DECEMBER 2021 # 82

the Medicine Maker®

The Innovation Awards 2021

It's time to celebrate! Welcome to our annual showcase of the top pharma development and manufacturing technologies to hit the market this year

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Let's Shake Things Up

As the pharmaceutical industry evolves, we need new ways to celebrate its achievements

As 2020 drew to a close, you may have committed to a private (or public) declaration to make the most of the year ahead. To savor the small moments. To seize new opportunities and – restrictions permitting – to do as much with your time as possible. I may have set my expectations for 2021 slightly too high, but fortunately, it's never really too late to do things differently…

Pharma has certainly proven this over the last two years. Though the industry is notorious for its risk-averse and hesitant approach to change, its reputation has skyrocketed because of its response to the COVID-19 pandemic. The industry was quickly able to prove that it was capable of information sharing on a grand scale and adopting new mindsets towards drug development during the most crucial moments of the global fight against the disease. A report published by market research company Ipsos MORI for the ABPI was one of many that provided evidence; their data revealed that 56 percent more of the British public have a more positive perception of the industry than in previous years – citing the sector's role in the development and distribution of COVID-19 interventions as reasons for their changed opinion (1).

To celebrate pharma's new attitude to drug development, manufacturing, and regulation The Medicine Maker has decided to do things a little differently too. Though we still want you to nominate the inspirational people driving innovation in our annual Power List, you'll also be able to celebrate the achievements of businesses at the heart of the medicine making endeavor in our newly launched Company of the Year Awards.

Prominent figures have helped influence the industry's trajectory over the last year, but we can't forget how, as a collective, professionals from businesses across the globe worked to make change happen on an international scale, sacrificing time and resources to protect our healthcare interests. Our new award will help give them the recognition they deserve.

Just like the Power List, the power is in your hands. You'll have the chance to vote for the best companies across six categories: Big Pharma, Biopharma Equipment, CDMO, API Supplier, Processing Equipment, and Biggest Talking Point.

It's simple to get involved. Check out the links below. And then join us for the celebration of the winners in April 2022!

Nominate for the Power List: tmm.txp.to/pl-2022

Vote for the Company of the Year Awards: tmm.txp.to/coya-intro

Maryam Mahdi
Deputy Editor

Reference

1. *Ipsos MORI, "Myths and Vaccines: Building pharma reputation in the face of misinformation." (2021). Available at: https://bit.ly/3Gl16Pg*

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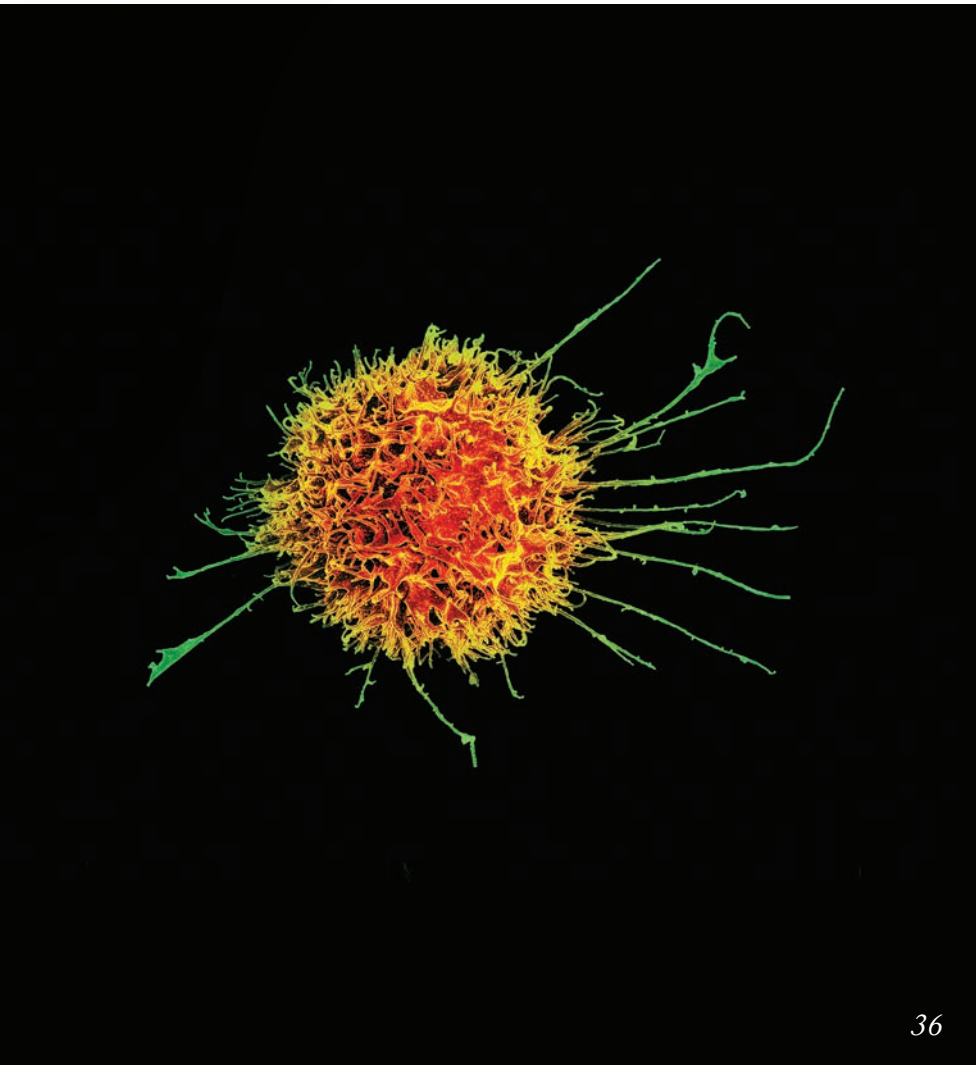

On The Cover

Celebrating the 2021 Innovation Awards

Upfront

In My View

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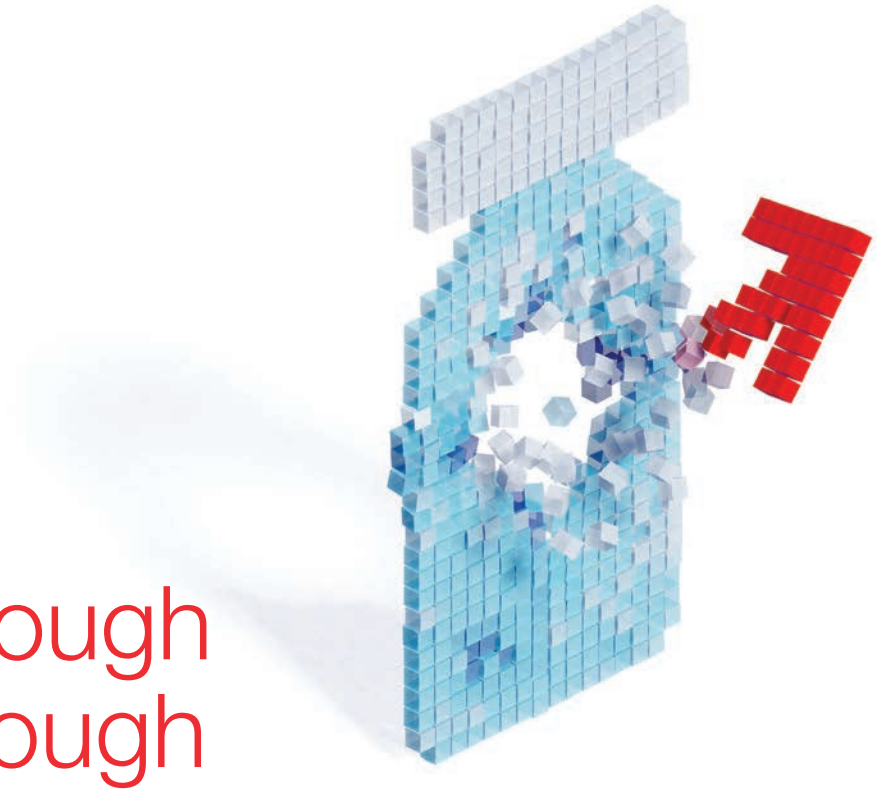

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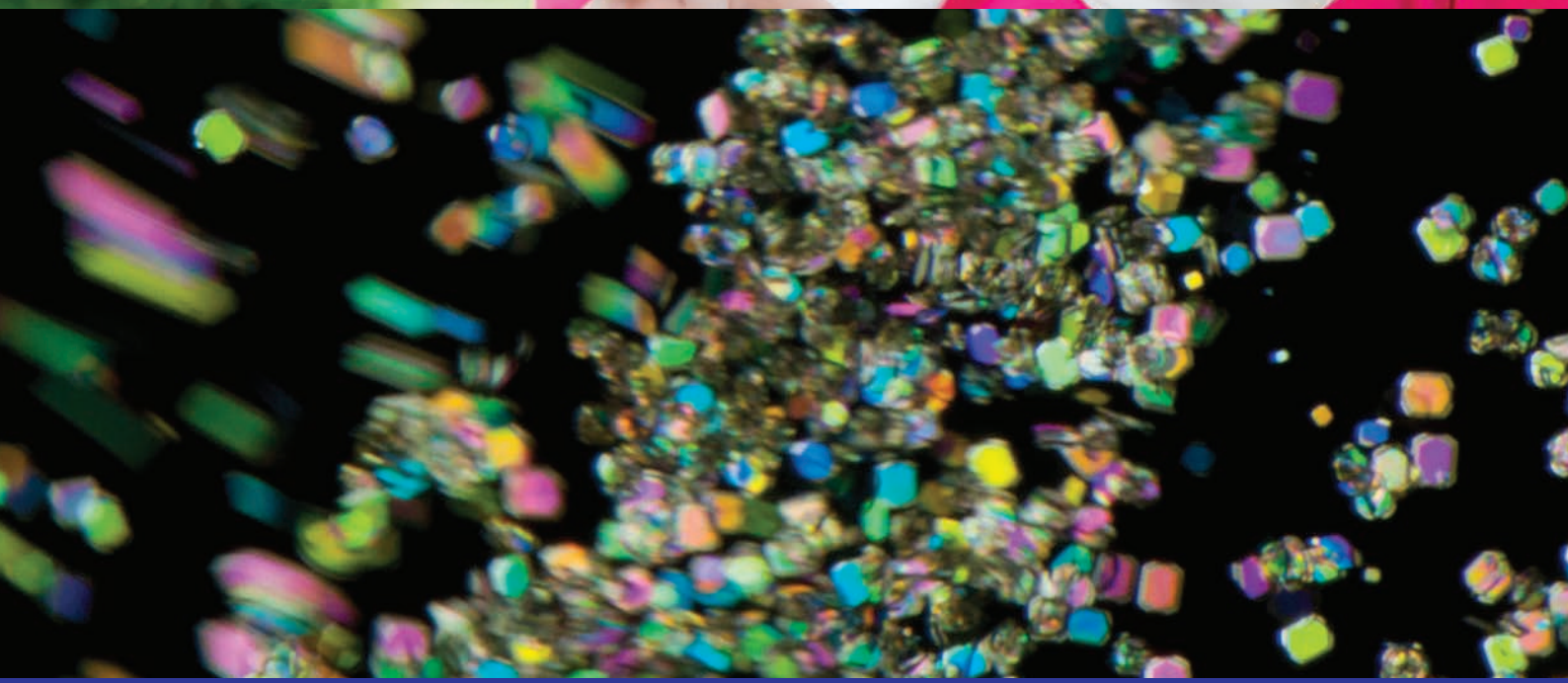

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the Medicine Maker

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Change of address info@themedicinemaker.com
Hayley Atiz, The Medicine Maker, Texere Publishing Limited, Booths Park 1, Chelford Road, Knutsford, Cheshire, WA16 8GS, UK

General enquiries
www.texerepublishing.com | info@themedicinemaker.com
+44 (0) 1565 745 200 | sales@texerepublishing.com

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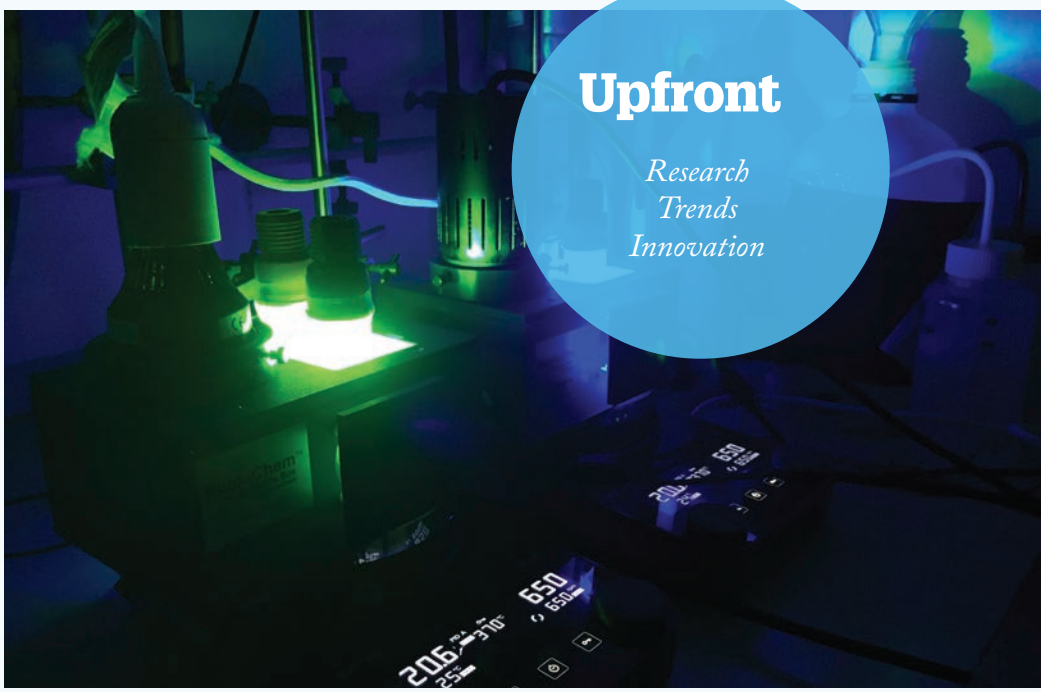

~~Green~~ Blue Light for Waste Reduction

Lower energy costs, fewer steps, less waste – a new photocatalyst-driven technique for drug production seems like a no-brainer

Chemistry researchers from the UK's University of Bath have developed a method for drug production that could help reduce energy consumption, chemical waste, and carbon emissions in the pharma industry (1).

The technique uses 420 nanometer blue light and a photocatalyst to facilitate chemical reactions that produce nitrogen-containing chemicals called primary amines, which are used in more than half of all pharmaceutical drugs. The blue light method requires less energy and fewer steps than traditional drug production, which is estimated to produce waste and drugs at a ratio of 100:1. Much of this waste material is then incinerated, contributing to CO2 emission figures that a recent study calculated to be higher than those of the automotive industry (2).

Lead scientist Alex Cresswell explains the new technique: "Once the photocatalyst has absorbed the light energy, it becomes reactive enough to tear away an electron from one of our reactants. This produces an entity called a "radical," – a molecule bearing an odd number of electrons. We harness the reactivity of that radical to achieve unusual reactions."

As a test, Cresswell's team used the blue light method to synthesize the multiple sclerosis drug Fingolimod, and were able to reduce the process from five to two steps. The drug is produced and sold by Novartis under the name Gilenya (with sales of US$3 billion in 2020).

The team is currently working alongside industry partners to further develop and commercialize the blue light technique. Cresswell is optimistic that medicinal chemists will adopt the method, but notes that scaling up presents technical challenges: "Light-mediated reactions are hard to scale up to the multi-kilogram or tonne scale, because the light doesn't penetrate very deeply into the reaction mixture. Flow chemistry offers the best solution to this – it would involve pumping the mixture through transparent tubing wrapped around a powerful light source. We've already shown that our reaction can be scaled up to decagrams in this way."

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1. *Journal of the American Chemical Society (2021). DOI: 10.1021/jacs.1c07401*
2. *Journal of Cleaner Production (2019). DOI: 10.1016/j.jclepro.2018.11.204*

INFOGRAPHIC

Nobody Stemmed Stem

Report lays bare the extent to which dubious stem cell businesses have proliferated across the USA

As of March 31, 2021 in the USA:

1,480 **businesses** operating

2,754 **clinics** engage in direct-to-consumer marketing of purported stem cell therapies

BUSINESS - IN BRIEF

Breakup at J&J, cybersecurity alarm bells, and a new manufacturing facility in Poland… What's new in pharma this month?

- Johnson and Johnson has announced it will split into two companies: one handling its consumer health products, and one handling pharma. The latter will complete its separation in 18 to 24 months. The move emulates other major pharma companies that have split off their consumer divisions to please shareholders.
- Following a rapid increase in ransomware attacks on the healthcare industry, a new study from ethical hacking firm Outpost24 has found a vast array of cybersecurity weaknesses in 85 percent of the top 20 pharma and healthcare applications.
- Nemera has begun construction of a new manufacturing facility in Poland. The site is to include 3400 m^2 clean room space for device assembly, and will house resources for the creation of new devices. The move follows a different species of Polish expansion in 2020, when Nemera bought Copernicus, a local injection device manufacturer.
- Zhejiang Huahai Pharmaceutical has overcome an FDA warning letter it received in 2018 regarding the discovery of a likely carcinogen in one of the company's products, which at the time dealt a major blow to trust in Chinese drug manufacturing. This removal of the FDA's warning comes significantly later than the lifting of European regulators' measures in 2019.

the Medicine Maker POWER LIST

'Tis the Season for… Awards

Show us what you're made of in The Medicine Maker Power List 2022 and the Company of the Year Awards 2022

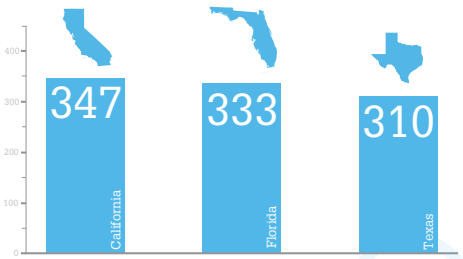
At The Medicine Maker, we don't worship power, but we do believe it's important to have people and technology to admire. Our annual Power List celebrates the former – and nominations are now open for the 2022 list. And our Innovation Awards – on page 24 – shine a light on the latter.

Submit your nominations at: *tmm.txp.to/pl-2022*

But drug development is not just about individual people – inspiring careers and groundbreaking new medicines cannot exist without the context that supports and creates them: companies. For 2022, we are launching the Company of the Year Awards to celebrate the best of the best across six categories. Check out the list and register your vote at: *tmm.txp.to/coya-intro*

The closing date for nominations for the Power List and voting for the Company of the Year Awards is March 17, 2022.

The three states with the largest concentrations of such clinics are:



Clinics in these three states comprise more than one-third of all in the country

Price range of treatments

Lowest price: **$1,200**

Highest price: **$28,000**

Average price: **$5,118**

Median price: **$4,000**

Source
Cell Stem Cell (2021). DOI: 10.1016/j.stem.2021.10.008

Credit: Katherine Hanlon / Unsplash.com

Cupping Combats COVID-19?

How a technique with roots in alternative medicine practice improves vaccine delivery

Though the origins of cupping are unclear – and, for some, controversial – a paper published by researchers at Rutgers University, New Jersey, USA, draws comparison between the ancient technique and a method for increasing uptake of DNA-based medicines, including vaccines for COVID-19 to patients (1).

In the traditional practice of cupping, one or several heated glass cups are placed on the skin, creating negative pressure and increasing blood flow. (Adherents of traditional Chinese medicine believe this facilitates the flow of "qi" – the term assigned to vital energy that is fundamental to the discipline but unproven by scientific inquiry.)

In the study at Rutgers, a smaller, handheld device operating on a similar mechanical principle was used on rats. Following a conventional vaccine injection, the 6 ml orifice was applied at the point of injection for 30 seconds, inflicting no pain and leaving no mark. It is thought that the force of suction against the skin then increases the uptake of vaccine particles by the dermis cells; certainly, when used on the Rutgers rats, the suction devices multiplied the subsequent immune response by roughly 100 times.

Study leader, Hao Lin, who has tried the method on himself (2), highlighted suction-based in vivo cutaneous DNA transfection as a highly-scalable platform for both laboratory and clinical applications for nucleic-acid-based therapeutics and vaccines. He also noted that minimal training was necessary for practitioners of the technique.

"We have demonstrated an alternative, safe, and effective transfection platform that yields high levels of transgene expression," Lin said in a statement (3). "Because of the inherent advantages of DNA, not least of which is avoiding cold-chain requirements of other vaccines, this technology facilitates vaccination programs in remote regions of the world where resources are limited."

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1. *EO Lallow et al., "Novel suction-based in vivo cutaneous DNA transfection platform", ScienceAdvances (2021). DOI: 10.1126/sciadv.abj0611*
2. *Rutgers University, "Combining ancient and modern medicine, scientists use cupping to deliver COVID-19 vaccine in lab tests" EurekaAlert! (2021). Available at: https://bit.ly/anc-mod-eur*
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Gilead Goes Ferreting

A partnership between Gilead Sciences and Georgia State University has tested a new oral antiviral for COVID-19

A study carried out on ferrets at Georgia State University's Center for Translational Antiviral Research, funded by Gilead Sciences and the National Institutes of Health, has tested the potential of a new oral variant of Gilead's remdesivir, the only as-yet approved antiviral treatment for COVID-19 (1). The approved form of remdesivir is currently available only via intravenous delivery.

In glad news for the participating mustelids, the study found that the drug was effective. If approved, the oral variant would improve access to remdesivir and allow patients to begin receiving doses outside of hospital – an option intravenous remdesivir does not offer. The rapid chemical conversion conferred by the pill delivers the same bioactive to patients, faster. In a statement, first author Robert Cox said, "Orally available antivirals will provide health care workers with a powerful weapon to combat the highly infectious SARS-CoV-2 variants that are active in the community now (2)."

The ferrets were not available for comment.

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2. *Georgia State University (2021). Available at: https://bit.ly/3oxPSjt*

IMAGE OF THE MONTH

Ironclad Innovation

University of Rochester PhD student Maria Camila Aguilera in the lab. She is co-lead author of a paper published in Science on a new method for coupling iron to other compounds, which could bring down costs in medicine manufacturing.

Credit: The University of Rochester <https://bit.ly/PhD-Maria/>

Would you like your photo featured in Image of the Month?
Send it to maryam.mahdi@texerepublishing.com

QUOTE of the month

"The top pharma companies in 2030 will be those that can ... ruthlessly (create) a path of prioritizing investments in promising countries and disease areas."

Aurelio Arias, Engagement Manager, Thought Leadership, IQVIA on the findings of the CPhI Annual Report https://bit.ly/ruth-less

Corporate Medicine, Government X-Rays

Pfizer's trial of a new medicine for COVID-19, produced with support from the US Department of Energy, could improve access to treatment

In a study of over 1200 participants recently diagnosed with COVID-19, researchers found that Paxlovid – a new oral antiviral treatment from Pfizer – reduced the risk of hospitalization or death in high-risk adults by 89 percent (1). The FDA and independent monitors have since recommended Pfizer move to the next stage of regulatory application. However, the FDA is not the only branch of the US government the drug has come into contact with. Paxlovid was planned, designed, and created using the ultrabright X-rays of the Advanced Photon Source (APS), a US Department of Energy (DOE) facility at the DOE's Argonne National Laboratory (2).

Should Paxlovid achieve authorization, it could be prescribed as an accessible, at-home treatment with the potential to combat multiple kinds of coronavirus. However, as wealthy countries begin placing large orders for the drug, some observers are concerned that the result will be reduced or nonexistent access to Paxlovid in the developing world (3).

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1. *DR Owen, Science (2021). DOI: 10.1126/science.abl4784*
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The Digital Future of Formulation

Next-gen drugs can be slow and costly to develop. To help medicines reach patients faster, businesses should consider how digital tools can help solve formulation challenges.

By Ferdinand-Paul Brandl

Whether producing generics or innovative pharmaceutical products, all formulators face a unique dilemma. Drug development is, by its very nature, a trial and error process, which results in slow operations – but developers are always under pressure to produce drugs quickly and cost-efficiently. Though high-quality formulations are the result of many experiments, companies (and their formulators) must juggle the various aspects of lab and manufacturing processes with their business needs for faster, cheaper R&D. But finding a happy medium isn't easy.

And there's another key challenge too: the small pool of talent companies have to draw on. Skilled formulators are a rare commodity. Although well-established businesses may have in-house expertise, smaller companies and startups can find it difficult to attract and retain the professional talent necessary for formulation development and manufacture. Businesses need to think about how they can tackle these hurdles.

Digital platforms are proving that they can be useful tools in helping formulators select the right active ingredients and excipients for drug products. Though they cannot replace the skill set of trained formulators, they can help companies make better decisions in a time-efficient, resource-effective manner – and help formulators push drugs through the development cycle more quickly.

At BASF Pharma Solutions, we have one purpose: inspiring medicines for better lives. We understand that not all companies are set up for developing robust drug formulations; it's our duty to help them develop superior quality drugs in shorter time frames. ZoomLab™, our virtual formulation assistant, provides companies with a variety of interactive tools to solve formulation challenges. With free access to excipient and active ingredient data, companies need not worry about characterizing molecules in the lab; they can find the excipients most likely to work with their active ingredients with a few clicks – saving time and money.

Listening and responding

Digital tools for formulation are still a relatively new concept. Though they have much to offer formulators, some experts are still sceptical about their use. We have found that customers in emerging markets like Africa, Turkey, and Russia tend to be more receptive towards new technologies and are eager to explore the benefits, while those in more established pharma markets, like Europe and North America, are typically more apprehensive. Their concerns often pertain to confidentiality – an understandable reservation. To access excipient and active ingredient data, formulators must share details about themselves and their projects, which could, theoretically, make them vulnerable. Companies have a right to and want to know what happens to their data when using digital systems. But, in our experience, once they have seen what digital tools can offer (and how their data can be protected), they show the same levels of openness as other international businesses.

We value data protection and are carefully listening to our customers to ensure that our tools meet their needs. We've also simplified the ZoomLab™ interface so that formulators can easily find answers to their questions. Our digital technical service team is also there to address concerns around the clock.

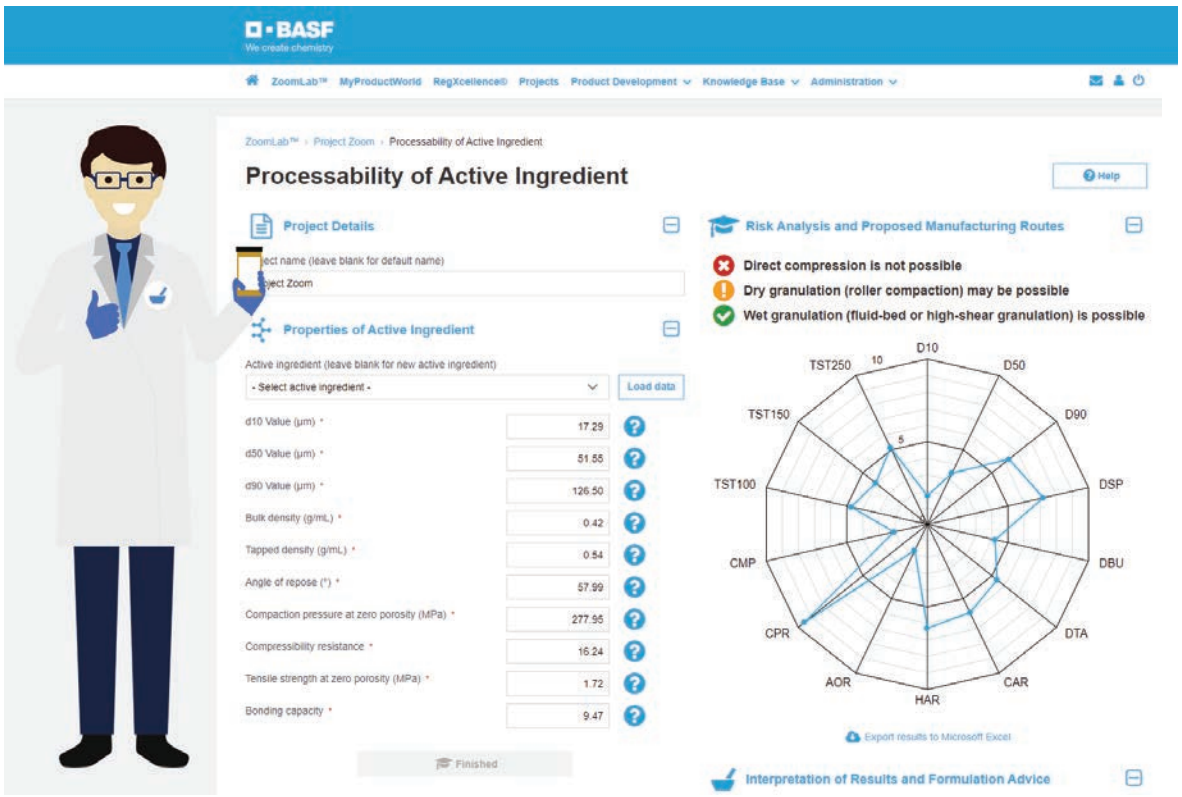
Continuous improvement

For developers to have smoother formulation journeys, the digital platforms they rely on must be easy to use. Our databases have been designed to guide formulators through every aspect of their drug development process – quickly directing them to the right information for their needs. As an educational tool, it can also help fill in knowledge gaps for companies with less experience in the formulation process.

"For developers to have smoother formulation journeys, the digital platforms they rely on must be easy to use."

Most importantly, we understand that as the pharmaceutical industry continues to make advances, ZoomLab™ will have to evolve to keep pace with change. In 2019, when we launched our platform, we focused solely on direct compression data. But our customers' needs are far-reaching. Since then, we have developed tools for film coating and poorly soluble drugs, and we're now exploring how the platform can be expanded to provide support for the development of topical formulations, such as creams and ointments, which typically require extensive expertise to produce under conventional circumstances. This evolution will certainly help businesses who often have challenges in hiring and retaining experienced formulation professionals. The guidance they would normally receive from such individuals can be supplemented through our platform.

Although these additional tools and resources have improved our customers' formulation journeys, we always aim to



expand our offering of service – incorporating customer feedback into our platform wherever possible. Therefore, we'll also be introducing a chatbot that can assist our customers with troubleshooting. The AI optimized system will direct them to the information and tools related to their queries – allowing them to address problems as soon as they are encountered. For example, if a developer has an issue during tableting they can instantly find support from our chatbot.

To make the most of the system, we realize that training will be necessary, so our new learning center will offer users access to case studies and tutorials in both video and PDF formats – helping to foster a positive learning environment within our community.

The full package

Though formulation is a key part of any drug's success story, we recognize that companies need guidance and support at all stages of development. Alongside ZoomLab™, our other virtual assistants, RegXcellence® and MyProductWorld can help developers as they push candidates from the bench to the bedside.

At the start of their R&D journeys, companies can access MyProductWorld and browse through our product catalog for pharma-grade samples of active ingredients and excipients. As companies draw closer to commercialization, they can turn to RegXcellence®, which can help cut down on quality assurance and regulatory paperwork. The platform allows users to download statements and audit information, and access advice from global regulatory experts for faster approvals. All of our virtual assistants are linked so when customers are ready to progress their products through development, they can access the right information for their next step quickly.

Can digital tools replace the formulator? This is absolutely not the intention! Rather, our tools are there to iron out kinks in development. And we challenge those companies who are still hesitant about the use of digital tools to give them a try! We're open to your ideas and are ready to listen to your concerns; the dynamic nature of the platform means that we can quickly integrate them.

As an excipient and active ingredient provider with one of the broadest portfolios on the market, we've always been open to learning about the needs of our customers. We understand that listening to and responding to your challenges helps ensure that best-in-class medicines find their way to patients. So we're always ready to talk.

Learn more about our Virtual Pharma Assistants here: info-mypharma.basf.com

Ferdinand-Paul Brandl is Head of Laboratory at BASF

Reduce, Refine... Replace?

How to use organ-on-a-chip technologies to make drug discovery more efficient

By Tomasz Kostrzewski, Director of Biology, CN Bio, UK

Why do so many drugs entering clinical trials fail? Too often, existing test models do not accurately predict human outcomes.

The rapid response to the COVID-19 pandemic has shown that safe and effective therapeutics can be developed and delivered to market efficiently by challenging – and improving – existing processes. We should now seriously examine other ways to improve existing drug discovery processes. Research suggests organizations could slash R&D costs by almost one third through the introduction of organ-on-a-chip (OOC) technology – alternatively known as microphysiological systems (MPS) – into their workflows, thus addressing the problem of human-relevance in traditional 2D cell cultures and animal models.

Adoption of MPS has risen over the last decade, but there are still misconceptions about their effective use and potential value. MPS are often framed as an eventual replacement for animal studies and, whilst there's a way to go before this becomes a reality, recently the European Parliament resoundingly passed a resolution to phase out animal testing in research, regulatory testing and education, which will put more focus on the use of new alternative methods (NAMS) such as OOC. Others are concerned about the acceptability of MPS data in Investigational New Drug (IND) submissions. In the meantime, MPS are being used to drive major improvements in the accuracy and efficiency of drug discovery. Researchers should understand that MPSs represent a concrete approach to reduce, refine, and complement existing tests, right now – rather than a futuristic proposal to sweep away the status quo.

Using microfluidics, MPS devices generate in vitro 3D models that faithfully recapitulate the in vivo phenotype and function of equivalent human (or animal) organ counterparts. They differ from static culture approaches in their use of fluidic flow to mimic blood circulation. In doing so, these systems facilitate microtissue development, improve physiological relevance, promote culture longevity, and facilitate inter-organ communication. Most MPS technologies are high content rather than high throughput – they compare tens or hundreds of molecules against a known target or pathway to deliver deep mechanistic insights.

At the beginning of the drug discovery process, MPS can be used to complement the reproduction and corroboration of target-specific data from patient-derived clinical samples, test animals, or other preclinical tools. MPS simulate an in vitro state that expresses the same targets as a human disease, helping to identify the role and relevance of these targets. Critically, MPS cultures are more physiologically relevant and cheaper than animal models. These same predictive models can also be carried through to lead optimization to complement and improve animal (in vivo) efficacy studies. They could unlock options to explore many more drug concentrations in vitro, helping to refine the effective therapeutic dose range ahead of animal studies. Through cross-referencing the results, potential cross-species issues would be flagged early. In my view, MPS are especially beneficial for testing the safety and efficacy of new human-specific modalities where differences in genetics, metabolism, or immunological response render animal models unsuitable.

MPS are better predictors of human-specific adverse effects than the standard range of pre-clinical safety toxicity tests. Standard animal and in vitro models have proved poor predictors of drug-induced liver injury (DILI) – a major contributor to late-stage drug failures and withdrawal from the market – due to their non-human metabolic profiles. Liver MPS provide researchers with the means to uncover potential adverse metabolite-driven effects early, reducing the risk and cost of late-stage failures. Additionally, disease modeling with MPS can identify increased DILI susceptibilities for classes of patients with underlying metabolic conditions, such as the hugely prevalent condition of non-alcoholic fatty liver disease, reducing the risk that therapeutics exacerbate pre-existing conditions.

Above and beyond the benefits of single-organ models, researchers can now also link multiple-organ MPS systems

together to represent the interaction and communication of complex human systems. At present only animal studies offer such insights, but interspecies differences can lead to costly, unforeseen late-stage problems. One clear multi-organ application is for human ADME profiling. By connecting a liver MPS to another "route of entry" organ (for example, gut or lung) to monitor drug transit through an interconnected system, MPS can provide researchers with a human in vitro alternative to animal or in silico first-pass metabolism studies for improved bioavailability determination. To increase the accuracy and precision of data translation, in vitro to in vivo clinical predictions can be extrapolated using physiologically based pharmacokinetics (PBPK) mathematical models.

By incorporating MPS into drug discovery and development at pivotal and strategic stages, we can cross-validate or otherwise supplement currently available datasets. Indeed, in combination with existing methodologies, MPS can highlight unexpected surprises before the clinic. For me, MPS represent an essential but complementary tool in the preparation and evaluation of IND data packages.

As these increasingly advanced in vitro models continue to prove their worth and take on new roles, we anticipate that there to be a natural "survival of the fittest" evolution. Unless parliamentary pressure accelerates this process, MPS will not suddenly replace or eliminate traditional approaches, but in the meantime, its complimentary use will provide a path to more insightful and efficient drug discovery.

Reference

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Please, Sir, May I Have Some Samples?

Biotech companies need good patient samples, but hospitals are not always obliging

By Robert Hewitt, Founder, Biosample Hub, Glanrhyd, UK

Biotech companies worldwide struggle to access high-quality patient samples to support their research and development. The root of the problem? The simple fact that patient samples most often originate in a healthcare setting in the public sector – but biotechnology companies are in the private sector and therefore have reduced access.

The easiest way for most biotech companies to obtain samples is to get them from a commercial broker. These companies are solely focused on providing clinical samples for industry and, naturally, they are driven by the need to make a profit. Scientifically speaking, the main disadvantage of using a broker is that sample provenance may be lacking (brokers tend not to reveal their sources for business reasons) and there may be uncertainty about the samples' quality and the reliability of the resulting research.

So what can be done to provide industry – and particularly small biotech companies – with the reliable, high-quality samples they need?

Best practice for any researcher is to obtain biosamples directly from the source; that is, from the hospital biobank that collected the sample from the patient. To encourage this, we need to make it easier for biotechs and hospital biobanks to find each other. Biotechs can search a number of directories to find suitable partners, but this is often a difficult approach. Many of the biobanks listed may not be open to working with industry or may give companies a low priority, leading to disappointing false leads.

In my view, Biosample Hub could be a potential solution. Biosample Hub is an international online platform dedicated to bringing biotechs and academic/hospital biobanks together, with use restricted to these two groups. It includes a directory of biobank and biotech members, a directory of sample requests, and social networking features. The only reason for biobanks to be on the platform is to supply industry, so the problem of false leads is minimized. One other key aspect of the platform is that it is not-for-profit, which overcomes the ethical concerns of many biobanks.

Another solution is to make it more attractive for hospital biobanks to work with industry. In other words, there need to be more and bigger incentives. The problem is that, in many hospital biobanks, local academic researchers get top priority and other researchers get second priority, leaving industry at the back of the queue. This is natural, because these biobanks are established as institutional initiatives, with the purpose of serving their own institution. The focus of academic biobanks is very much on research productivity as measured by publication impact and, unfortunately, industry, for reasons of intellectual property, faces restrictions about how much work it can publish and when.

The incentive of funding should encourage hospital biobanks to work with industry, because biobanks need funding and

often operate on shoestring budgets. One approach is for biobanks to charge industry a cost-recovery fee for samples, and also to charge fees for additional sample processing services, such as cutting sections or extracting DNA. This approach seems to be especially well understood by French biobanks, who use the term "valorization" for the process of adding value to their samples. Almost half of the biobanks that have joined Biosample Hub are French and most offer additional sample processing services.

Another approach is to make external grant funding of biobanks conditional on service to industry. This could be aided by mandating that funded biobanks make their sample access policies public, requiring annual reports on sample distribution, and perhaps even having industry representatives on sample access committees. Patient representatives are well accepted, so why not industry representatives?

New regulations could have a major impact on how biotech companies source their clinical samples in future. For example, the new European regulation governing manufacture of in vitro diagnostic devices (IVDs) comes into force on May 26, 2022; to demonstrate conformity, makers of IVDs must show that the biospecimens used to validate their devices have undergone acceptable preanalytic processing. This will require the sourcing of samples from biobanks certified to meet specific quality management standards. As a result, diagnostics companies will need to obtain samples from known sources that provide full provenance information.

This need will put pressure on commercial brokers to change their business practices and reveal the source of their samples. One way in which brokers may mitigate this is by using binding contracts with both the provider and the requester of samples to prevent them from interacting independently of the broker. Of course, not all companies or biobanks will be comfortable with such restrictions…

There are technological solutions, however, that can be used to ensure the reliability of samples' provenance information. Blockchain is one example that allows tracking of biospecimen transfers from the patient donor to the researcher in a secure, transparent, and ethical manner, with all transactions documented in an incorruptible shared digital ledger.

Right now, biotech companies often find access blocked for a variety of possibly short-sighted reasons. Ultimately, to speed up development of new therapies, diagnostics, and vaccines, biotech companies need access to top-quality patient samples – and we need to find solutions that facilitate this.

A New Focus for Cancer Therapeutics

As oncolytic virotherapy comes into industry focus, a range of challenges including variable target virus selection, clinical patient access, and manufacturability require industry progress. Here, I share insights and crucial considerations to successful marketization.

By Joe Sinclair, Vice President, Business Development and Corporate Strategy, Vibalogics

There were 17 million new cancer cases and 9.5 million cancer deaths worldwide in 2018 according to estimates from the International Agency for Research on Cancer (IARC). The global burden is expected to grow to 27.5 million new cancer cases and 16.3 million cancer deaths within the next two decades in correlation with the growth and aging of the population (1). The total cost of treatments in the US alone now sits at US$150 billion per year (2).

Historical first-line cancer treatment options have included surgery, chemotherapy, radiotherapy, and hormone therapy – which suffer from critical drawbacks including strong side effects, invasive procedures, and eventual waning efficacy and tumour resistance to treatment.

Recently, industry and patients are focusing on the therapeutic potential of treating cancer with immuno- and virotherapies, including immune checkpoint inhibitors, gene-mediated cell therapies, and therapeutic vaccines, among other approaches. Attention is rapidly converging on a particular modality, as oncolytic viruses (OVs) have shown strong potential to complement existing therapeutic options, either as a monotherapy or in combination with other immunotherapies, traditional treatment options, or even other OVs. OVs can be tailored to attack any cancer cell without targeting healthy tissue, while providing impressive efficacy (3, 4) and a strong safety profile with limited side effects (5). The further engineering and augmenting of OVs can amplify the activity and response to these treatments, including oncolysis, and the critical release of tumour antigens to stimulate an innate immune response from the body directed at the tumour.

With all of this in mind, it is no surprise that there is substantial energy

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in the market right now, with around 160 emerging biotechnology companies exploring this new modality and area of research. Thus far limited OV therapies have been commercially approved, with only one marketed approval by the US FDA (Amgen's talimogene laherparepvec (T-VEC)) and one recent approval by Japan's MHLW (Daiichi Sankyo's teserpaturev (Delytact)). However, many more are in early-to-late clinical development.

There are, however, several limiting factors currently preventing OVs from achieving their full potential with broader clinical progress and additional market commercialization. To open the door for widespread commercialization and use of OVs, the following four challenges must be resolved:

- Virus variability and multiplicity: a single OV capable of targeting a broad range of cancers in most patients has yet to be found. Each cancer has a specific genetic profile, which means that presently no virus or vector has been shown to be universally effective. In addition, targeting the mass of tumour tissue is very different from targeting the totality of individual cancer cells.
- Heterogeneous immune responses: Some patients have immunity to certain virus platforms commonly used to create OVs. This can undermine the strength of the immune response elicited or even dampen the ability of the OV to achieve oncolysis (6, 7).
- Access to trial participants: Sourcing patient numbers sufficient for studies to ensure adequate representation of all possible patients for a particular OV candidate is a major challenge, especially as patient access is generally limited to those who are refractory or relapsed from first line and traditional treatment options.
- Adequate manufacturing capability: Very few companies have capacity or specialist equipment tailored to the broad requirements of this field. Requirements include cleanroom grades, technologies supporting avian production systems (specific pathogen-free eggs, chicken embryo fibroblasts), continuous cell substrates, and applicable adherent and suspension production platforms. In short, the still advancing industry suffers from limited options of viable early and late-phase partners, incurring supply challenges during development and manufacturing production.

But the recent approvals have shown that there is a viable pathway to commercialization. To help maximize the chances of successful marketization, I can offer four key points to keep in mind.

First, plan your development roadmap before embarking on the project. Rigorous development is critical in linking product and process, and the processes required for OVs differ greatly from the needs of other therapies. Planning a given project's development process and downstream milestone targets from the outset can help ensure that you have the necessary time and resources to devise your strategy, and support discovery, development, manufacture, and testing requirements that align to a timely regulatory filing. Proper planning in advance can minimize risks along the way.

Second, choose the right virus candidate for your needs. Each virus platform will have different strengths and weaknesses when it comes to its ability to be genetically modified, the cells it preferentially infects, and how it reproduces once it has infected the target cell. Bearing this in mind, it is crucial to select the candidate with the optimal profile for the cancer you intend to target. Failure to fully consider the unique features of your virus candidate at the beginning of the project could lead to issues further down the line.

Third, you need access to appropriate cell lines. A range of cell lines have already been evaluated for OV development. Nevertheless, for each cell line, you must consider all compatibility requirements. These depend on the type of OV being developed, susceptibility to infection of the host cell line, viral propagation, and overall productivity of the production system, as well as whether the cell line is adherent, a suspension, or suspension adapted. It is also wise to consider upfront the licensure requirements/agreements for the free-and-clear use of cell lines in a commercial setting, especially when translating processes from academic research.

Finally, you must develop an appropriate testing program. Live viruses are highly complex. This complexity is reflected in the need for robust analytical assays to characterize and release the OV. Experienced analytical specialists can help ensure GMP release of raw materials, virus and cell banks, as well as drug substance and product for appropriate identity, purity, potency, titer, residuals, and safety requirements. Bioanalytical assays and post-treatment patient monitoring should also be incorporated into any OV analytical program, where applicable.

Complex, challenging, yet rewarding research in the OV field is well underway, and a rapidly increasing number of exciting discoveries remain in progress through preclinical and clinical trials. The specialist expertise and dedicated equipment required can be difficult for OV developers to acquire, implement, and operate in-house, particularly as an business with limited capital.

However, by remaining aware of the considerations outlined above – and by seeking the support of expert CDMOs and virotherapy partners where necessary – it is possible to maximize the likelihood of a commercially and economically viable product. OVs are transformational therapies, and soon – with focus and determination – they will have their chance to change patients' lives.

References available in the online version of this article

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Keep Calm and Use Pools

How pooled cell populations helped accelerate COVID-19 vaccine development – and what that means for the therapeutics of the future

By Trent Munro, Senior Group Leader at the Australian Institute for Bioengineering and Nanotechnology at the University of Queensland, and Director of the NCRIS funded National Biologics Facility, Australia

The COVID-19 pandemic gave a huge boost to the vaccine field, with scientists throwing every technology they had into the arena to help find a vaccine candidate as quickly as possible. My group contributed to the fight by putting our "molecular clamp" technology platform forward.

The surface proteins on many viruses, including SARS-CoV-2, are highly complex molecules that can be unstable when made in isolation. One challenge is the fact that these molecules exist in two main conformations, depending on pre- or post-target binding (pre-fusion conformation or post-fusion conformation). When viral surface molecules are made in isolation, they enter into an energetically favourable form: the post-fusion form, which obscures important epitopes that may be important for a vaccine to ensure right protective immune response. To overcome this challenge, you can synthesize the molecule in a way that "locks" it into the pre-fusion form, which is most recognized by the immune system and more able to generate the right type of immune response.

For SARS-CoV-2, it is possible to design a "lock and key" mechanism by placing new amino acid substitutions into the molecule. The approach builds on previous work with closely related viral proteins from MERS and SARS, and is used for many COVID-19 vaccines; however, it is also very specific to this type of spike protein and is not a broadly applicable technology. Moreover, it requires a significant structural understanding of the molecule.

At the University of Queensland, Australia, we've been working on a different approach to vaccines that we hope could become a platform technology applicable to a range of different viral proteins; notably, we were working on this long before COVID-19. In short, we genetically fuse the trimer forming domain to viral surface proteins, which locks the molecule into its pre-fusion conformation. We refer to this as a molecular clamp; after all, it essentially clamps the trimer in place. We've shown that the approach works for a range of different viral proteins, including Ebola, influenza, RSV, and MERS. We have also managed to attract from The Coalition for Epidemic Preparedness Innovations (CEPI).

In early 2020, we were preparing for a clinical trial of an influenza candidate, which would be the first human proof-of-concept for our molecular clamp approach. We used CHO expression technology to make the vaccine, which worked, but based on my experience from industry, I knew there were better systems out there that could drive high levels of expression. I was fortunate to be aware of the Lonza GS expression system and the power of genetically engineered GS knockout CHO cells.

When we pivoted to COVID-19, we had to think about technologies that would allow us to produce enough doses of the vaccine (if successful) to vaccinate millions of people. I reached out to Lonza because I felt their GS XCEED expression system was the most powerful and easily accessible CHO expression platform.

> *"With pools, you simply need the characterization and comparability studies to demonstrate to regulators that the material you are generating is suitable for purpose."*

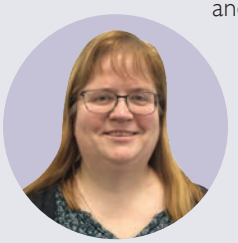
It starts with understanding

Today, we understand how different expression systems work, the importance of critical quality attributes for the molecules we make, and how to control them. We also have access to different types of bioprocess controls, as well as chemically defined media. However, the regulations were set many years ago and have not adapted to new technologies. We also need to consider that there have been examples where companies have made poor decisions during cell line process development, so regulators are keen to ensure no shortcuts are taken that might impact product safety or efficacy.

When making a cell line to produce a therapeutic protein or vaccine, there is a perception that cloning from a single cell creates a higher degree of overall stability, and creates a robust cell line for manufacturing.

What Is a Pool?

By Alison Porter, Head of Expression System Sciences at Lonza



Simply put, a pool is a mixed population of stably transfected cells.

During transient transfection, the recombinant DNA does not integrate into the host genome and therefore does not replicate, so it will eventually be lost as cells divide. On the other hand, stable transfection begins transiently, but is followed by an infrequent but critical event where recombinant DNA will integrate into the host genome, meaning the product gene can be replicated. Descendants of those transfected cells will also express the product.

Transient transfection is typically used during the drug discovery and screening stage when researchers are assessing multiple variants and need relatively small amounts of material fast. Stable transfections are then used when creating a suitable cell line for manufacturing. This is because integration is important if long-term gene expression and large amounts of material are required. Typically, stable transfection will also require a cloning step to meet regulatory requirements.

A pool can be described as a halfway house between a transient transfection and a clonal cell line from a stable transfection – in fact, a pool is a typical starting point from which to clone. A pool takes longer to create and obtain material from than a transient transfection, but less time than a clonal cell line. However, although a pool can generate more material than a transient cell line, it can generate less than a clonal cell line (but this difference is reducing as the industry becomes more familiar with pools and as technologies and techniques advance).

At Lonza, we first started investigating and using pools in the early 2000s. We initially used pools to supply some customers with material very early on in development, but we quickly found that pools became a main part of the cell line construction workflow because we found that they could help to significantly reduce timelines. Today, the use of pools has increased substantially; they are frequently used to select the best starting point to clone from, to get a head start on upstream process development, and to develop material to feed other project stages.

Over the last 10 years, there have been many interesting conversations about the use of pools in the industry, including whether it's possible to use material generated from pools for toxicology studies or even for phase I trials. But the real accelerant that has pushed pools to the front and centre is the COVID-19 pandemic – where there was a need for significant reductions in timelines. I expect us to see the use of pools being pushed even further in the future, particularly for developing antibodies, where the industry has so much experience already.

Lonza's GS GENE EXPRESSION SYSTEM is well established and can help create transient material, clonal cell lines, and pools – and we provide the protocols as well as actual physical materials. We use the system ourselves when creating cell lines and developing processes for customers, but we also out-license the same system for customers to use in their own laboratories.

Trent Munro and I have known one another for some time; he was aware of our technologies and contacted us to request access to the GS SYSTEM in his lab – in short, that's how our fantastic collaboration began!

Regulators need to ensure that manufacturers will make a safe, effective product the same way with each manufacturing run, and many would argue that using a clonally-derived cell line is the golden path.

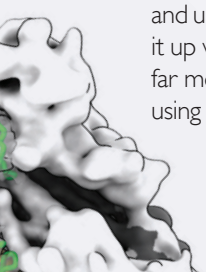
I would argue that this is not necessarily the case. The most important element is knowledge; you must understand your expression system and how your expression system matches your bioprocess, and you must understand how to isolate a population of cells to create a robust manufacturing platform. This connectivity and understanding – and being able to back it up with an appropriate data package – is far more important than whether you are using a clone, a pool, or a different origin for the manufacturing process. With pools, you simply need the characterization and comparability studies to demonstrate to regulators that the material you are generating is suitable for purpose. Ultimately, regulators are data driven and will make decisions based on the quality and robustness of your data package.

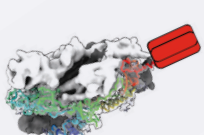
Harnessing the full potential of pools

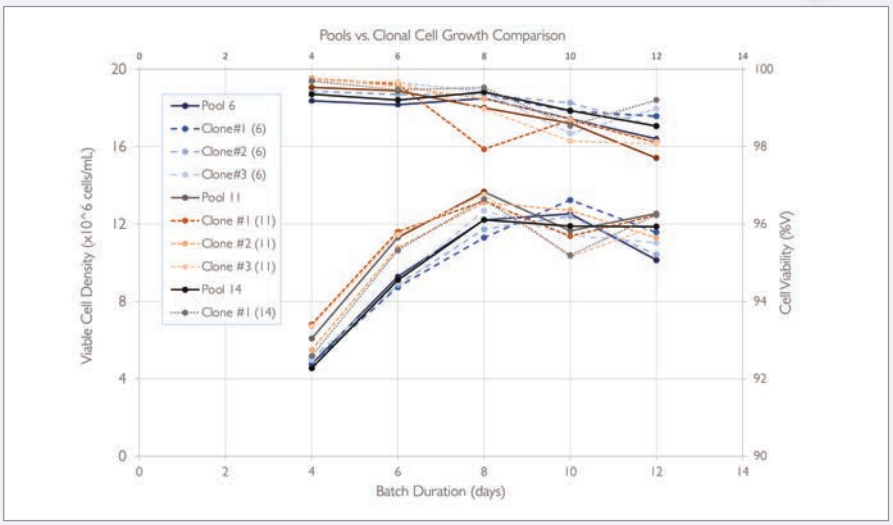
I believe that the combination of stable pools and well-characterized processes is a powerful method to accelerate early development. And new technologies, such as the Lonza GS platform, are amenable to the creation of stable pools that are suitable for manufacturing. These pools can potentially be used for early-stage material, early clinical, or even for commercial manufacturing, depending on the data for the individual program and molecule.

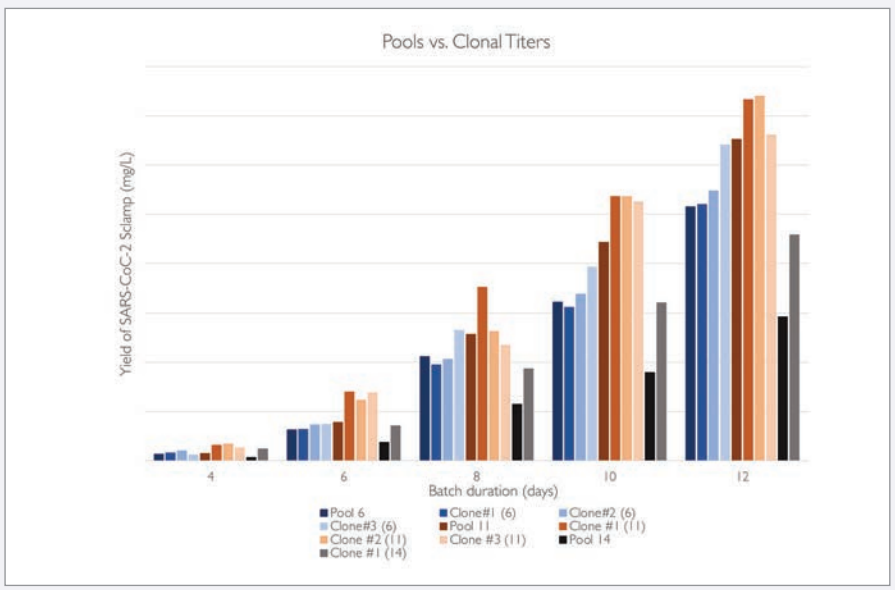
In our vaccine program, we had no time to use clones. COVID-19 forced us to move fast. We worked with partners to quickly define our critical quality attributes and set the bar for comparability – and that gave us the confidence to use a pool-based expression system.

We demonstrated biological proof of concept by looking at animal studies in mice, hamsters, rabbits, and ferrets – at the time we didn't know what would be the best animal challenge model for COVID-19. It was critical that we









Abridge fed batch culture expressing SARS-CoC-2 Sclamp (~600kDa) in shake flasks using the Lonza GS XCEED system with v8.10 processes. Solid lines represents pools, dotted lines are the clonal cell lines, number in the bracket for clonal cell line shows which pool they were derived from. Cell growth and titers produced by pools is comparable to those of the clonal cell lines.

generated high quality material to go into those studies and for our preclinical GLP toxicology studies. The only way we could generate this material fast enough was to use pool-derived material. That said, we did also produce some clone material – and it was indistinguishable from what we produced from pools.

We were fortunate to be able to work on our program at different locations in Australia and run parallel clinical lots. The Lonza production process worked well and we tech transferred to a larger biotech company – CSL – which was able to transition to commercial, clonally-derived production in just a few months. This speaks to how well the CMC process was set and how well the pool process worked. The other piece of the puzzle was the technical support from the Lonza team. This made for a truly seamless tech transfer experience from construct generation, through to pool creation, and then upstream process optimization. Their deep understanding of the system allowed for first time success of our clinical lot. Despite Lonza being busy with other manufacturing projects they were always responded quickly to any queries we had and were keen to help us as much as they could.

"It doesn't matter if materials are generated from a pool or a clone – as long as they are characterized accurately. I believe that pools of genetic material could become a regular tool for speeding up the development process."

Reviewing the results

Our program went through phase I and delivered good immunology data in terms of the level of immune response. But we hit an unusual snag. In our molecular clamp approach, the trimerization domain contained two peptides derived from

the GP41 HIV protein – and the GP41 molecule is used in a number of screening tests for HIV. Participants who received the vaccine not only generated an immune response against the COVID-19 spike protein but also to small elements derived from GP41, which cross-reacted with some HIV screening tests to produce a false positive. At the same time, efficacy data began to be released for the Oxford-AstraZeneca vaccine, as well as the Pfizer and Moderna programs.

We had to decide whether to pause development or push forward into phase III with the caveat that the vaccine could cause a false positive in some HIV screening assays. When we discussed the issue with HIV experts, everyone agreed that diagnostics can be changed, so it was a tractable issue. However, the reality of interfering with the HIV diagnostic algorithm is complex. In some countries, for example, a positive result in a lab can lead to the patient being given antivirals without a secondary check. Clearly, inducing a false positive for HIV with our vaccine had the potential to cause issues, so we ultimately decided to halt our COVID-19 program.

I'll be honest; it was a tough decision to make! We were confident it was a good vaccine and, as it was made in a CHO cell system, it only came with mild side effects. If we had proceeded with the program, I think we probably would have been the first protein-based COVID-19 vaccine to reach the market. Right now, there's still no protein-based vaccine widely approved for COVID-19, but we are hoping that changes any day...

On the positive side, however, we do now have human validation that our molecular clamp approach can drive a robust immune response. Over the past several months, our team has been busily exploring a new trimerization domain that is not derived from GP41. We are calling it "Clamp 2.0" and we're looking at a range of different viral antigens and potential vaccines for commercial targets. We're also keeping an eye on the COVID-19 variants and we continue to work with CEPI.

Accelerating beyond the pandemic

Today's sophisticated analytical tools allow us to understand molecules very early on; we can pull apart a molecule and really understand what residues are important at an amino acid level, what affects activity, what could change, what is a liability, and so on. It doesn't matter if materials are generated from a pool or a clone – as long as they are characterized accurately. I believe that pools of genetic material could become a regular tool for speeding up the development process. Getting into phase I studies is absolutely critical and every day you can save is beneficial! Having an artificial separation between clonally derived populations or pools seems like an antiquated way of working. We really should just be focusing on the quality of the molecule and how we use that material and our ability to create a reproducible process.

We're really pleased with our partnership with Lonza. Being based in Australia, we are a long way from Europe and the US, and having access to the Lonza system during the pandemic really empowered our work. We're now working on several different COVID-vaccines with researchers in Australia, and we're also looking at the production of monoclonal antibodies for COVID-19. We wouldn't be able to do that with the quality and the speed that we have today if it wasn't for the generosity and the partnership with Lonza. Lonza has spent years developing the GS SYSTEM to get it to where it is today, and the combination of the GS knockout cell line and cell culture platform result in a robust upstream platform. The GS XCEED expression system brought great benefits to our project because it allowed us to move fast – speed was clearly crucial at the start of a public health crisis.

But this technology is not just applicable to a pandemic. Getting new therapeutics to patients as quickly as possible – in all therapeutic areas – is important. And technology like this can help developers to move much faster. I firmly believe that using pools of genetic material early in development can bring huge benefits to a project.

Why Did We Choose a CHO Expression System for Vaccine Production?

With Trent Munro

Some companies are using a baculovirus approach to a COVID-19 vaccine, including Sanofi and Novavax. These vaccines have very different types of post-translation and modification profiles compared with a vaccine derived from mammalian cells. So far, the immunology data coming out of these vaccines looks good, although we'll learn more as additional clinical data emerges or as they are rolled out more broadly.

In our program, we wanted to replicate the glycosylation pattern of the virus as closely as possible – CHO makes sense here. But we also wanted a production system that was a good fit for the installed base of bioprocess capabilities available in CDMO networks and across the biopharma industry – and capacity for CHO production technology is huge. Finally, CHO secretes molecules at a good yield.

Clover Biopharmaceuticals is another COVID-19 vaccine developer that is using a CHO-based production system – and promising data has come out of their phase III program. For me, Clover's data proves the validity of using CHO as a production system for COVID-19 vaccines. And, more broadly speaking, I believe CHO is a sensible choice for vaccine production.

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We're now barreling towards holiday season – and that means it's also time to celebrate The Medicine Maker Innovation Awards! Here, we showcase the top technologies released during 2021 – as nominated by our readers via an online form.

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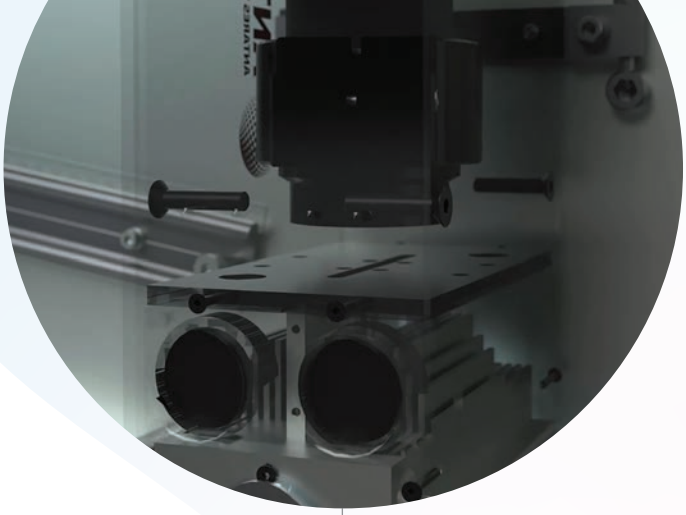
How? Go to http://tmm.txp.to/2021/innovationwinner to vote for your top pick of 2021. Voting will close on March 16, 2022 – and the grand winner will have the opportunity to tell the development story behind their innovation in a 2022 edition of The Medicine Maker.

Interested in the 2022 Innovation Awards? Nominations will open in April 2022.

Now without further ado, let's meet the winners of 2021…



AI-POWERED VISUAL INSPECTION

An artificial intelligence-based platform applied to visual inspection machines

Stevanato Group

Artificial intelligence meets visual inspection: Stevanato Group has launched an AI-based platform based on deep learning models that applies human-like decision making to its automatic visual inspection equipment. The goal is to overcome the traditional trade-off between detection rate and false rejection rate. The company claims that false rejects can be reduced tenfold and that the detection rate can yield up to 99.9 percent accuracy – both for particle inspection and cosmetic defects detection. The cloud-based platform is compliant with US CFR 21 Part 11 and EU GMP Annex 11, and also meets data integrity needs. It also includes advanced monitoring tools, such as heat maps and confusion matrix, for model performance evaluation.

AV PRINT INSPECTOR

Vision system for whole-label inspection

Antares Vision Group

This high-resolution vision system provides inline layout inspection for webs and labels at speeds of up to 80 m/min, and can be incorporated into new or existing labeling, printing or packaging machines. Antares Vision created the system to meet demands for increasingly sophisticated – and often print-on-demand – applications. The standard head size handles labels and web applications up to 4 inches wide, with 6-inch and 12-inch options also available. The technology supports all major vision system tools for quality control across a wide range of layout features including 1D/2D barcodes, optical character recognition (OCR) and verification (OCV), pattern matching, color check, and pattern matching. In addition, it can define as many as 40 unique regions of interest, each with independent parameters and reportable defect statistics.

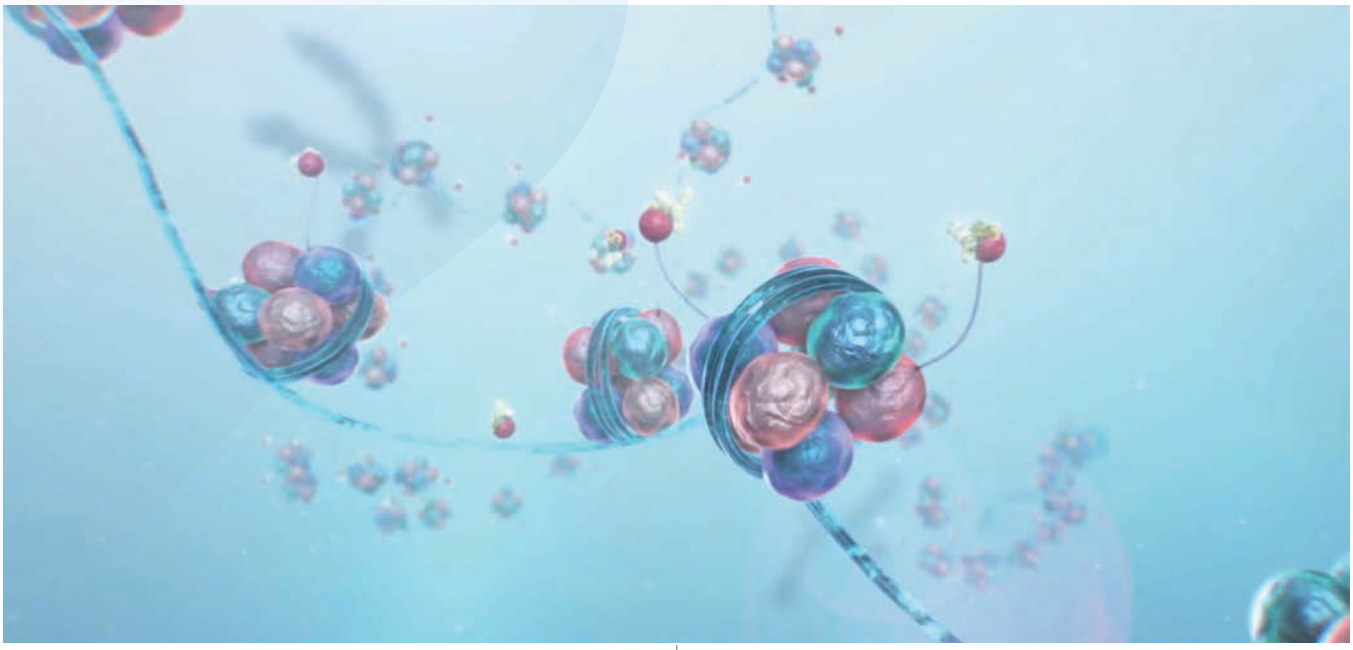
CHOSOURCE CHO-K1 ADCC+ CELL LINE

Expression cell line to develop afucosylated antibodies with increased therapeutic efficacy

Horizon Discovery, a PerkinElmer company

The CHO-K1 ADCC+ expression line is the newest addition to Horizon's CHOSOURCE platform, built from its elder cousin, CHO-K1 GS KO, by knocking out a gene in the fucosylation pathway. The CHO-K1 ADCC+ cell line helps increase antibody binding affinity to the FcgIIIa receptors present on effector cells to enhance antibody-dependent cellular cytotoxicity activity. As a consequence, the cell line should improve the potency and efficacy of therapeutic antibodies and fusion protein biotherapeutics, and potentially reduce dosage requirements and side effects for patients. The cell line can also replicate human-like post-translational modifications, significantly reducing the potential immunogenic response.

According to Horizon, use of afucosylated antibodies and fusion proteins is expanding from oncology applications to other areas, including infectious diseases and autoimmune conditions.



DOMINA

An automated tablet press designed with the fourth industrial revolution in mind

IMA Active Division

IMA claims to have channeled the benefits of its popular Prexima series into Domina, including isolation of the processing area, robust structure, and accessibility. Domina also uses Industry 4.0 technology to maximize production while minimizing errors; the system's KORTEX HMI system offers control of all the machine's functions while advanced algorithms constantly control the status of the machine and the production quality. The self-learning algorithms can quickly find the right set-up and ensure consistent tablet quality.

EPIMOGRIFY

Applying epigenetics to identify optimal culture conditions

Mogrify

Mogrify collaborated with the Duke-National University in Singapore and Monash University in Australia to co-develop epiMOGRIFY. The technology utilizes epigenetic sequencing to identify the optimal culture conditions required to maintain cells and support reprogramming in chemically defined media. Using ChIP-Seq, epiMOGRIFY identifies the trimethylation levels of the protein histone H3K4, a known marker of cell identity genes. A unique epigenetic profile of the cell is then built in the context of other human cell types. Using a regulatory network engine, key signaling ligand-receptor pairs are identified, according to their influence. The identified ligands can then be incorporated into culture medium and matrix to improve the control and maintenance of cell identity.

epiMOGRIFY-predicted factors have been validated for the maintenance of astrocytes and cardiomyocytes in vitro in chemically defined media, and promoted their generation from neural progenitors and embryonic stem cells, respectively. According to Mogrify, epiMOGRIFY-defined conditions demonstrated an improvement in cell growth, survival and differentiation efficiency when compared to existing undefined conditions.

GENVOY-ILM T CELL KIT FOR MRNA

Lipid nanoparticle reagent kit that delivers RNA into human T cells

Precision NanoSystems

Current gene delivery methods have their challenges; for example, the non-viral electroporation method can be harsh on cells, making it difficult to generate quality cells at high yields, whereas conventional viral vector delivery methods can be expensive and cumbersome to manufacture. The GenVoy-ILM T Cell Kit for mRNA can deliver RNA into human primary T cells, while maintaining high cell viability, and can also be tuned and scaled across Precision Nanosystems' NxGen microfluidic platform from discovery to the clinic.

The kit launched with proof-of-concept datasets with therapeutic relevance, such as expressing tumor-killing receptors and introducing gene knockouts. Optimized protocols are also available that can help researchers to explore the lipid nanoparticles at the discovery stage without any specialized knowledge of the technology.

HIPERSEP PROCESS M

Fast, powerful HPLC chromatography system

Novasep

Hipersep Process M is the newest addition to the Hipersep line and is designed for the purification of peptides, oligonucleotides, insulin, and other synthetic molecules. The system can perform chromatography runs up to 100 bars and is also suitable for purification processes that require high temperatures (up to 85 °C). High temperatures are managed and maintained autonomously by a system of thermoregulation functions. The flow range can obtain 60–500 l/h, or 20–200 l/h with the "Low Flow" version.

The system is compatible with Novasep's Prochrom columns LC110 to LC450 mm, and can also be customized with modular options depending on needs. According to Novasep, this latest addition to the range features optimizations to meet the complexity challenges of new modalities, as well as cleaning requirements related to production.

HISCREEN FIBRO PRISMA

Protein A fiber chromatography unit for rapid cycling

Cytiva

Suitable for early process development applications, HiScreen Fibro PrismA is a single use, protein A fiber chromatography unit for rapid cycling chromatography purification of mAbs. Specifically, it can be used to purify mAbs and Fc-containing fragments in cycle times less than five minutes – compared to hours for standard chromatography resins. The adsorbents have a protein A cellulose fiber matrix with an open pore structure where mass transfer is governed by convective flow. This structure allows high mAb binding capacities at very short residence times by using rapid cycling chromatography. Dynamic binding capacity is around 30 mg IgG/mL matrix independent of the residence time.

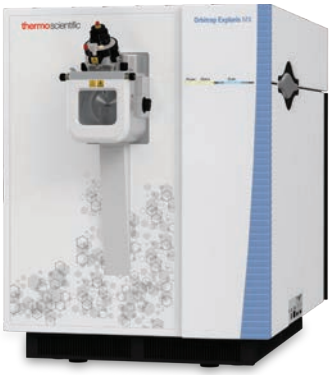
The unit can be run on an ÄKTA chromatography system for real-time UV, pH, and conductivity detection.

MAM 2.0 WORKFLOW

Suite of physical and digital tools to enable multi-attribute monitoring

Thermo Fisher Scientific

The MAM 2.0 workflow is a connected platform that helps bridge the gap between development and manufacturing by providing knowledge and data transfer that can easily be shared across departments and teams. The updated workflow includes instrumentation, software, installation, training, and ongoing support from Thermo Fisher Scientific. The company says that the platform provides site-specific insight on multiple product quality attributes and has the potential to replace multiple single-attribute assays into one information-rich assay, which should help accelerate drug development. Additionally, the MAM 2.0 workflow can be used to facilitate implementation of mass spectrometry in quality control environments.



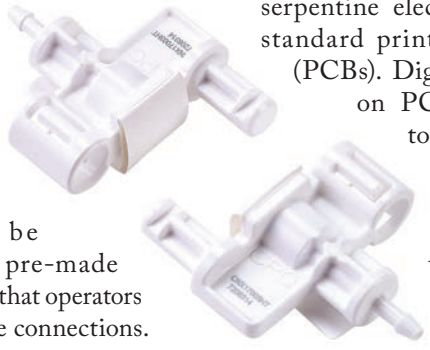
This image shows the Thermo Scientific Orbitrap Exploris MX mass detector, a key component of the MAM 2.0 workflow

MICROCNX SERIES CONNECTORS

Sterile connector for small-volume closed processing

CPC (Colder Products Company)

These aseptic connectors (available in sizes of 1.6 mm, 2.4 mm, and 3.2 mm) are a simple way to connect tubing in small-format assemblies. CPC says that users simply need to "pinch-click-pull" – pinch to remove the protective cover; click together the connector halves; and pull out the protective membranes. In comparison, tube welding involves more steps and a precise technique to create a successful weld. According to the company, a user can complete up to four MicroCNX connections in the time it takes to create one weld. Using aseptic connectors also eliminates the need to purchase, calibrate, validate, and maintain tube welders. The connectors can be incorporated into pre-made tubing assemblies so that operators know where to make connections.



MOBIE

High-resolution ion mobility mass spectrometry

MOBILion Systems

Mobie is designed to accelerate and simplify the workflows of challenging analyte classes, including peptides, proteins, lipids and glycans. The driving technology is Structures for Lossless Ion Manipulation (SLIM). SLIM was invented by Richard D Smith of the Pacific Northwest National Laboratory, and sets itself apart from other ion mobility platforms thanks to its path length of 13 meters, which enables high resolution that can separate molecules with only very minor differences to improve reliability and reproducibility in the lab. The technology also has serpentine electrode patterns on standard printed circuit boards (PCBs). Digitizing separations on PCBs allows Mobie to break linear path boundaries with virtually limitless path lengths without any ion loss.

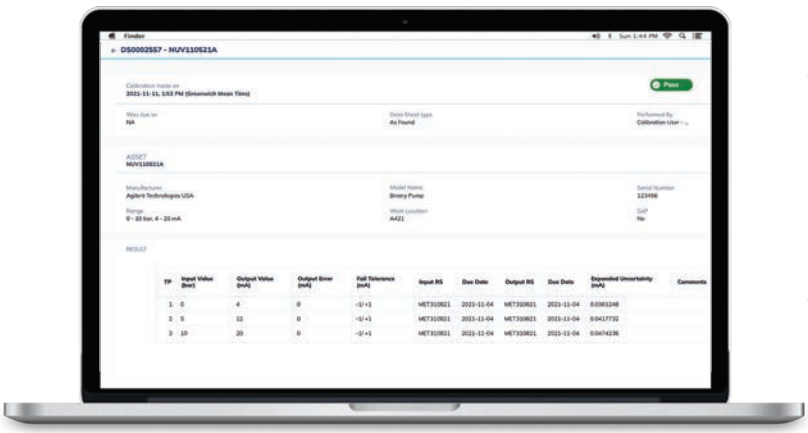
NUVOLO CONNECTED WORKPLACE - CALIBRATION

Data management system for planning, scheduling, and documenting equipment calibration

Nuvolo

Many pharma companies still use spreadsheets or disparate systems to conduct and record equipment calibrations. Nuvolo Connected Workplace Calibration solution centralizes all information on one platform and reduces the amount of manual interventions required. The platform minimizes errors through automatic calculations so that technicians can easily see if the equipment falls within standards or needs adjustment. It also establishes quality, safety, and regulatory compliance through traceability. Details of the Reference Standard used, along with the calibration results, allow maintenance and quality teams to keep track of details such as asset and device location, manufacturer, model, serial number, asset tag, calibrated date, and calibration due date.

Nuvolo believes their solution will reduce errors and save time. As all data is saved in one place, companies can also easily access records for audits and other reporting.



ORBITRAP IQ-X TRIBRID MASS SPECTROMETER

A mass spectrometer with a range of specialized features for small molecule scientists

Thermo Fisher Scientific

Small molecule scientists can use the Thermo Scientific Orbitrap IQ-X Tribid MS to reveal complex chemical structures for unknown compound identification and a greater understanding of small molecules. Intelligent software enables real-time library search; the local and customizable library can be used to selectively detect and characterize unknown compounds that are structurally related to known compounds. The system also features an ultraviolet photodissociation option, providing insights on the lipid double-bond localization and site specific glucuronidation, while the 1,000,000 resolution option enables fine isotope detection and improved confidence in results.

SOLOPURE

Closed-barrier system that provides Grade A aseptic environment for sterile manufacturing

ILC Dover

soloPURE can be used as a VHP-in-place isolator system with disposable, flexible-film walls or can be installed as a fully single-use assembly with a six-sided, bonded structure whereby all product-contacting surfaces can be disposed of after use. For sensitive products that cannot be handled inside a VHP sterilized environment, the single-use assembly can be Gamma Irradiated to ensure a sterile internal working environment.

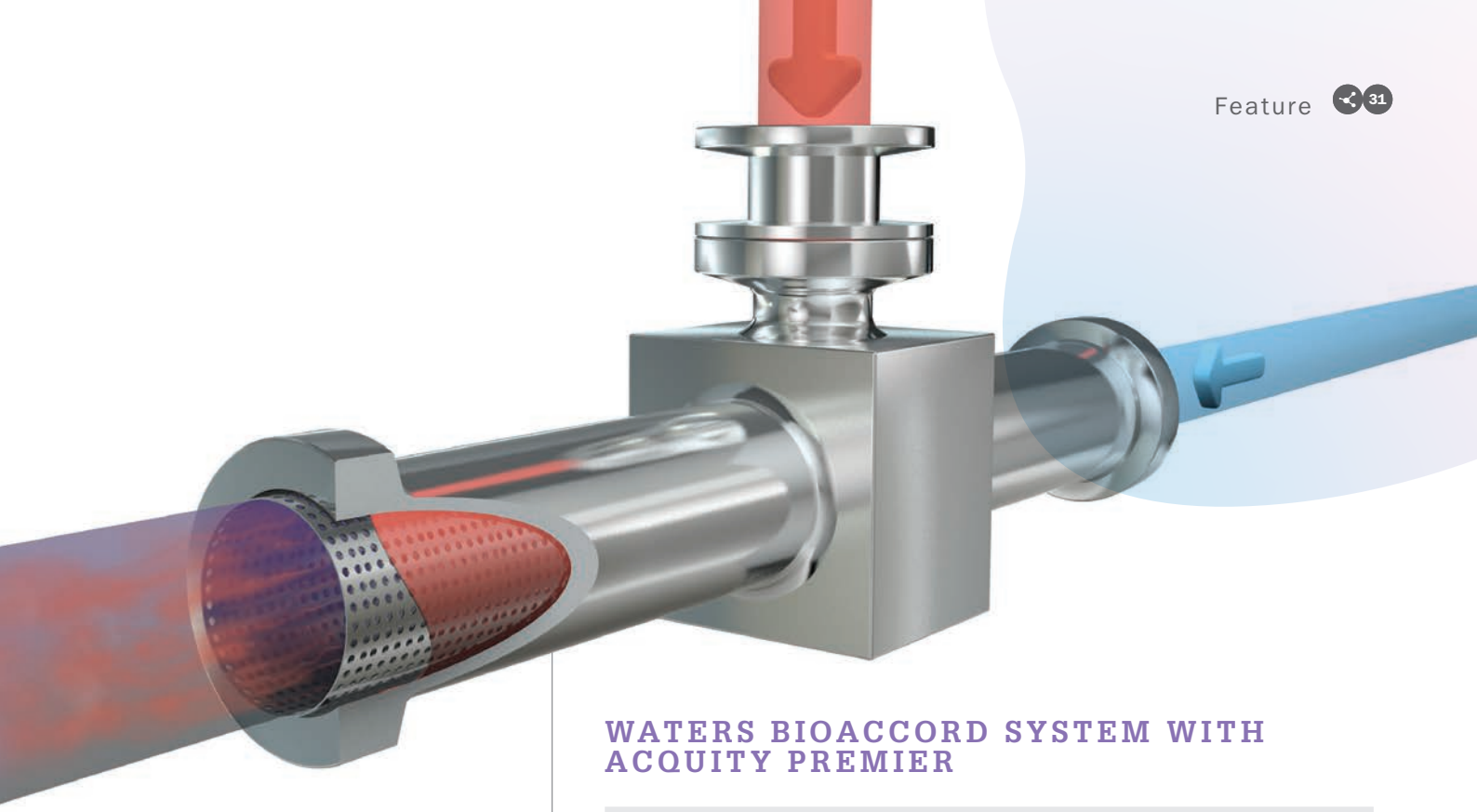
Despite being made from flexible-film, the isolator has the same working functions as a stainless steel counterpart with a 21 CFR control system, Grade A aseptic working environment, 0.45 m/s airflow, and integration with all associated entry/exit methods commonly found in a fill-finish process. Bolt-on modules are also available that provide more capabilities, including lyophilization loading and VHP transfer.

STARMAP V2.0

AI platform that predicts drug development success

Nanoform Finland Plc

Starmap uses sparse-data AI to augment experimental results from Nanoform's CESS nanoparticle engineering process with expert knowledge to allow reliable predictions to be made about the potential success of nanoforming drug molecules. Essentially, Starmap is a digital version of the CESS technology that enables in silico experiments in large quantities. And that could allow libraries of previously unsuccessful drug molecules to be assessed for the process, opening up new possibilities for drugs previously discarded. The platform could have applicability in drug discovery and development, as well as in lifecycle management for existing marketed drugs and 505(b)(2)-like product development strategies.



VERSATILE LNP PRODUCTION

A scalable approach for manufacturing lipid nanoparticles

Micropore Technologies

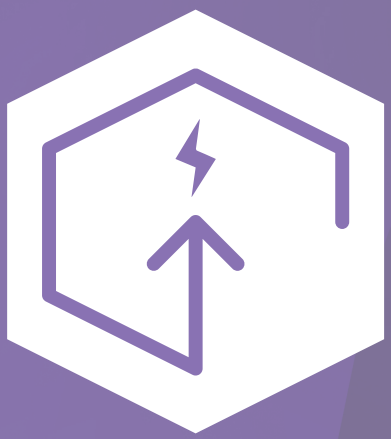
Micropore Technologies has developed what it refers to as a "Generation 2" manufacturing process for making polynucleotide lipid nanoparticles that can be used in mRNA-based vaccines and other therapeutics. The company has further developed its AXF technology into a micromixer suitable for the manufacture of LNPs loaded with mRNA. The approach results in mRNA-loaded LNPs with a very small hold-up volume and zero mRNA degradation resulting from a low operating pressure (<2 bar). In addition, there are no moving parts and users have the ability to scale from 0.2 to 200 L/h on the same unit.

WATERS BIOACCORD SYSTEM WITH ACQUITY PREMIER

High-res LC-MS system that simplifies multi-attribute monitoring

Waters Corporation

Broader LC-MS adoption by biopharma late-stage development laboratories has two barriers to entry: cost and complexity. Waters is trying to address these with the launch of the BioAccord System with Acquity Premier. The system eliminates analyte-to-metal surface interactions using Acquity Premier technology, simplifies the detection of critical quality attributes using high-quality mass spectral data, and enhances the recovery of hard-to-detect sample analytes and assay-to-assay reproducibility. When analyzing biologics, information is currency; by solving the analyte-to-metal interactions obstacle, scientists can get detailed information about samples from the very first injection. The system also automatically monitors its own performance, helping to improve productivity by maximizing system uptime and minimizing reanalysis.



the Medicine Maker

THE INNOVATORS

WHETHER BETTER ENSURING PATIENT SAFETY, IMPROVING PROCESS EFFICIENCY, OR JUST MAKING LIFE IN THE LAB OR FACILITY EASIER – MEET THE COMPANIES ADVANCING PHARMACEUTICAL DEVELOPMENT AND MANUFACTURE

THE FUTURE OF STERILE CONTAINMENT

soloPURE™ is a newly developed sterile isolator from industry containment leaders, ILC Dover. The focus around sterile injectable drug substances has grown in recent years due to the COVID-19 pandemic, as well as changes to global regulations regarding the manufacture of these critical, life-saving products. To help accommodate the changes in regulation and demand, ILC Dover has developed a system that complies with the most stringent industry regulations and provides a cost-effective method to get new products to market quicker. soloPURE is a closed isolator system with a completely disposable working chamber that allows for rapid campaign change overs. The central chamber is made of a PVC flexible film which can be bio-decontaminated using either conventional VHP methods or as a pre-sterilized, gamma irradiated entity. Also, the isolator has been developed to perform to the same criteria as its hard wall counterparts, obtaining a grade A particle count and maintaining the correct laminar airflow parameters. The overarching benefit of the soloPURE is that the price point is around half that of the next best alterative hard wall solution, allowing smaller developing biotech companies to bring new products more affordably to market.

www.ilcdover.com/products/solopure-flexible-aseptic-isolator/

ACCELERATING THE DELIVERY OF LIFE-SAVING TREATMENTS

The COVID-19 pandemic intensified pharmaceutical supply chain and fill-finish capacity shortages that have existed within the industry for many years. One of the fundamental concerns in fill-finish manufacturing is glass friction created by glass-to-glass and glass-to-metal contact. This resistance can limit filling line efficiency and speed, reducing yield and generating damage that can create particles, breakages, and cracks. The pharmaceutical industry has come to accept these limitations as a standard cost of doing business, but innovations in glass packaging are enabling a step-change in performance that shatters these old assumptions.

In response to the pandemic and the need for a modern-day primary packaging solution, Corning introduced Velocity® Vials, a USP Type I borosilicate vial externally coated with Corning's proprietary technology. Velocity Vials are engineered to deliver better economics, better quality, and an environmentally sustainable design. Velocity Vials' protective uniform coating can improve filling line efficiency from 20% to 50% compared to conventional vials, while also lowering packaging production costs and providing a fast regulatory process for post-market drugs. In addition, Corning's new coated vials can enable up to a 96 percent reduction in glass particulates and a three-times reduction in the likelihood of damage that leads to cracks and breaks, ultimately helping to improve drug safety and purity.

Corning's latest innovation can improve fill-finish productivity and quality, thus lowering manufacturing costs, which can ultimately lead to lower drug costs. The increased efficiency and throughput of Velocity Vials can also help drive faster manufacturing of essential medications to meet rising global demand. The Coalition for Epidemic Preparedness Innovations (CEPI) and The Gates Foundation have identified vaccine manufacturing, including fill-finish operations, as bottlenecks in the vaccine supply chain. They note that this issue is even more exacerbated in low-income countries.

Pharmaceutical companies and fill-finish contract manufacturers can leverage the improved efficiency of Velocity Vials as a drop-in solution to increase throughput, thereby producing more vaccines and other drug products in less time.

Velocity Vials join Corning Valor® Glass and pharmaceutical glass tubing as the company's newest innovation as it builds a comprehensive, end-to-end pharmaceutical packaging portfolio. With the invention of Velocity Vials, the company extends its longstanding leadership role in the life sciences industry and broadens the reach of Corning's unique capabilities while strengthening the supply chain for the future.

NextGen

R&D pipeline
New technology
Future trends

The Four Most Promising Adoptive Cell Therapies

A whistle-stop tour of the mechanisms, benefits, manufacturing challenges, and clinical potential of CAR T cells, TCR T cells, TILs, and NK cells

By Marwan Alsarraj, Biopharma Segment Manager, Digital Biology Group at Bio-Rad

For far too long, patients with cancer had access to only a few treatment options – and none were ideal. Surgery is invasive and risky, while radiation and chemotherapy are toxic and offer variable success rates. In the last decade, however, thanks to advances in increased understanding of genetics and the immune system, researchers have developed more personalized, targeted therapies that promise better outcomes for cancer patients. Immunotherapy, including adoptive cell therapy, defines a new generation of cancer treatments that could drastically change clinical strategies and outcomes.

Here, I review the mechanisms, benefits, manufacturing challenges, and clinical potential of the four most promising types of adoptive cell therapies: chimeric antigen receptor (CAR) T cells, T cell receptor (TCR) T cells, tumor infiltrating lymphocytes (TILs), and natural killer (NK) cells.

Our biological watchdog

The core purpose of the immune system is to discriminate between "self" and "non-self" and destroy anything that does not belong. The human immune system identifies pathogens ranging from bacteria to viruses and activates lymphocytes, such as T cells and B cells, to attack them. However, the immune system struggles to recognize tumors, which can often grow rapidly and spread unchecked throughout the body.

Adoptive cell therapy, also called cellular immunotherapy, uses immune cells to treat cancer. As of 2021, only one type of adoptive cell therapy has received approval from the FDA: CAR T cell therapy. The first approved CAR T cell therapy treats acute lymphoblastic leukemia. Today, there are five CAR T therapies on the market, treating a range of blood cancers, including multiple myeloma and mantle cell lymphoma.

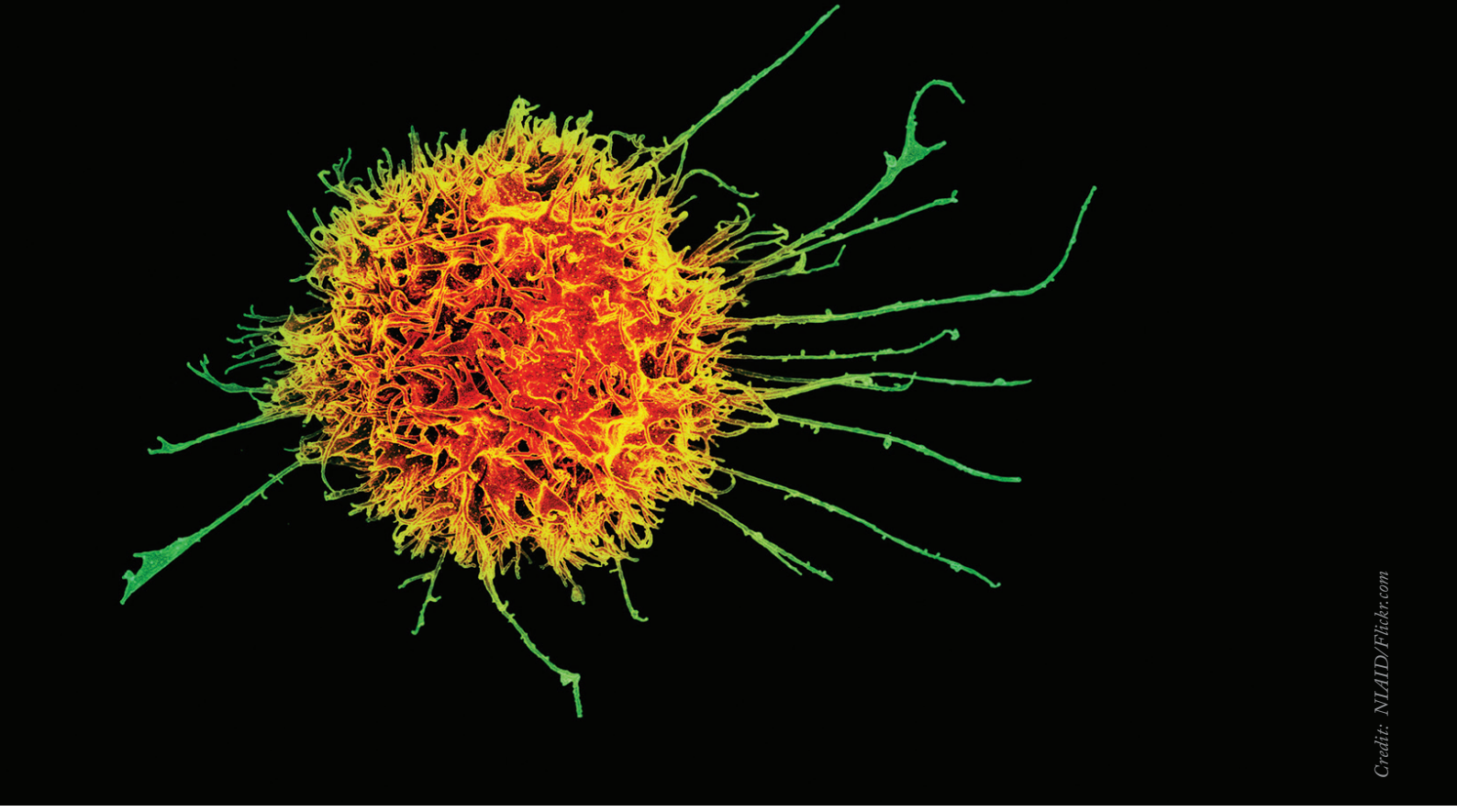
However, other types of adoptive cell therapies are now in advanced stages of development and are likely to enter the clinic soon. Tumor infiltrating lymphocytes (TILs), for example, are on the verge of approval, having already received a breakthrough designation for treating advanced cervical cancer and an orphan drug designation for advanced melanoma (Iovance's LN-145 and Instil Bio's ITIL-168, respectively). T cell receptor (TCR) T cells have also shown promise in the laboratory but have not yet reached the clinic – and the same is true for natural killer (NK) cells.

Though promising, no one type of adoptive cell therapy is perfect. These therapies are challenging to develop and manufacture efficiently, and it is difficult to predict how individual patients will respond to treatment. In addition, each therapeutic approach offers distinct benefits and harbors specific limitations.

CAR Ts

CAR T cells have demonstrated incredible success in the clinic. Engineered to express the chimeric antigen receptor (CAR) protein, CAR T cells seek out tumor cells that express certain surface markers and destroy them. In a way, CAR T cells recognize tumor cells as infectious agents.

Today's approved CAR T cell therapies are autologous, meaning they are derived from a patient's own T cells. This process offers safety benefits for patients but also poses a manufacturing problem. To develop CAR T cells, a patient has their blood drawn, and then the blood is sent to a laboratory, where scientists extract the T cells and genetically engineer them using viral vectors or transposon systems



Credit: NIAID/Flickr.com

to express the CAR protein. Next, they expand the cells and return them to the clinic, where a physician infuses the patient's modified T cells back into their body. Since the cells originally came from the patient, the chance of the patient experiencing an immune reaction to the cells is minimal.

But autologous CAR T cells are hard to manufacture efficiently. The process often takes weeks – time that patients may not be able to afford. To address this issue, scientists are developing allogeneic CAR T cells that could be manufactured in advance and administered "off the shelf." This option poses a different set of pros and cons: while allogeneic CAR T cells could potentially reach patients in days instead of weeks, their foreign nature puts patients at risk of either contracting graft-versus-host disease or seeing their immune system kill off the transfused cells before they can have an effect.

As T cells are complex living cells, CAR T cell manufacturing and development requires rigorous quality control. Biomanufacturers cannot entirely predict how the cells will act either in vitro or in vivo. Therefore, they cannot predict the success of the cells' development or application in the clinic. For instance, viral transduction of the CAR transgene is not guaranteed, and variations in copy number can lead to varying clinical success: if transduction is not successful, the treatment won't work, and if the copy number is too high, the treatment can become toxic. Furthermore, the cells could potentially contain replication-competent viruses that can infect patients. Finally, researchers cannot always predict how long CAR-T cells will persist once administered to patients, so they must conduct serial monitoring to assess the ongoing viability of the treatment.

New technologies can help in this regard. As one example, droplet digital PCR (ddPCR), which detects rare nucleotide variants and quantifies them directly, can be used to assess the quality of CAR T cells. ddPCR can quantify nucleic acids down to one copy per genome, qualifying it as technology suitable for serial monitoring of CAR T persistence in the blood.

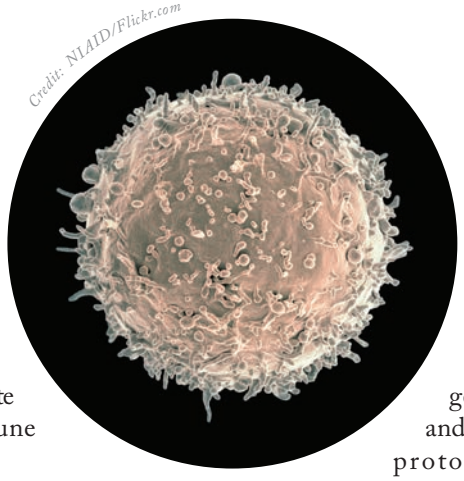
All current FDA-approved CAR T cells treat blood cancers, as the CAR T cells in use today cannot infiltrate solid tumors. However, scientists are starting to identify novel targets that will enable CAR T cells to attack solid tumors.

More than 630 CAR T cell trials are registered on ClinicalTrials.gov as either recruiting or ongoing. By 2028, the market may reach $8 billion in size (1).

T cell receptors

Like CAR T cell therapy, TCR therapy involves genetically modifying T cells, yet the two therapies work via different mechanisms. CAR T cells target specific antigens present on the surface of cells, which explains why they struggle to infiltrate solid tumors. In contrast, TCRs can target any antigen, whether it is present on the cell surface or within the cell, suggesting that this therapy might be applicable to other types of cancer (2). TCR T cells bind to a cell's major histocompatibility complexes (MHCs), the innate immune system's protein structures that tag cells for destruction, thereby enhancing the body's natural immune response.

Like CAR T cells, TCR T cells are personalized to each patient, slowing down the development process and delaying treatment. As researchers continue to study the feasibility of developing allogeneic


Credit: NIAID/Flickr.com

CAR T cells, TCR T cell development should benefit, as well, creating two viable forms of T cell mediated therapy.

TCR T cells are running behind CAR T cell therapies in development, but around 280 TCR clinical trials are recruiting or ongoing, according to ClinicalTrials.gov.

Tumor infiltrating lymphocytes

Lymphocytes that successfully enter tumor tissue are called TILs – and scientists are looking to exploit this ability to treat cancers that are off-limits to current CAR T cells. Unlike CAR T and TCR T cells, TILs do not need to be genetically modified. Since they specifically infiltrate tumors, they already recognize all the antigens needed to fulfill their intended purpose. Instead, these cells merely need to be expanded ex vivo to enhance their effect within the body.

But this expansion process is not simple, making the cells difficult to scale up for commercial use. While T cells can be harvested via a blood draw, TILs can only be collected after resecting tumor tissue from a patient. The tissue needs to be dissected, plated, and digested to isolate the T cells. Finally, the cells get expanded and returned to the patient. From biopsy to reinfusion, the process takes about six to eight weeks and requires significant technical skill. This convoluted process might explain why, despite over 20 years of research, this therapy has not yet reached the clinic. Unsurprisingly, researchers are investigating new methods to simplify the development process.

Despite the hurdles, about 300 clinical trials for TILs are currently enrolling or active on ClinicalTrials.gov.

Natural killers

Unlike the first three adoptive cell therapies, NK cell therapy does not involve T cells; NK cells are a different type of lymphocyte that specifically targets tumor cells, granting them unique therapeutic potential. NK cells do not need to be genetically modified to identify tumors or any specific antigen on tumor cells. Instead, they attack tumor cells directly and release chemokines and cytokines that activate the adaptive immune system.

NK cells do not sufficiently kill off cancer cells on their own because tumors release inhibitory molecules that suppress their activity (3). However, activating them ex vivo, expanding them, and modifying them to express the CAR protein could help them overcome inhibition and kill tumor cells (4).

Allogeneic, unmodified NK cells are safe, indicating that they could potentially be standardized and offered off-the-shelf (5). But manufacturers still have several hurdles to overcome to make the approach viable for clinical use; for example, it is difficult to expand NK cells in vitro and they also struggle to infiltrate tumor tissue, meaning they might not be suitable for use against solid tumors. They also do not persist in the blood for as long as CAR-T cells. But given NK cells' natural ability to target tumor cells, scientists are optimistic about their therapeutic potential. After further research and development, these could become cheaper, easier to produce, and more widely available than CAR T cells (6).

Over 300 NK cell trials are currently enrolling patients or ongoing for people with cancer on ClinicalTrials.gov – and forecasters expect the market to reach $5 billion by 2026 (7).

Making a difference

Together, these four adoptive cell therapies could give many people with cancer a chance to live a better, longer life. Though they all present unique development challenges, hundreds of clinical trials are underway to investigate their therapeutic potential. The science will continue to advance as researchers discover how lymphocytes interact with tumor cells and as the field refines genetic engineering and ex vivo expansion protocols. With this additional knowledge, it will become easier to produce these "living drugs" effectively.

The FDA supports the development of adoptive cell therapies and understands the challenges inherent in developing them – and that's why the agency has released several guidelines on cell therapy manufacturing (8). Through the combined efforts of academic researchers, biopharmaceutical companies, and regulators, these four adoptive cell therapies could reach their clinical potential and make a significant difference in patient outcomes.

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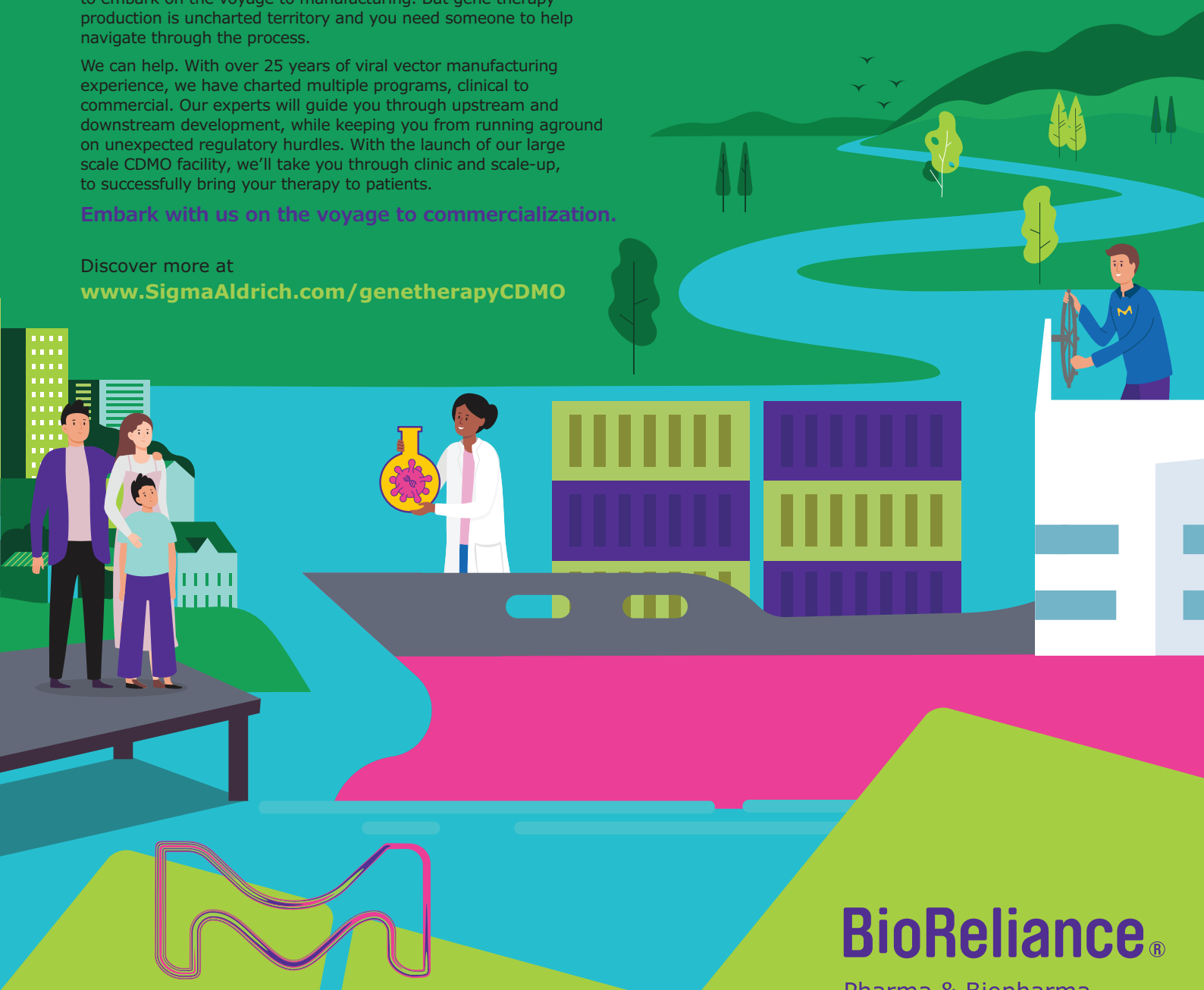

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Natural Born Therapeutics

Two leaders from the Trinity Centre for Natural Products Research in Ireland explain how nature can create molecules that go beyond the human imagination

With Helen Sheridan, Associate Professor of Natural Product Chemistry and Academic Director of NatPro, and Gaia Scalabrino, Executive Director of NatPro, Trinity Centre for Natural Products Research, Ireland

Why look for bioactives in nature?

Nature is a complex and fascinating system. Our planet's diverse environments – oceans, grasslands, arctic ice, thermal pools – all present unique and sometimes challenging environments for organisms. As a result, species that live in these environments have generated complex and varied natural scaffolds far beyond the imaginations of human scientists.

Therapeutic molecules usually derive from the more complex "secondary" metabolite pathways in nature that give rise to alkaloids, polyketides, terpenoids and so on. These classes frequently display anticancer, immunomodulatory, analgesic, and other properties needed in human medicine. One example of a key bioactive among the more than 40 percent of drugs that originate from nature is paclitaxel, a cancer drug derived from the bark of the Pacific yew tree. As with many natural materials, using naturally sourced paclitaxel at scale is not sustainable, so this drug is produced in the laboratory using a number of different approaches. Today, we know it as Taxol.

Once a potential therapeutic candidate from nature has been identified, isolated, and its properties established, difficulties often arise in cultivation conditions, processing methods, sustainable supply, IP constraints, and regulations. Many natural products have very complex chemical scaffolds with multiple chiral centers, which makes procuring sufficient quantities of material for clinical evaluation a serious hurdle. They are often too difficult to synthesize economically (think 40–60 synthetic steps) and are produced only at low levels in plants.

If an interesting bioactive is found in a marine species, the challenges are even more significant. The marine environment brings all the associated difficulties of harvesting wet plants at depth and contamination of plant material by microbes (which, in some cases, we now believe to be the primary producers of the active metabolite). A good example of a drug that has faced these scale and marine challenges is the alkaloid trabectedin (Yondelis), isolated from the sea squirt Ecteinascidia turbinata. It takes one tonne of these animals to isolate one gram of trabectedin. Many different methods have been explored to generate this drug, including commercial mariculture. The solution? Synthesis of the molecule from an advanced chemical intermediate isolated from a bacterium.

What is NatPro's focus?

Nature is the source and starting point of our work. The products nature gives rise to broaden our scientific knowledge and the myriad ways we can apply it. At NatPro, we've gone beyond traditional phytochemistry, isolation, and characterization to include AI as part of our strategy. We use a mixture of network pharmacology and advanced computer applications to predict the biological and disease targets of plant extracts and isolated molecules. It's an efficient, cost-effective way to combine the potency of nature with the accelerative power of technology.

We focus on both terrestrial and marine sources of bioactives. Some natural products we study are herbal medicine plants, cereals, micro-, and macro-algae; others are byproducts of industry, such as spent grain and fruit pulp. We look at crude extracts, small stable and volatile molecules, and essential and fixed oils – all derived from terrestrial and marine plants and microbes. Currently, we are supporting a small-to-medium enterprise (SME) in assessing the quality and stability of their commercial tinctures to optimize their production. One example of work we are doing for this SME involves generating data that inform the selection of optimal locations and conditions for growth to increase chemical content and allow producers to access high-value organic international markets.

In another project – a collaboration with industry at an earlier stage of development – we are completing background work for an early study in clinical aromatherapy intervention. We're looking at using a blend of aromatherapy oils as a complementary aid for reducing stress in patients receiving chemotherapy. Part of this project involves unlocking regulatory constraints on the novel development of such products.

As a research center, we want to reframe natural products. We explore innovative approaches in the use of biomass generated as byproducts in other processes, seeking ways to repurpose them using novel processing/biotransformation approaches. One tangible example is a project we worked on at the European level, exploring the use of brewers' spent grain to create functional foods. We applied metabolomic and chemometric techniques to identify the chemical fingerprints of this spent and fermented grain. Applied more broadly, our approach could create added-value products from biomass and byproducts in breweries and distilleries across Ireland and the UK. At present, we are discussing this area of work with industry partners.

What have been the key successes?

"Success" is very subjective. At NatPro, we

Nemera
we put patients first

From design to manufacturing, we partner in your device strategy

NEMERA: YOUR DRUG DELIVERY DEVICE SOLUTIONS PARTNER:

Patients first. Always.
Partnering in drug delivery devices. Holistically.
Going the extra-mile. Together.

take pride in building valuable relationships and disseminating high-quality science. We have developed a multidisciplinary, cross-cultural team of researchers, nurtured partnerships across numerous industry sectors, run educational civic science programs in communities and schools, and offered fellowships and scholarships to students in areas where natural products could morph into innovative solutions (such as therapeutics, functional food, and cosmetics) – and we did it all during a pandemic!

At a national level, NatPro is contributing to policymaking for Ireland's national bioeconomy. We're taking a lead in the area of natural products, with Helen Sheridan serving as the natural products representative in the government's expert advisory group. This is a privileged role and we recognize the importance of best using national natural resources effectively while contributing to global environmental and climate goals.

Looking to the future, NatPro has also secured the hosting of an international conference on natural products to be held in Dublin in 2023. This will bring together several hundred candidates from academia and industry worldwide, offering enormous international science and networking opportunities. Watch this space!

What are your hopes for the future?

The natural product market is rising globally across sectors, driven by social, environmental, and economic needs. Importantly, consumers are becoming more aware of nutrition and health. At NatPro, we aim to contribute to the development of innovative products and to support Ireland at the forefront of this positive wave in the global natural product ecosystem by harnessing national natural resources, key research expertise, and commercial capacity.

Our ambition is to become a national center for natural products research, joining a collective global network. In this vision, we would also link with a regional hub that could act as a center for the processing of natural product biomass and conversion to higher-value extracts and finished products for national and international markets.

Our active roles in startups, experience in working with SMEs, and training in lean startup methodologies with the I-Corps SFI Academy and the US NSF I-Corp have benefited us enormously. Using this experience, we plan to create innovative products, spinning them out from the center or by creating startups to address unmet and urgent medical needs. We are especially interested in serving as a global accreditation center for commercial products to promote added-value products marketed at high-quality standards.

How does the Centre draw on its Irish heritage?

Innovation is a global affair, and we relish partnering with international stakeholders, but if we ask what is "uniquely Irish," there's much to say!

One project we are engaged with is of real national significance in Ireland. Its name is Unlocking Nature's Pharmacy from Bogland Species (UNPBS). We're turning the lens of "medicine hunting" on the flora of the Irish boglands. This means we're applying historical ethnomedical use, contemporary science, and advanced metabolomics to direct and inform the search for species with therapeutic and commercial potential. We are bringing together the remaining knowledge of traditional Irish healing plants to modern practices.

The Irish boglands represent a rich and diverse source of biodiversity. Many plants growing on the bogs have been used traditionally as healing plants, such as bog myrtle (Myrica gale) to treat wounds and acne; bogbean (Menyanthes trifoliata) for skin diseases or rheumatism; and chickweed (Stellaria media) for warts.

The UNPBS project involves extensive civic and educational engagement. We work closely with state agencies, not-for-profits, SMEs, schools, farmers, communities, and other stakeholders to focus on biodiversity and ethnomedicine and to deliver positive outcomes in research and education.

Gaia Scalabrino's story

I consider myself fortunate to have grown up in a cross-cultural environment, raised between Europe and Africa. I have been exposed to a variety of Mediterranean landscapes; I have dived among colourful corals, walked in the Savannah among amazing flora and fauna, and met a number of different African tribes. Exploring this rainbow of environments and people taught me to appreciate diversity and made me ever more curious about the power hidden within the beautiful natural world I saw with my naked eyes. To that end, I studied chemistry and, in the 1990s, I completed a PhD in Natural Product Chemistry. I then moved to industry, with particular focus on drug development. I wanted to strengthen the bond between the beauty of nature and human health and wellbeing. This is still a goal I am passionately working towards.

The diverse experiences of my youth gifted me an adventurous spirit, which is why I enjoy growing enterprises from inception and managing product development programs towards commercialization. Risks and change are part of this dynamic work environment, and these drive me. I worked in strategic and operations roles in startups and as an advisor to SMEs based in the EU and US, supporting the development of drug candidates from bench to market. Now, at NatPro, Helen and I are cultivating a new research center to create innovative products and sustainable solutions derived from nature and with applications across sectors. Helen and I have complementary skills and personalities. We share curious minds and an entrepreneurial focus, which make the venture stronger and the journey more exciting.

Helen Sheridan's story

I was born a scientist. My mother described my first experiments as observational – collecting and sorting caterpillars in glass bowls and drawing dots in my notebook corresponding to each one… my first lab books! At the age of eight, I started teaching local children in the summertime, out in our front garden with a small blackboard and a lot of enthusiasm! When I was 12, I had my first chemistry explosion in our sitting room. There was a blue stain on the ceiling for some years after…

I did a Bachelor of Science in University College Dublin. I loved every second of it and was strongly drawn to chemical sciences, microbiology, and zoology. In 1983, I completed my PhD on the chemistry of fungal infestations of pine trees. We were looking for bioactive molecules, medicines, and agrochemicals. At that time in Ireland, there was a lot of investment in forestry and science "followed the money." Unfortunately, it still does.

All of my research has been in natural products. I got a scholarship from the French and Irish governments to study for a short period in the "Centre national de la recherche scientifique" (CNRS) at Gif-Sur-Yvette in Paris, where I worked in the labs of Nobel laureate Derek Barton on the chemistry of the anticancer triterpenes – the quassinoids from the Simaroubaceae species. There, I met a wonderful scientist, Judith Polonsky, who instructed me in the art of phytochemistry while also showing me the cultural history of Paris, French literature, and La Couple.

From Paris, I went to the University of Oxford on a Royal Commission for the Exhibition of 1851 Overseas Travelling Fellowship, where I worked on penicillin biosynthesis under the direction of Jack Baldwin.

I then returned to Ireland on a postdoctoral fellowship from the Irish government and worked at University College Dublin for a year. In 1985, I secured my lectureship in the School of Pharmacy in Trinity College Dublin (TCD). I was allocated a tiny lab with no equipment and no sink! But I did have one massive advantage – I was in a multidisciplinary school of pharmacologists, pharmaceutical botanists, medicinal chemists, and formulation scientists. We worked on multidisciplinary research long before it came into vogue.

I worked on metabolites from plants, plant cell cultures, fungi, and marine microalgae. One plant that I identified from traditional cultural use – a fern of the genus Onychium – gave us the lead for a novel molecular class that I subsequently brought to human clinical trials for the treatment of inflammatory bowel disease alongside my colleague, Neil Frankish, who handled the pharmacology arm of the research. On that leg of my academic odyssey, I co-founded the TCD spinout company Trino Therapeutics, where Gaia Scalabrino and I first worked together.

The Cell + Gene Curator: 2021 Retrospective

Looking back on 12 months of top stories from cell and gene therapy's avant garde

The Cell + Gene Curator collates the week's discoveries, process innovation, and business updates. Want it all in your inbox? Go here: *https://www.texerenewsletters.com/cellandgene*

Subscribed already? Good. Not quite sold? Keep reading.

Below, we round up a selection of some of the most striking and significant news we've curated over the past year – from collaborations between giants to great leaps forward in research and innovation.

January

In the quest to fine-tune CAR T cell therapy, researchers from the Dana-Farber Cancer Institute created a switchable CAR T cell that can be turned on or off with lenalidomide. A tag was added to the CAR T cells, which marks them out for degradation when the FDA-approved cancer drug is administered. The team also built an ON-switch CAR that only attacks tumor cells after lenalidomide treatment.

Bluebird bio announced that it would split into two independent publicly traded companies by the year's end – one focused on genetic diseases and the other on cancer. The company made good on its promise in 2021 and completed the split.

February

Researchers from Yale and Sapporo Medical University in Japan found significant improvements in motor function in patients with sustained, non-penetrating spinal cord injuries after an MSC infusion. For more than half of the patients, substantial improvements in key functions – such as the ability to walk or use their hands – were observed within weeks of stem cell injection, the researchers report.

The FDA approved Bristol-Myers Squibb's anti-CD-19 CAR T, Breyanzi (liso-cel), a treatment for adult patients with certain types of large B-cell lymphoma.

March

Researchers from Oregon Health & Science University set out to discover the short-term budget impact of a potential gene therapy for sickle cell disease among Medicaid programs with the highest prevalence of the disease. For a gene therapy priced at $1.85 million, they estimated a mean one-year budget impact of $29.96 million per state Medicaid program, or $1.91 per member per month increase in spending, in the 10 states of interest.

The UK's National Institute for Health and Care Excellence recommended Zolgensma, Novartis' £1.79m gene therapy for spinal muscular atrophy in babies.

April

The FDA approved its fourth CAR T cell therapy. Abecma from Bristol Myers Squibb and bluebird bio was cleared for use in adult patients with relapsed or refractory multiple myeloma, becoming the first anti-BCMA CAR T on the market. The approval was based on phase II data from the KarMMa trial, which revealed an overall response rate of 72 percent and a stringent complete response rate of 28 percent.

Researchers from Anhui Medical University, China, reviewed recent developments in CAR-macrophage-based treatments for solid tumors, citing "great potential" despite issues around cell proliferation and migration.

May

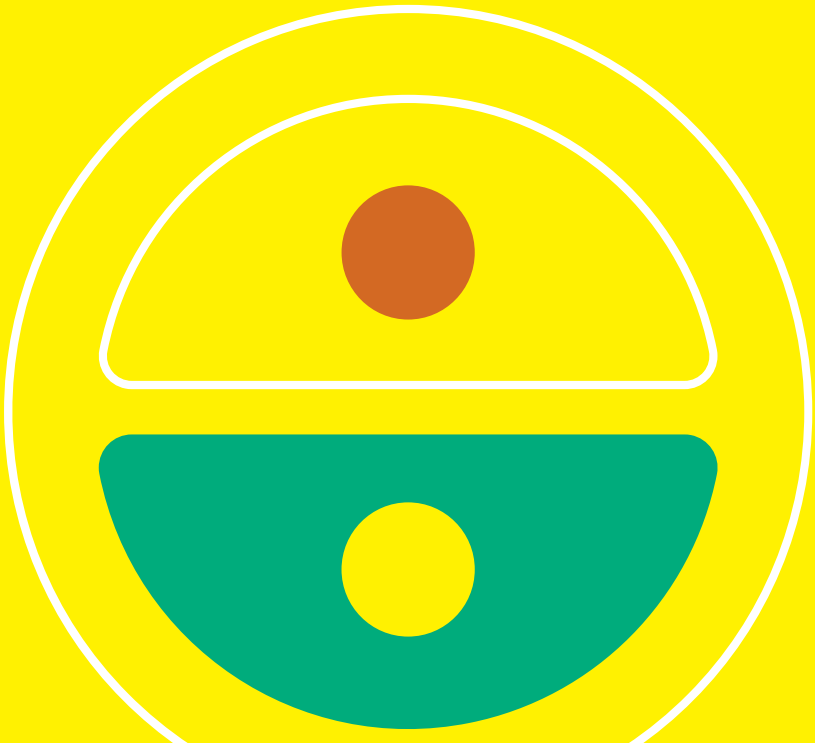
Researchers partially cured a patient's blindness with an AAV-vector encoding algae genes. The international team engineered a light-sensitive protein called ChrimsonR, which is found in unicellular algae, and then inserted it

cytiva

Accelerating the path to new therapies is ~~un~~attainable

The demands of innovation are evolving ever faster with each new discovery, each new molecule, each new insight. At Cytiva, we evolve with you, helping advance forward with flexible, modular solutions. We shorten the time to the next milestone and to market with automated manufacturing processes.

Together, we'll accelerate brave science.



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into modified viruses that were injected into a patient's eyes. With the treated eye, and while also using engineered goggles, the patient was able to locate, count, and touch different objects.

The International Society for Stem Cell Research released updated guidelines for stem cell research and its translation to medicine (https://bit.ly/3EUrzmJ).

June

Unproven stem cell therapy is a global problem that requires a global solution, according to three experts. The researchers called for a WHO Expert Advisory Committee on Regenerative Medicine to tackle the issue at the international level and provide guidance.

A deep learning system designed by Japanese researchers accurately identified individual skin stem cells grown under artificial conditions and tracked their motion, opening a possible means to improve the speed and efficiency of growing skin grafts (https://bit.ly/3J0bYVh).

July

Researchers studying how cells repair damaged DNA in low gravity used CRISPR to introduce double-strand breaks. The astronauts on the International Space Station who performed the experiments were the first to successfully edit a genome in space. Ok, this isn't technically a cell or gene therapy story, but should be of particular interest to CRISPR researchers out there.

Promising preliminary results rolled in from Aurion Biotech's IOTA trial, in which cells from two donors were used to treat 50 patients with corneal endothelial disease.

August

Researchers from the University of Zurich developed an in vivo prime editing (CRISPR-based genome editing technology) approach for the liver. They reached up to 58 percent editing rates in mice and were able to correct the disease-causing mutation of the phenylalanine hydroxylase (Pah)enu2 allele in phenylketonuria mice with an average efficiency of 8 percent (and up to 17.3 percent), which reduced blood phenylalanine levels.

In a fundraising round led by Lilly Asia Venture, Richard Wang's startup Neukio Biotherapeutics secured US$40m angel financing for allogeneic iPSC-CAR-NK development.

October

An African American family announced they were taking Thermo Fisher Scientific to court over their use of immortal cells taken from Henrietta Lacks at Johns Hopkins Hospital, shortly before she died of cervical cancer. The HeLa line cloned from her cells has been commercialized by various companies and has played a major role in modern medicine.

A team from the Technical University of Denmark enhanced CD8 T cell therapy by carrying out a systemic delivery of tumor-associated antigens in mice (https://go.nature.com/3GHMvhf).

November

A team of MIT and Harvard researchers designed an RNA-based control switch that could work to selectively trigger production of therapeutic proteins to help treat cancer and other conditions. The tech detects particular mRNA sequences in cells then triggers production from a transgene. It selectively eliminates the danger of off-target effects arising from the expression from incorrect cells, and so offers exciting new "control-circuitry" to the field of RNA therapeutics (https://bit.ly/3DUBLtS).

Australia's Carina Biotech contracted Singapore's CellVec to manufacture clinical-grade lentivirus. The move marked the opening move in Carina's new LGR5 CAR T manufacture process.

December

In mid-October, Vertex Pharmaceuticals announced positive phase I/II clinical trial data for their first patient dosed with VX-880, the company's stem cell therapy for type I diabetes. The treatment, Vertex reported, was well tolerated, improved glucose control, and saw a 91 percent decrease in the patient's need for insulin treatment. Now, the story has continued not through the medium of press releases, but via a profile of this "first man" published in the New York Times (https://nyti.ms/3GCEeem). His name is Brian Shelton. And the man behind the medicine is one Doug Melton. Melton began work on stem cell treatments for type I diabetes at Harvard after his son was diagnosed with the disease in 1991, but he had to dive into privately funded research after George W Bush outlawed spending of federal money on research using human embryos. The treatment Doug Shelton received is the result of that work.

Russia's Belgorod State National Research University launches lab for modeling and gene therapy of human diseases, as part of project to create Genetic Technology Research Institute by 2025.

The Cobalt-60 Pioneers

Richard Wiens, Director, Strategic Supply & Marketing, at Nordion explains the importance of Cobalt-60 – and why Nordion is a key player in this field

How is Cobalt-60 used in the pharma industry, and what is Nordion's role?

Gamma irradiation, using Cobalt-60, is used for a variety of applications in pharma, including the sterilization of drug packaging and single-use bioprocessing equipment. Sterilization of drug components such as APIs using gamma irradiation has also been on the rise.

Gamma radiation has been used safely and effectively for more than 50 years, so the process is widely understood and there is a large global network of sterilization providers with the necessary experience and expertise. These are all reasons that gamma is responsible for sterilizing more than 30 percent of the world's single-use medical devices.

Nordion is one of the pioneers in using Cobalt-60 for gamma irradiation. We have been building irradiation facilities and shipping Cobalt sources around the world for more than 50 years – and continue to be a leader in the space. Today, our customers include both contract sterilizers and medical device manufacturers.

There has been talk about using x-ray as an alternative to gamma; how do the technologies compare?

From a physics standpoint, the product can't tell the difference between the energy delivered by Cobalt-60 and x-rays from an accelerator. However, theoretical equivalence doesn't always play out in practical terms. The challenge with x-ray as a sterilization modality is that there is limited real-world experience at commercial scale. As more commercial x-ray facilities are constructed and operated, we should get better clarity of the true practical differences.

Everyone in the industry supports the idea of using the appropriate sterilization modality for the job. Gamma has a proven track record and accounts for a majority of radiation sterilization today, and there isn't a compelling reason established to make the switch.

Is there a Cobalt-60 shortage?

Cobalt-60 supply has been under pressure in recent years, but the amount of Cobalt-60 being made available to the market continues to grow, through initiatives at both Nordion and other producers. The latest addition to the mix is the re-introduction of production in Argentina from a reactor that had been offline for refurbishment. Not only is the new supply welcome, but the reactor will now operate for another 25-30 years, adding to the reliability of the Cobalt -60 supply chain.

Other projects are also helping to increase Cobalt-60 supply. Most of the world's Cobalt-60 is produced in a particular design of nuclear reactor called a CANDU. We have two projects – one in Canada and one in Romania – where existing CANDU units are being equipped to produce Cobalt-60. The Canadian project is at the stage where a significant amount of the engineering has been completed, and fabrication of the equipment has begun.

In another CANDU project, Nordion's largest supplier of Cobalt-60, Bruce Power, is looking at how they could increase the amount of Cobalt-60 being produced in their reactors.

The other major design of reactor currently producing Cobalt-60 is the RBMK, a Russian design. Nordion's supply partners in Russia have been working since 2017 to add new reactors to the Cobalt production fleet, and the first of this new Cobalt-60 will be harvested and shipped to the global market in 2022.

This image shows the interior of the Jefferson Institute for Bioprocessing state-of-the-art GLP pilot-scale bioprocessing facility featuring single-use end-to-end production capabilities. Printed with permission from the Jefferson Institute for Bioprocessing Nov 5, 2021.

Lastly, Nordion has been working with Westinghouse Electric Company to develop technology to produce Cobalt-60 in Pressurized Water Reactors (PWRs). This innovation is exciting as it brings scalability; more than two thirds of the approximately 450 reactors operating globally today are PWRs. We'll begin deploying the technology in the US, which has 65 operating PWRs alone, with a view towards first production in the mid-2020s.

Nordion also continues to increase recycling efforts so that Cobalt-60 being returned from the field after 20 years of use can be mixed with new Cobalt-60 and sent back out for another 20 years.

What is your advice to pharma manufacturers and other users of gamma?

Gamma is here to stay. The technology is proven and reliable and there is a large global network of experts and providers that understand it and can guide prospective users. It is also well suited for many pharmaceutical applications. In addition, the commitment that Nordion has made to ensure Cobalt-60 supply for the long term helps to ensure that Gamma will continue to be the workhorse of radiation sterilization for many years to come.

Learn more at www.nordion.com

Business

Economic drivers
Emerging trends
Business strategies

The New CDMO on the Block

Can ten23 health really make a difference to the planet while fully supporting its biopharma customers? We find out.

Featuring Hanns-Christian Mahler, CEO of ten23 health

You're a new CDMO – what's the story behind the company? And why is sustainability so important to you?

ten23 health was officially founded in May 2021 – and we went live the following September. We are offering development, manufacturing, and testing services for injectables out of our two sites in Switzerland.

Patients are our key priority, and we believe that businesses today should be "net positive" in the impact they have on society overall. We also believe that modern businesses should be based on new ways of working, so we put people at the heart of all we do and place a lot of emphasis on how we work together. Every decision should be made with the planet in mind. For us, fairness and sustainability merge into "fairstainability," and should be more than just terms in a corporate sustainability report. As a business, we strive to leave the world in a better shape than it would be without us.

What are the challenges of being sustainable in this industry?

Firstly, there is no clear definition of sustainability; many people aren't sure what it really means. Is it a planet focus? Or is it about greenhouse gas emissions? For us, sustainability means having a focus on both the planet and people. It means reducing waste, such as plastic. It means considering everything we do as a company, what our suppliers do, and what is being done with our services and products – and how all these things affect the world around us. We consider the impact and harm we may do, and how we can reduce, reuse, recycle, and develop other solutions. Only as a last resort do we consider offsetting. As a business, we want to make sure all our employees are thinking about the consequences of actions on a daily basis – even the small things: "Do I need to print this contract?" or "Can I commute by public transport or bike?"

Secondly, it is difficult to obtain meaningful and relevant information about sustainability efforts from suppliers. For example, which computer (hardware) companies operate sufficiently sustainably? What about insurance providers? There are many labels and many claims – most companies strive to achieve some sort of certification for sustainability efforts – but it is sometimes difficult to make a judgement based on relevant first-hand information. In any case, are these labels the best channel to communicate that sustainability is really a key focus for that company – especially in a world of greenwashing? Nevertheless, we've found there is limited interest in entering deeper conversations about sustainability

"We're also thinking a great deal about how we cope with the amount of single-use plastic in the industry."


Hanns-Christian Mahler

with some providers…

Thirdly, there are remaining technical challenges in the pharma and CDMO environment. As an example, pharma companies rely on single-use plastic materials during lab activities (for example, tubes, pipette tips, and so on) and for manufacturing (for example, bags, tubings, filters). Clearly, they can be considered a necessary evil to eliminate the risk of cross-contamination or to mitigate the challenges of cleaning validation. But it's hard to escape the fact that there is a lot of plastic in today's operations.

As a final thought, pharma companies often say they focus on the patient, but sustainability is an afterthought. Personally, I don't think this should be an "either–or" discussion. You can focus both on the patient and sustainability – for the benefit of patients, all people, and the planet.

How do you plan to address these challenges in the services that you offer?

We consider "sustainability" very broadly, including carbon dioxide, water, energy, and plastic. We think about this for all business decisions, including choice of laptops, cell phones, pension fund insurance, and so on. We've even installed a composter in Basel to manage and handle our own organic waste. We also operate on 100 percent renewable energy – and we want to go even further.

In our efforts to focus on the planet, we collaborate (and plan to collaborate with) specific partners who can help us measure, minimize/reduce and offset, and provide other opportunities for us to give back.

We are discussing sustainability topics with our employees and we hope we can make them aware of topics that may be overlooked in daily life – be it meat consumption, commuting, or business travel. We also support our employees in their carbon footprint assessment and – despite the risk of greenwash – we do strive for sustainability certifications. We are receiving support from different providers, including Swiss Triple Impact, Leaders For Climate Action, and B corp.

Going back to a pharma specific challenge, we're also thinking a great deal about how we cope with the amount of single-use plastic in the industry. There is certainly a multiyear journey ahead of us!

How did you come to partner with Seven Clean Seas?

I personally came across Seven Clean Seas because of their partnership with the Berlin startup Einhorn – a company with a great focus on sustainability. One of their founders, Waldemar Zeiler, also wrote a fantastic and thought-provoking book ("Unfuck the Economy"). I started to support Seven Clean Seas with some personal contributions over time and, when founding ten23 health, it seemed obvious to partner with them. They have a focus on cleaning plastic waste from nature and beaches to preserve the habitat for animals. It's great to be able to support something like this.

How have others in the pharma industry responded to the formation of the company and your dedication to sustainability?

There have been a few different reactions! I have received a lot of very positive feedback, with some saying it was about time that a pharma CDMO had a real focus on the "triple bottom line" – in other words, not being solely led by financial decisions in its directions and strategy, but also deeply considering people and the planet. Others have noted that such idealism is not scalable or that we must be hippies… (What's wrong with rebels and hippies?)

Personally, I hope that we at ten23 health can provide a few examples that others may follow. It is time for the pharma sector to embrace sustainability in its entirety.

How would you encourage others in the pharma industry to think more sustainability?

Try to leave the world in a better place than it was before. Think net positive.

Scaling Advanced Therapies

Sitting Down With… Jason C Foster,
Chief Executive Officer and
Executive Director, Ori Biotech

What led you to the sciences?

A sizable portion of the mail in my spam folder is addressed to "Dr Foster", and I often wonder: who is that? I only have a marketing degree from Columbia...

After completing my undergraduate degree at University of Virginia, I went to Washington DC, where I eventually became a lobbyist for various healthcare organizations. It was a great chance for me to witness policymaking first hand. But once you've seen the "sausage" getting made, you can't unsee it! I became quite disillusioned and turned my eyes to the private sector where healthcare innovation was happening. I went to Columbia Business School to assist that transition, and in 2003 ended up in marketing at Merck-Medco.

How did your move to the UK come about?

When we talk about our lives in retrospect, we make everything sound so well-planned, but reality is a little more haphazard. My then employer asked if I'd like to take charge of expanding the business in Europe. At that time, we had a two-year-old, my wife was five months pregnant, and we had just bought a house. Call us crazy, but we went for it! We sold our house, picked up sticks, and moved to London. Today, the city is our home and my family loves it here. Both my kids are proper Brits, accents and all. They play cricket, netball, and other strange sports that I don't fully understand.

What led you to Ori Biotech?

When I met the founders of Ori, I was living a cushy life as a consultant, investor, and non-executive director. However, the compelling story of cell and gene therapy (CGT) pulled me back into a full-time operational role. When I learned that we had cures for cancer that patients can't access because of prohibitively expensive costs, I decided that was an untenable outcome and something had to be done. Every year, ten million people die of cancer and another ten million people per year are diagnosed with it. Having a chance to positively impact that number excited me, and that's why I decided to get involved with Ori Biotech.

I began by helping Ori secure its seed stage investment. If you ask my lead investor what happened next, he'll tell you that I briefly lost my mind and pledged not only my financial capital but my human capital as well by joining the business full-time.

A grand challenge – so where to begin?

Ori's mission is to democratize patient access: how do we deliver these living medicines, personalized to an individual patient, at large scale? Solving this problem means re-thinking the challenges from the ground up: tabula rasa. What is unique about Ori is that our technology has been developed in a bespoke fashion by experts in CGT manufacturing to specifically solve the problems of this sector. This has resulted in truly novel full-stack technology including hardware, software, data services, and automation that we use to solve the problem holistically. It's already been demonstrated that the industry can't solve these new problems with old thinking and repurposed technologies.

Another part of our approach has been to form ecosystem partnerships with best-of-breed tech companies in other parts of the CGT value chain. For example, in the modular cleanroom space we've formed partnerships with industry leaders like G-CON and Germfree. Their modular technologies allow our customers to operate without investing tens or even hundreds of millions of dollars into a facility of their own. On the digital side, we have partnered with organizations like Cardiff's TrakCel, California's Vineti, and ATMPS, based here in London. They manage data flows from the patient to the manufacturing facility and back again, which lets us track and trace the chain of identity and chain of custody. Handling personalized medicines is a zero defect scenario – mixups can't happen.

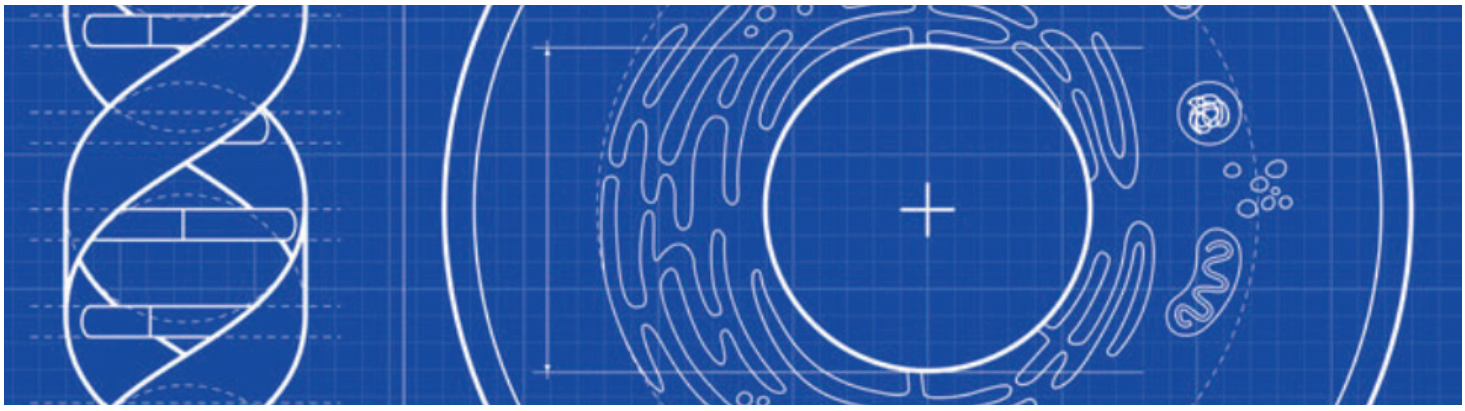
Through these collaborations in manufacturing, data tracking, and more in raw materials and software, we're trying to shine a light into the black box of CGT manufacturing. We want to have full transparency at every point in the vein-to-vein process. We don't want our therapy developers, CDMOs, and academic partners to continue to have to spend time and money cobbling together technologies that were never meant to work together. We want to bring to the market a pre-integrated platform where the heavy lifting has already been done, and does not need to be repeated.

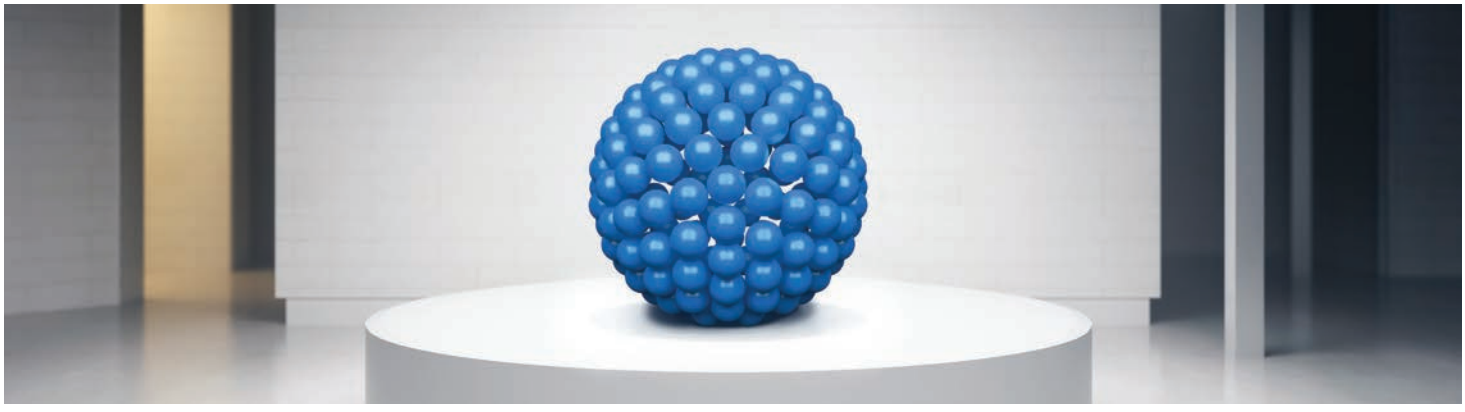
Are you optimistic about the future?

I couldn't be more positive about the future of CGT! Despite all the technical and budgetary constraints we face, I agree that advanced therapies are the third pillar of medicine. To help this industry achieve its potential, we need to form a collective mindset.

At a fundamental level, we need to reset the measuring stick for success to be the number of patients successfully treated. Just getting products into the clinic or approved is no longer good enough. We also need to enable widespread patient access for these incredible therapies which have curative potential. Working with innovators, therapy developers, academic researchers, and CDMOs to try and solve these problems will be really important. Essentially, the only way to achieve this is with a cooperative effort – we need to play nicely together in the pre-competitive sandbox.

Last year, around US$20 billion was invested in advanced therapy, and in the first three quarters of 2021 over $25 billion was invested. Investors go where opportunities are – and that means they need proof that CGT is a viable treatment modality – otherwise, the whole field could be in danger of going down in history as little more than an interesting research project. "Fascinating science, admirable approach... but not never quite got there," they'll say. We cannot let that happen.





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