount of sample required for the measurement.

ATA Scientific offers a range of technologies to enable robust manufacture and characterisation of complex drug delivery systems and particularly LNP-based therapies. If you would like to learn more about how to better characterise your LNPs, reach out to our team of analytical specialists at
+61 2 9541 3500 or
enquiries@atascientific.com.au.

1. https://bit.ly/47TqidH

Injectable tissue prosthesis to aid in muscle regeneration

Researchers from the Institute of Basic Science (IBS) in South Korea have developed a novel approach to healing muscle injury, by employing an injectable tissue prosthesis in the form of conductive hydrogels and combining it with a robot-assisted rehabilitation system. Their work has been published in the journal ***Nature***.

Imagine you are swimming in the ocean when a giant shark approaches and bites a huge chunk of meat out of your thigh, resulting in a complete loss of motor/sensor function in your leg. Traditional rehabilitation methods for these kinds of muscle injuries have long sought an efficient closed-loop gait rehabilitation system that merges lightweight exoskeletons and wearable/implantable devices. Such assistive prosthetic systems are required to aid the patients through the process of recovering sensory and motor functions linked to nerve and muscle damage.

Unfortunately, the mechanical properties and rigid nature of existing electronic materials render them incompatible with soft tissues. This leads to friction and potential inflammation, stalling patient rehabilitation.

The new hydrogel system (IT-IC) can protect the gel from destruction by external forces. In conventional covalently crosslinked hydrogels, fragmentation occurs due to the destruction of covalent bonds during the injection process, but IT-IC hydrogels maintain covalent bonds due to stress dissipation with multiple bonds containing biphenyl structure and allow injection into narrow areas.

To overcome these limitations, the IBS researchers turned to a material commonly used as a wrinkle-smoothing filler, called hyaluronic acid. Using this substance, an injectable hydrogel was developed for tissue prosthesis, which can temporarily fill the gap of the missing muscle/nerve tissues while it regenerates. The injectable nature of this material gives it an advantage over traditional bioelectronic devices, which are unsuitable for narrow, deep or small areas, and necessitate invasive surgeries.

Thanks to its 'tissue-like' properties, the hydrogel seamlessly interfaces with biological tissues and can be easily administered to hard-to-reach body areas without surgery. The reversible and irreversible cross-links within the hydrogel adapt to high shear stress during injection, ensuring good mechanical stability. The hydrogel also incorporates gold nanoparticles, which give it decent electrical properties. Its conductive nature allows for the effective transmission of electrophysiological signals between the two ends of injured tissues. In addition, the hydrogel is biodegradable, meaning that the patients do not need to get surgery again.

The researchers put their idea to the test in rodents that had had a large chunk of muscle removed from their hind legs. By injecting the hydrogel and implanting the two kinds of stretchable tissue-interfacing devices for electrical sensing and stimulation, the researchers were able to improve the gait of the rodents. The hydrogel prosthetics were combined with robot assistance, guided by muscle electromyography signals. Together, the two helped to enhance gait without nerve stimulation. Furthermore, muscle tissue regeneration was effectively improved over the long term after the conductive hydrogel was used to fill muscle damage.

The injectable conductive hydrogel was found to excel in electrophysiological signal recording and stimulation performance, offering the potential to expand its applications. It thus presents a fresh approach to the field of bioelectronic devices and holds promise as a soft tissue prosthesis for rehabilitation support.

"We've created an injectable, mechanically tough and electrically conductive soft tissue prosthesis ideal for addressing severe muscle damage requiring neuromusculoskeletal rehabilitation," said Professor Shin Mikyung. "The development of this injectable hydrogel, utilising a novel cross-linking method, is a notable achievement. We believe it will be applicable not only in muscles and peripheral nerves but also in various organs like the brain and heart."

"In this study, the closed-loop gait rehabilitation system entailing tough injectable hydrogel and stretchable and self-healing sensors could significantly enhance the rehabilitation prospects for patients with neurological and musculoskeletal challenges," added Professor Son Donghee. "It could also play a vital role in precise diagnosis and treatment across various organs in the human body."

The research team is currently pursuing further studies to develop new materials for nerve and muscle tissue regeneration that can be implanted in a minimally invasive manner. They are also exploring the potential for recovery in various tissue damages through the injection of the conductive hydrogel, eliminating the need for open surgery.

Combined spectrophotometer and cell counter

Pacific Laboratory Products' anvajo Fluidlab R-300 combined spectrophotometer and cell counter is a handheld device for in-lab or remote use. Featuring a pocket-sized instrument and easy-to-use cuvettes or sample carriers for cell counting, it is suitable for all to use.

The anvajo Fluidlab R-300 combines two central laboratory technologies — spectrometry and cell counting — in one portable device. It can be used with the dedicated anvajo sample carriers as well as standard cuvettes in a broad range of applications.

The product features deep neuronal networks and machine learning for classification of optical outputs. A dedicated sample carrier system enables the testing of a large variety of fluids, and quantitative results are available within minutes for immediate decisions.

The unit's small size makes it easy to use and to move, with no recalibration after transport. There are also no maintenance costs due to the autonomously performable sensor check and status update.

Pacific Laboratory Products
www.pacificlab.com.au

Microbiology lab automation range

Cell Biosciences has been appointed a distributor of the Alliance Bio Expertise (A.B.E.) range of microbiology laboratory automation equipment.

The range includes automated microbiology media preparators allowing preparation of media from 1 up to 50 L. These units can be integrated with the A.B.E. petri dish or tube and bottle fillers.

Filled petri dishes can be wrapped using the Minima wrapping machine, combined with a carefully selected film in order to avoid condensation.

Cell Biosciences Pty Ltd
www.cellbiosciences.com.au

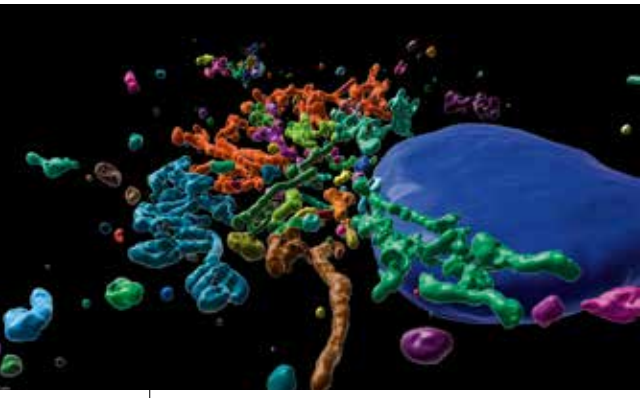


Image analysis software with AI

Oxford Instruments has released Imaris 10.1, the latest version of its microscopy image analysis software suited to applications such as cancer, cell biology, developmental biology, neuroscience, quantitative analysis of organoids, segmentation and visualisation of greyscale images in CT and MRI imaging, and automated segmentation of SEM images.

Over the last 30 years, Imaris has continuously improved on its visualisation technology for 3D/4D fluorescence images to accommodate ever-increasing image sizes while introducing a range of analytical tools for cell biologists, neuroscientists and other life science disciplines. To best serve the image analysis community, Imaris has integrated a trainable AI segmentation tool for challenging images, which is now available to all Imaris users.

This latest release integrates AI segmentation tools into the main image analysis workflows, improving ease of use and providing better and more versatile segmentation tools. A native trainable AI pixel classifier is an integral part of the big data capable surface segmentation model. Using the Imaris AI pixel classifier simplifies and improves the segmentation and object detection in challenging fluorescent datasets. In addition, it opens doors for 3D scanning electron microscopy (SEM) segmentation and shape recognition.

Key features include efficient training on thick slices (visualising biological structures); a smooth and slick brush training tool; real-time predictions preview; automated use on multiple images (with retrain option); and fast computations for big datasets (100s of GBs).

SciTech Pty Ltd
www.scitech.com.au

Air filters

Camfil Absolute V-shaped air filters provide extra-high-efficiency final filtration in air-conditioning systems, housings and diffusers for systems that require a very high airflow and low pressure drop.

Absolute V filters are usually used in make-up-air or recirculation units as a final HEPA stage to protect terminal HEPA filters in cleanrooms. They can also be used in exhaust air to help remove harmful ultrafine particles, whether chemical, biological or radioactive.

The range is available in filter classes E10 to H14, with an MPPS of 85% to 99.995%, and is suitable for very high airflows greater than 3400 m^3/h. The media is pleated using Camfil's patented controlled media spacing (CMS) technology for optimal airflow and media performance. Together with intermediate hot-melt separators, the product is designed to ensure uniform pleat spacing and the ability to form a rigid self-supported media pack. The product's gasket seal is a seamless polyurethane foam gasket applied to its flange that is designed to eliminate the risk of air bypass.

The Absolute V family includes Absolute VG and Absolute VE. Absolute VE features an enclosing frame of galvanised sheet metal that forms a rugged and durable enclosure. Absolute VG is made from lightweight plastic and is completely fire combustible upon disposal.

Each Absolute V filter is individually tested and certified to EN 1822 with a separate scan test protocol and serialised on the product label.

Camfil Australia Pty Ltd
www.camfil.com.au

Live cell transport incubators

Transportation of delicate living cells in biomedical research has long been a challenge. Conventional cryopreservation has limitations, particularly when dealing with fragile cells such as engineered iPSC-derived hepatocytes, often leading to cell damage and reduced viability. Cellbox Solutions offers a solution with its Cellbox Ground and Flight systems.

The Cellbox serves as a live cell transport incubator, specifically engineered for the secure transport of organoids, tissue patches, cellular 3D prints and other non-freezable cell types. It can be used when samples need to traverse across a campus, between institutes or even from one part of the globe to another.

The innovation lies in the portable nature of the Cellbox, eliminating the need for cryopreservation or cooling during shipment. A fully temperature- and CO_2-controlled environment means that samples are maintained in a suitable incubation state during transportation. The Ground version uses a pressurised CO_2 cylinder for transportation by car, train or foot, while the Flight version employs sublimation of dry ice, enabling it to comply with flight regulations and thus making it capable of transporting live cells by air.

The solution was recently demonstrated in a collaboration between CellBox Solutions and time:matters, a biomedical company that was faced with the challenge of transporting engineered iPSC-derived hepatocytes from France to Canada. The active portable CO_2 incubator was found to maintain the cells at 37°C and 5% CO_2 during the 16-hour transatlantic journey, resulting in a 91% cell viability rate upon arrival.

ATA Scientific Pty Ltd
www.atascientific.com.au

*Ivor Campbell**

iStock.com/AndreyPopov

Can AI replicate the human touch in healthcare provision?

Anyone who recalls the 'turbo' trend of the 1980s will have a foreboding sense of déjà vu about the sudden ubiquity of artificial intelligence in every aspect of our lives.

What began with Swedish motor manufacturer Saab unveiling its 99 Turbo Coupé in 1977 suddenly had manufacturers scrambling for their own version of the latest technological buzzword in everything from alarm clocks to hairdryers. The craze reached its apotheosis with the spoof launch, by *Viz* magazine, of the Satsuma Castanet XR4 Turbo supercar, which promised potential buyers that, if they bought one, they would never sleep alone again.

If you believe the latest hype around AI, then the screamingly unreliable chatbots with whom you are invited to engage while trying to renew your home insurance are poised to take over the world, consigning humanity to the role of trussed-up gimps. But while most of the general chatter around the technology can, most charitably, be dismissed as 'uninformed', there are already some encouraging signs of its potential to change the world of public healthcare provision, substantially for the better.

Some months ago, it was revealed that researchers at the University of Aberdeen, NHS Grampian and an industry partner had made a significant breakthrough in using AI to speed up the detection of breast cancer. Their three-year project, funded by UK Research and Innovation, involved analysing 220,000 mammograms from more than 55,000 patients, using artificial intelligence-powered breast screening technology.

This proved highly effective at identifying potentially missed cancer cases, known as interval cancers, that would have remained undetected under current screening procedures until patients developed symptoms; this breakthrough could lead to recalling 34.1% of women who developed

interval cancers. Meanwhile, in another study of 80,000 mammograms of women who had undergone screenings in Sweden, an AI-assisted system detected 20% more cases of cancer than human radiologists.

The global market for AI in medical diagnostics is experiencing significant growth, projected to reach $2.85 billion in 2023 — up by 43.1% on the previous year. The market is expected to grow by 42.5% annually over the next four years, when it will be worth $11.75 billion.

It includes services such as medical imaging, robotic process automation, machine learning, natural language processing and rule-based expert systems, along with sales of various medical devices used in providing AI-based diagnostics services. AI also has the potential to identify, and even design, up to 50 new therapeutic drugs in the next decade, representing a $50 billion opportunity for the global pharmaceutical industry, with a 20–40% reduction in preclinical costs.

There is fevered speculation about how the technology might be used in other areas of medical technology to improve patient outcomes and reduce the burden on hard-pressed, and often under-resourced, medical practitioners.

Imagine a future where AI-powered smartphone cameras could analyse skin conditions, providing instant feedback on potential issues. By enhancing early detection, AI can save countless lives and improve overall healthcare outcomes.

It may also soon be able to contribute to the development of personalised medicine, with treatment plans tailored to each individual patient's unique characteristics, including their genetic makeup, lifestyle factors and medical history.

By analysing vast datasets and applying predictive analytics, algorithms can identify optimal treatment options and predict potential responses to specific therapies. The integration of artificial intelligence in surgery has the potential to optimise treatment efficacy, minimise adverse effects and improve patient satisfaction.

However, while pharmaceutical corporations, medtech manufacturers and national healthcare providers see only the benefits of huge cost savings, quicker and more effective ways of treating more patients and better health outcomes, not everyone shares their unequivocally optimistic view.

AI will undoubtedly change the roles and responsibilities of medical professionals, with routine diagnostics being handled by AI systems,

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freeing up doctors to focus on more specialist and complex tasks. Just as motor mechanics have shifted to specialise in managing onboard computing systems in cars, medics may need to adapt and evolve their roles to work alongside AI systems.

For this they will need to learn new skills and some employers may struggle to find enough qualified AI experts, or be prepared to pay a premium to secure their services. The likelihood is that many AI developments will end up being concentrated in a few consultancy firms, leading to potential monopolisation of expertise, and potentially an increased cost for end users.

The growing use of AI in health care also raises important ethical considerations. While technology can provide data-driven recommendations and diagnostics, it lacks the capacity for empathy and sensitivity.

The human touch is crucial in health care, especially when addressing mental health issues. A balance must be struck between using AI for efficient diagnostics and ensuring that human healthcare professionals maintain a central role in providing emotional support and understanding to patients.

A recent study by University of Arizona Health Sciences found that 52% of participants would choose a human doctor rather than AI for diagnosis and treatment. Researchers found that most patients aren't convinced the diagnoses provided by AI are as trustworthy of those delivered by human medical professionals.

The omnipresence of AI monitoring and its capacity for data collection may also raise concerns about privacy and individual agency.

While AI may offer real-time insights into our health and provide us with tailored recommendations, it also poses a risk of intrusion and control over personal lives. Patients may experience anxiety and uncertainty when AI systems predict their future health outcomes, leading to potential psychological impacts.

Some of the benefits of a healthcare system are in its powers of mediation to protect patients from the impact of existential reality.

A system that can tell an 18-year-old patient, using AI, that they are going to have a lifestyle-related cancer by the age of 40, will also have a duty of care to ensure the patient is psychologically equipped to deal with such news, and also to present them with advice on how to change their lifestyle.

While some people may want to hear how long they have to live, years in advance, the main beneficiaries of such information will be life insurance companies who will see an opportunity to deal increasingly in greater certainty, while minimising, or even eliminating, risk.

While there will be some patients who believe that having a chip implanted under their skin, which permanently monitors their health, will drastically improve their life chances, there will be others for whom it is an unacceptable intrusion.

While we may still be in the early days of AI in health care, already there is an urgent need to establish ethical guidelines and regulatory standards to govern its use.

Ensuring transparency, accountability and patient autonomy must be prioritised. Decision-making algorithms must be explainable and unbiased, and the data collected must be handled responsibly and securely to protect patient privacy.

Times and attitudes change and driving a Satsuma Castanet XR4 Turbo would now be considered distinctly antisocial. Creating a solid framework for the ethical and manageable implementation of AI in health care will ensure it doesn't follow the same pathway.

Ivor Campbell is Chief Executive of Callander-based Snedden Campbell, a specialist recruitment consultant for the medical technology industry.

Continuous capacitance flexible probe and controller

Where liquids are non-conducting or where there are free-flowing powders, Hawker Electronics can offer a capacitance detection system that detects the presence of the media to be monitored; this can be a point level for on/off control, alarms or a continuous level measurement. The company's FLEXICAP variable capacitance systems with Flexilevel wall-mounted unit and cable probe lengths with length over 3 m and up to 13 m are available.

A capacitance probe works in two ways: with conducting liquids and non-conducting liquids. The capacitance principle uses two detector plates and one insulator. By changing one of the factors, the user can measure its change and give a continuous output signal.

For conducting liquids, an insulated cable with a stainless steel conductor is used. As the conducting liquid rises and falls in the tank, the change is detected and an output signal is produced.

For non-conducting liquids, two concentric or parallel rods are used and the non-conducting liquid rises and falls within the orifice or gap. The change is detected and an output signal produced.

The system enables the user to measure to the top of the tank and it is unaffected by foam or turbulence. Probe length must be decided in advance for accurate measurement.

The probe will give a signal over its length and it will be detected by the controller. The controller will give digital indication, four programmable trip points and a diagnostic trip point to detect cable break and short circuit between the controller and the probe.

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

DNA and RNA library prep kits

The NEBNext UltraExpress DNA and RNA Library Prep Kits offer speed and efficiency in library preparation for Illumina sequencing. Designed by New England Biolabs (NEB), the cutting-edge kits offer researchers a novel approach to library prep, reducing time, labour and consumables while maintaining high quality.

Experience rapid RNA library preparation with the NEBNext UltraExpress RNA Library Prep Kit (NEB #E3330). A streamlined 3 h workflow means high-quality RNA libraries are created from a wide RNA input range (25–250 ng total RNA) in a short amount of time, whether in a single day with poly(A) mRNA enrichment or rRNA depletion kits, or as a standalone protocol.

For DNA library prep, the NEBNext UltraExpress DNA Library Prep Kit (NEB #E3325) offers speed and efficiency. In less than 2 h, the user can generate high-yield, high-quality libraries from a broad input range (10–200 ng pre-sheared DNA).

Without compromising quality for speed, the NEBNext UltraExpress DNA and RNA Library Prep Kits are designed to simplify workflow with fewer steps, use fewer consumables, employ a single protocol for all inputs and be automation compatible. NEB says the kits will help users to accelerate their research and make their discoveries at the bench greener and more efficient.

New England Biolabs
www.neb.com

Assay-ready NGS workstation

Hamilton Robotics' NGS STAR assay-ready workstation is a comprehensive solution for next-generation sequencing (NGS) applications from whole genome to whole transcriptome sequencing and targeted sequencing applications. The fully automated library preparation system can be customised for use with assay chemistries from leading industry partners, processing 96 libraries at once.

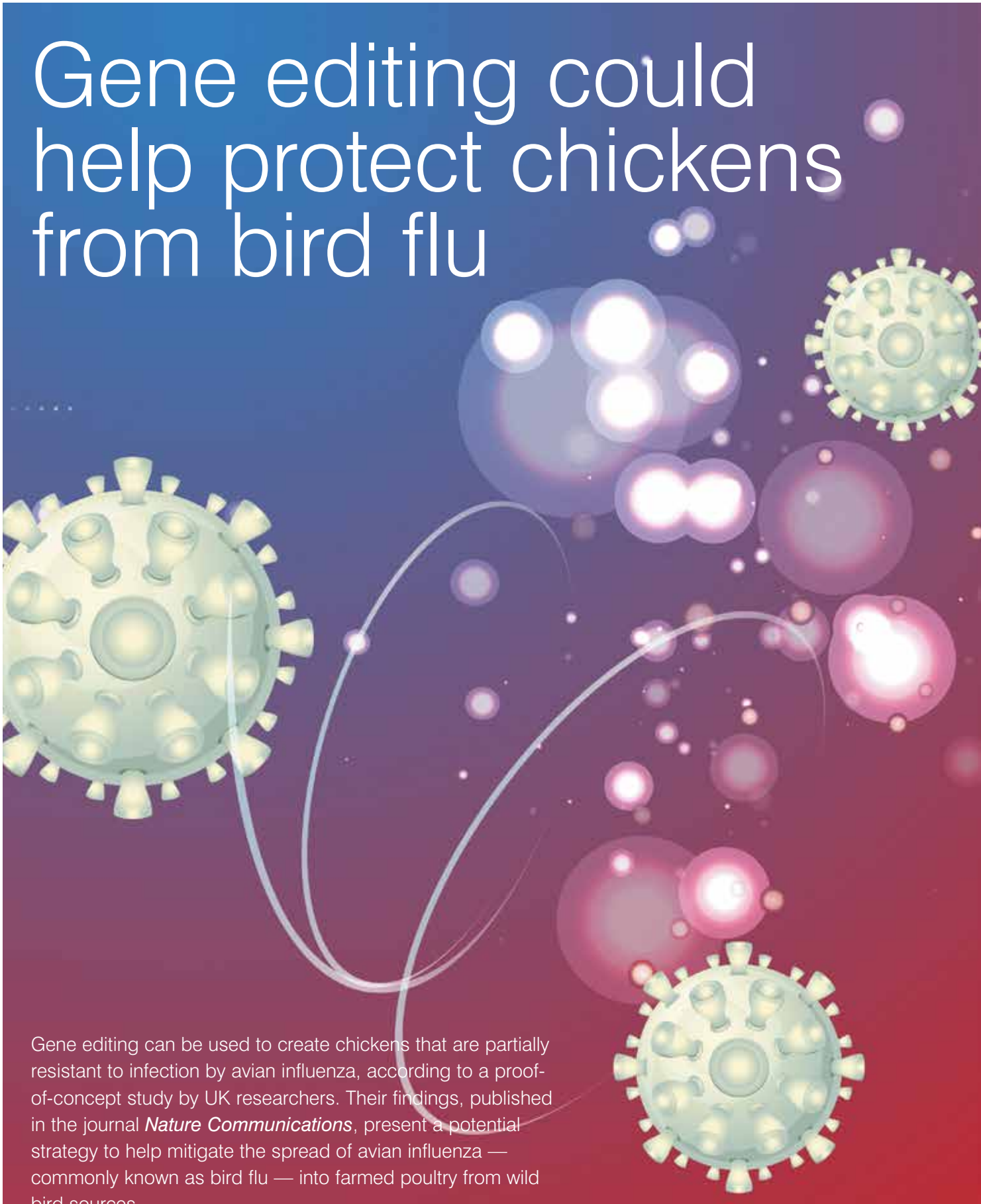
The workstation is a versatile system that delivers substantial value to customers. The NGS library prep workflows were developed with industry-leading partners, including Illumina, Integrated DNA Technologies, IDT New England BioLabs, Oxford Nanopore Technologies, Pacific Biosciences, QIAGEN, Roche KAPA, Thermo Fisher Scientific and Twist Biosciences.

The NGS STAR uses an open deck layout so that every system is fine-tuned to the lab's specific NGS workflow, throughput and assay needs. At the same time, the system is easily updated to keep pace with protocol updates or as requirements evolve over time. Users can also choose from a wide range of options to customise their system. The product is available as an open or enclosed solution, with a variety of cooling and airflow configurations.

As a fully automated system, the workstation is designed to reduce the number of cumbersome preparation steps required by current methods during runs of one to 96 samples. User-friendly software guides operators through the automated process, and automated barcode verification results in proper placement of samples, reagents, plates and tips. Each step in the aspirate and dispense process is continuously monitored for accuracy so that users can remain confident about getting consistent results throughout its operation.

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

Gene editing could help protect chickens from bird flu



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Gene editing can be used to create chickens that are partially resistant to infection by avian influenza, according to a proof-of-concept study by UK researchers. Their findings, published in the journal ***Nature Communications***, present a potential strategy to help mitigate the spread of avian influenza — commonly known as bird flu — into farmed poultry from wild bird sources.


A non-gene-edited chicken (left) pictured next to an *ANP32A* gene-edited chicken (right). Image credit: Norrie Russell.

Bird flu is a major global threat, with a devastating impact in both farmed and wild bird populations; and in rare instances, mutations in the bird flu virus allow it to infect people and cause serious illness. Efforts to control the spread of the disease are urgently needed — but poultry vaccination against avian influenza has not yet been reliable due to the rapid antigenic drift of field viruses, and is controversial owing to political and economic implications.

In chickens, avian influenza viruses hijack the host protein ANP32A to help replicate themselves. Scientists from The University of Edinburgh, Imperial College London and The Pirbright Institute have now altered the section of DNA responsible for producing the ANP32A protein, by editing the *ANP32A* gene in chicken germ cells (precursors of reproductive cells).

When the *ANP32A* gene-edited chickens were exposed to a normal dose of the H9N2-UDL strain of avian influenza virus, nine out of 10 birds remained uninfected and there was no spread to other chickens. The birds showed no adverse health or egg-laying productivity effects when monitored for over two years.

The research team then exposed the gene-edited birds to an artificially high dose of avian influenza virus — 1000 times higher, to be exact — to further test their resilience. While five out of 10 birds became infected, the amount of virus in the infected gene-edited chickens was much lower than the level typically seen during infection in non-gene-edited chickens. The gene edit also helped to limit onward spread of the virus to just one of four non-gene-edited chickens placed in the same incubator. There was no transmission to gene-edited birds.

The scientists found that in the *ANP32A* gene-edited birds, the virus had adapted to enlist the support of two related proteins — ANP32B and ANP32E — to replicate. Following lab tests, they found that some of the mutations enabled the virus to utilise the human version of ANP32, though its replication remained low in cell cultures from the human airway. But while experts have said that additional genetic changes would be needed for the virus to infect and spread effectively in humans, the research team concluded that the single *ANP32A* gene edit is not robust enough for application in the production of chickens.

To prevent the emergence of escape viruses — viruses that adapt to evade the gene edit and cause infection — the research team targeted additional sections of DNA responsible for producing all three proteins (ANP32A, ANP32B and ANP32E) inside lab-grown chicken cells. In cell cultures in the lab, growth of the virus was successfully blocked in cells with the three gene edits. The next step will be to try to develop chickens with edits to all three genes.

"Gene editing offers a promising route towards permanent disease resistance, which could be passed down through generations, protecting poultry and reducing the risks to humans and wild birds," said principal investigator Professor Mike McGrew, from The University of Edinburgh's Roslin Institute. "Our work shows that stopping the spread of avian influenza in chickens will need several simultaneous genetic changes."

Professor Wendy Barclay, from Imperial College London, added, "This work is an exciting collaboration that fuses our expertise in virology with the world-leading genetic capability at the Roslin Institute. Although we haven't yet got the perfect combination of gene edits to take this approach into the field, the results have told us a lot about how influenza virus functions inside the infected cell and how to slow its replication."

Members of the scientific community have had a cautiously optimistic reaction to the news. Professor Raina MacIntyre, Head of the Biosecurity Program at UNSW's Kirby Institute and an expert in influenza and emerging infectious diseases, noted that avian influenza spreads globally not just through poultry trading, but also through wild waterfowl such as ducks and geese as they migrate between countries and continents. "So engineering farmed chickens alone is not enough," she said.

"The other main concern is influenza A viruses are highly mutable and subject to continual antigenic drift; this means the virus itself will likely evolve to overcome engineered traits in the birds," MacIntyre added. She did say the technology could potentially be used for influenza vaccine manufacturing.

"Many vaccines are manufactured using embryonated hens' eggs," she said, "… [so] having engineered eggs that are resistant to highly pathogenic avian influenza can be of great benefit for vaccine manufacturing. Having said that, new vaccine technologies for influenza vaccines are becoming more common now, and reliance on eggs for vaccine manufacturing may not be as common in a few years."

Associate Professor Dimitri Perrin, lead of the Biomedical Data Science group from Queensland University of Technology (QUT), said it is crucial for any gene edit to ensure that there are no unintended modifications or unintended consequences elsewhere in the genome. "One edit could produce the desired effect on one specific function but also a detrimental effect for another one," he said.

While Perrin said it was encouraging that no differences were found, a single edit was not sufficient to achieve perfect results. "Targeting more genes increases the desired effect, but also the risk of other detrimental outcomes," he said. "More research is needed to strike the right balance."

Professor James Wood, Head of Department of Veterinary Medicine at the University of Cambridge, concluded that the study provides an important proof of principle for the genetic control of avian influenza. He said it is essential that the scientists demonstrate the same benefits, and the same health checks, in live birds as they did in the chicken cells that had three genetic mutations introduced.

"It would further be highly valuable to determine if these changes were advantageous in turkeys and ducks, other important food species — and it will be important to demonstrate protection in animals against the more virulent viruses circulating as well," he said.

ASID 2024 Annual Scientific Meeting

March 7–9, Wellington, New Zealand
The Australasian Society for Infectious Diseases (ASID) ASM is a leading Australasian meeting for adult and paediatric infectious disease and clinical microbiology specialists. The theme for the 2024 event is 'Challenging dogma in ID'.
The conference offers an opportunity for connecting clinicians, microbiologists and other health professionals with a common interest in infectious diseases and provides a friendly forum for the exchange of scientific advances in the prevention, diagnosis and management of clinical infectious diseases.
https://asid2024conference.net/

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ICCPDTLM-24
January 23–24, Perth
https://worldacademics.net/event/index.php?id=2196176

Lorne Proteomics 2024
January 31–February 3, Lorne
https://www.lorneproteomics.org/

Lorne Proteins 2024
February 4–8, Lorne
https://www.lorneproteins.org/

AMAS XVI — The Sixteenth Biennial Symposium
February 5–9, Brisbane
https://amasconference.squarespace.com/

Lorne Cancer 2024
February 8–10, Lorne
https://www.lornecancer.org/

Lorne Genome 2024
February 11–13, Lorne
https://www.lornegenome.org/

International Conference on Nanoscience and Nanotechnology
February 13–15, Melbourne
https://iconnference.com/

Lorne Infection & Immunity 2024
February 14–16, Lorne
https://www.lorneinfectionimmunity.org/

Molecular Approaches to Malaria (MAM) 2024 Conference
February 18–22, Lorne
https://mam2024conference.com.au/

Quantum Australia 2024
February 20–22, Sydney
https://sydneyquantum.org/event/quantum-australia-2024/

Cutting Edge Symposium Resilience in the Anthropocene
February 27–28, Hobart
https://events.csiro.au/Events/2023/October/4/Cutting-Edge-Symposium-on-Resilience-in-the-Anthropocene

Pathology Update 2024
March 1–3, Adelaide
https://www.rcpa.edu.au/Events/Pathology-Update

World Science Festival Brisbane 2024
March 15–24, Brisbane
https://www.worldsciencefestival.com.au/

Science Meets Parliament 2024
March 20–21, Canberra
https://scienceandtechnologyaustralia.org.au/smp2024/

TSANZSRS 2024
March 22–26, Gold Coast
https://tsanzsrsasm.com/

AusMedtech 2024
May 22–23, Adelaide
https://www.ausmedtech.com.au/

Accreditation Matters 2024
June 25–26, Sydney
https://nata.com.au/events/accreditation-matters-2024/

ASM National Meeting 2024
July 1–4, Brisbane
https://www.theasmmeeting.org.au/

National Science Week 2024
August 10–18, Australia-wide
https://www.scienceweek.net.au/

Biomolecular Horizons 2024
September 22–26, Melbourne
https://www.bmh2024.com/

AusBiotech 2024
October 30–November 1, Melbourne
https://www.ausbiotechnc.org/

17th APFCB Congress
October 31–November 3, Sydney
https://apfcbcongress2024.org/

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