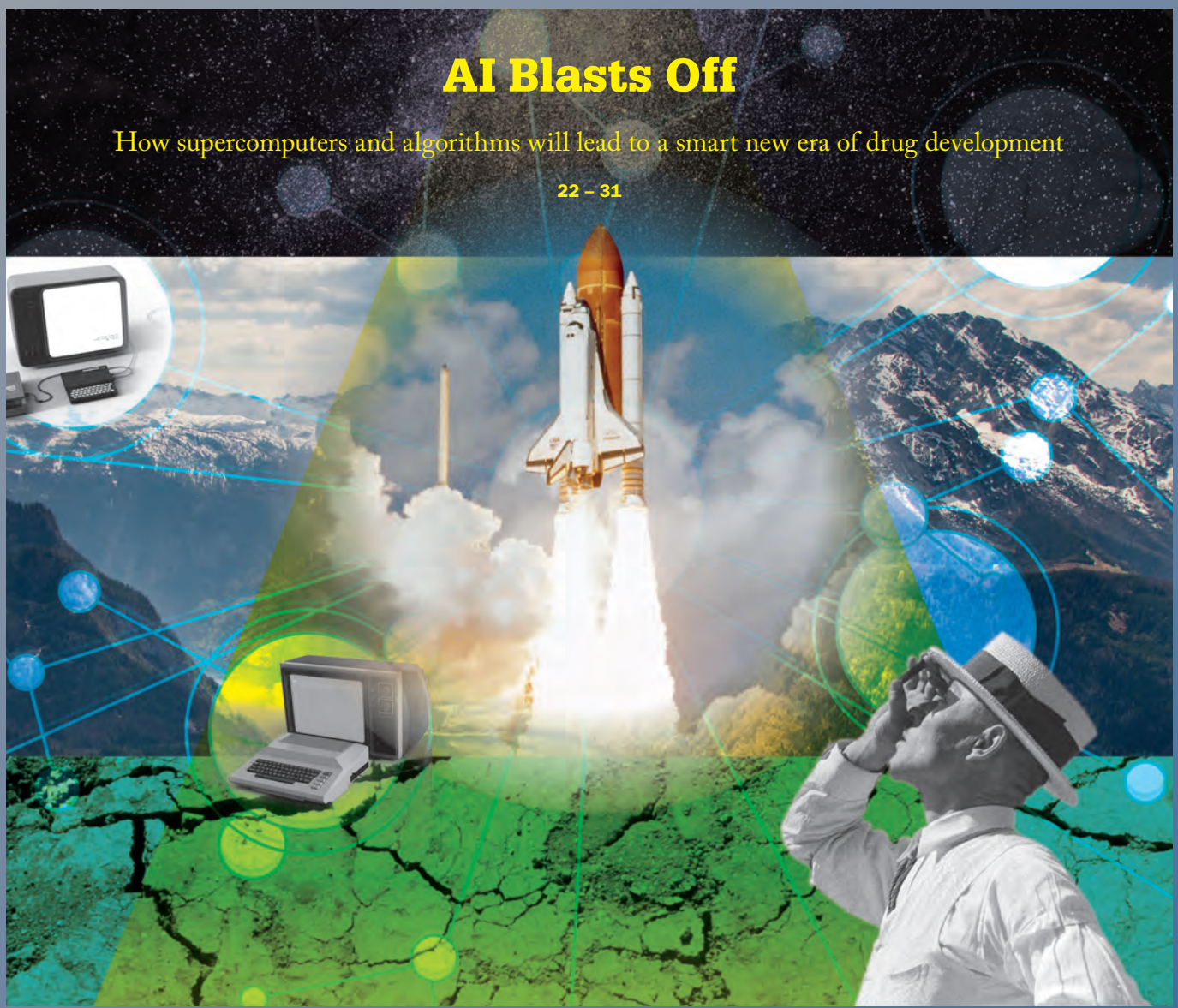
JUNE 2021 # 76

the Medicine Maker®

AI Blasts Off

How supercomputers and algorithms will lead to a smart new era of drug development

22 – 31



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What Do We Do About Distribution?

COVID-19 vaccine rollout is a lottery, with some countries faring much better than others

Over 70 percent of people over the age of 18 have received a first dose of COVID-19 vaccine in the UK. And over 40 percent have received two doses.

But when it comes to my country's progress, I can't say I'm particularly proud. The UK has received a steady supply of vaccines ever since the first approvals. Meanwhile in some low-income countries, even frontline healthcare workers have not yet been vaccinated. And in other wealthy European countries, there are still substantial numbers of vulnerable people who are not vaccinated. I have four relatives (aged 63–75) living overseas in EU countries; two have received a first dose but were turned away from booked appointments to receive their second doses because of a lack of supply (one month later and still no sign). The remaining pair have yet to receive their first dose...

In a post written for the London School of Economics and Political Science's EUROPP blog, Gareth Davies reported that EU states agreed early on that it would be "unacceptable" for some states to vaccinate their populations while others had nothing (1). Vaccines have been distributed in the EU on a per capita basis. Meanwhile, the UK is rapidly vaccinating people in their early thirties. Details of contracts between pharma manufacturers and various governments have not been revealed, but it could be that UK contracts have clauses for preferential supply. British nationalists have applauded the UK's shrewd negotiating skills. Though I am grateful that I can be vaccinated, I'm not able to justify the fact that I am receiving it ahead of others who need it more. Clearly, there are inequalities in global vaccine distribution.

Some believe that a waiver on COVID-19 vaccine patents may help. In a shock announcement last month, the Biden administration declared that the US would support such a move, despite the US previously opposing patent waivers (2). But pharma industry advocates, including IFPMA, PhRMA and EFPIA, are strongly against interfering with patents – and claim that it could damage the global battle against the virus by distracting from the manufacturing and scale up challenges.

I can't say if patent waivers are the correct way forward. There are powerful arguments on both sides of the debate (see page 10). But I do know that desperate times call for desperate measures – and a global death toll of over 3.5 million sounds desperate to me. We need to thoroughly explore all avenues to see if they have merit – even if they may be controversial in some camps.

Stephanie Sutton
Editor

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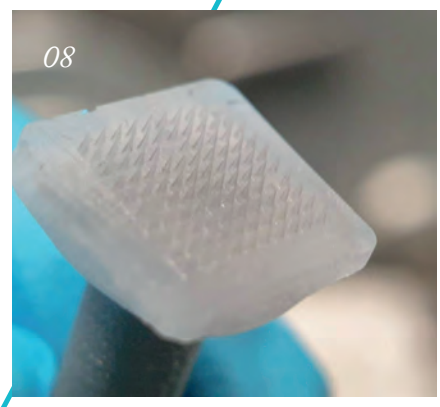

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AI takes off in the pharma industry

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the Medicine Maker

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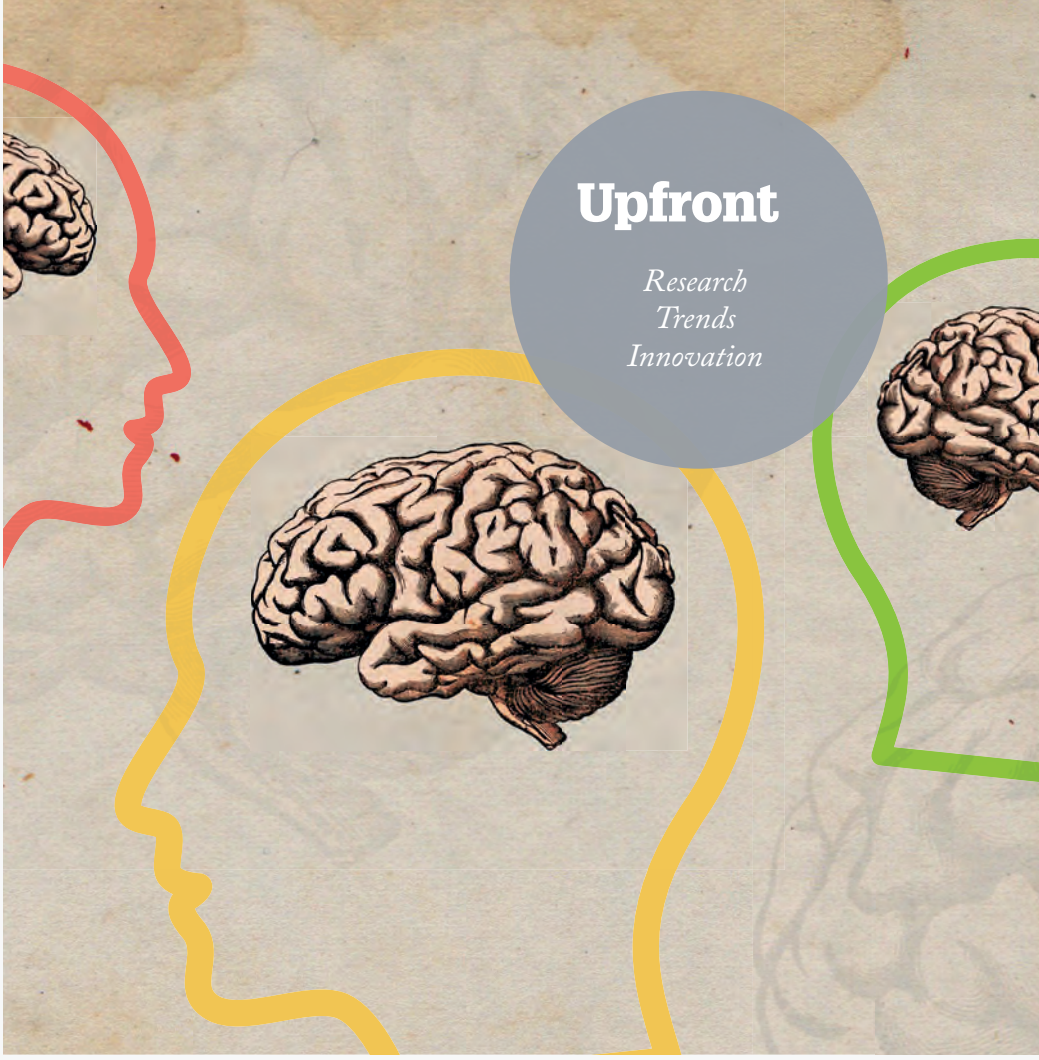

Results That Last

Could zinc finger therapy hold the key to treating Alzheimer's disease?

Imagine treating Alzheimer's disease (AD) at the genetic level. Now consider researchers at Sangamo Therapeutics who have found that gene regulation therapy helps prevent the build-up of tau protein in the brain (1).

"The tau protein is predominantly found in neurons. One of tau's main functions is to stabilize the microtubules – small structures within the nerves – that are important to ensure impulses are conducted between neurons," says Amy Pooler, Head of Neuroscience at Sangamo. "In AD, the tau protein is abnormal and tangles into various forms of toxic aggregates that disrupt communication between neurons, and ultimately lead to cell death."

The team decided to attempt lowering expression of the tau gene at the transcriptional level using gene-silencing zinc finger protein transcription factors (ZFP-TFs) – and observed specific, durable, and controlled reduction of endogenous tau production.

"With our ZFP-TFs, we have the potential to shift the treatment paradigm for AD from symptom management to lasting cures," says Pooler.

Sangamo CEO Jason Fontenot hopes the research can be applied to other debilitating neurological disorders – and the company has formed partnerships with the likes of Biogen and Novartis to look at how the approach can be applied to other therapeutic areas. Fontenot says, "Genome regulation is just one tool in our genomic medicines kit. Though our collaborations in this space just kicked off this past year, we are encouraged by our progress in moving the research forward."

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INFOGRAPHIC

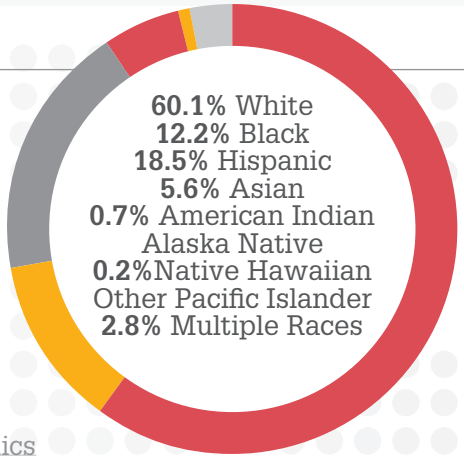
The Minority Report

Are US clinical trials truly representative?

Source: Parexel (2021). Available at https://bit.ly/3uqw3eK.

In 48 clinical trials for drugs approved in the US in 2019:

9% of participants were black
72% of participants were white
18% of participants were Hispanic
9% were Asian



US demographics

BUSINESS IN BRIEF

Manufacturing violations, regulatory probes, and advertising campaigns... what's new in business?

- Due to alleged manufacturing and records violations at Eli Lilly's Branchburg, New Jersey site, the US Department of Justice (DOJ) has issued the company a subpoena. During a 2019 inspection, it was found that documents related to manufacturing processes were missing. Reports also suggest that some documents were altered to minimize the extent of quality control issues. The DOJ is now requesting that the company, which is complying with the investigation, provide the documentation.
- AstraZeneca is reportedly holding discussions with the US government to move its COVID-19 vaccine production from Emergent BioSolutions' plant to another CDMO. Previously, a batch of J&J's vaccine was contaminated with ingredients from AstraZeneca's.
- AstraZeneca is also being probed by the UK's antitrust watchdog, the Competition and Markets Authority, for its acquisition of Alexion – a company focused on developing therapies for rare diseases. The US$39 billion deal must be cleared by the authority to allow AstraZeneca to expand its offering for areas of unmet need. The final decision will be issued by July 5.
- The Pharmaceutical Research and Manufacturers of America has launched a lobbying group against President Biden's plans for a patent waiver for COVID-19 vaccines. The organization has developed a digital advertising campaign to protest the administration's proposed idea with Google advertisements that read, "Biden's Harmful Vaccine Stance" and "Biden's Damaging IP Stance."
- AbbVie faces questioning from the US Senate for its tax record. The company, which is under investigation for its approach to drug pricing, is now under scrutiny as its American arm continues to lose money and questions arise as to why it doesn't pay more in tax. Senator Ron Wyden penned a letter to the company's CEO inquiring about its current financial situation. "It appears that AbbVie shifts profits offshore while reporting a domestic loss in the United States to avoid paying US corporate income taxes," he said in the letter.

A Tailored Solution

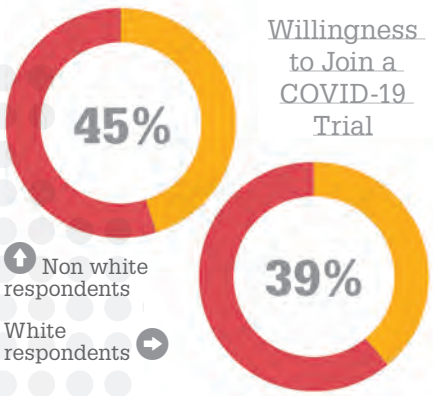
Reinventing drug delivery with polymeric threads

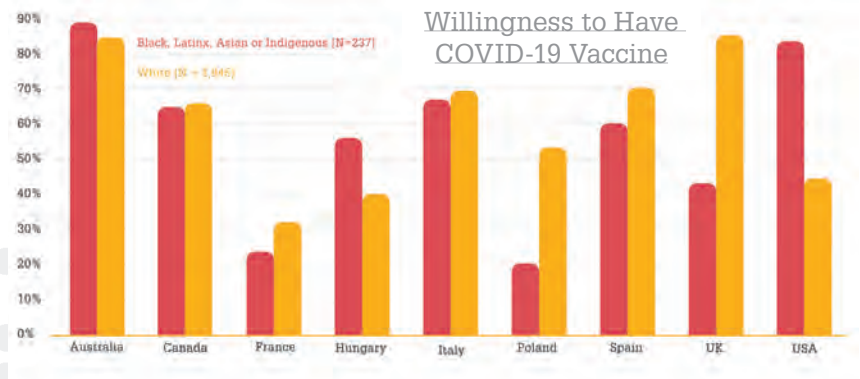
Researchers at the University of California, Riverside have used a technique known as electrospinning to develop a membrane made of polymeric threads that enables localized administration of drugs to sites in the body (1). The membrane is loaded with therapeutic material and embedded into a hydrogel, and the researchers expose it to shock waves that generate an electrical charge, allowing for controlled release of medicines.

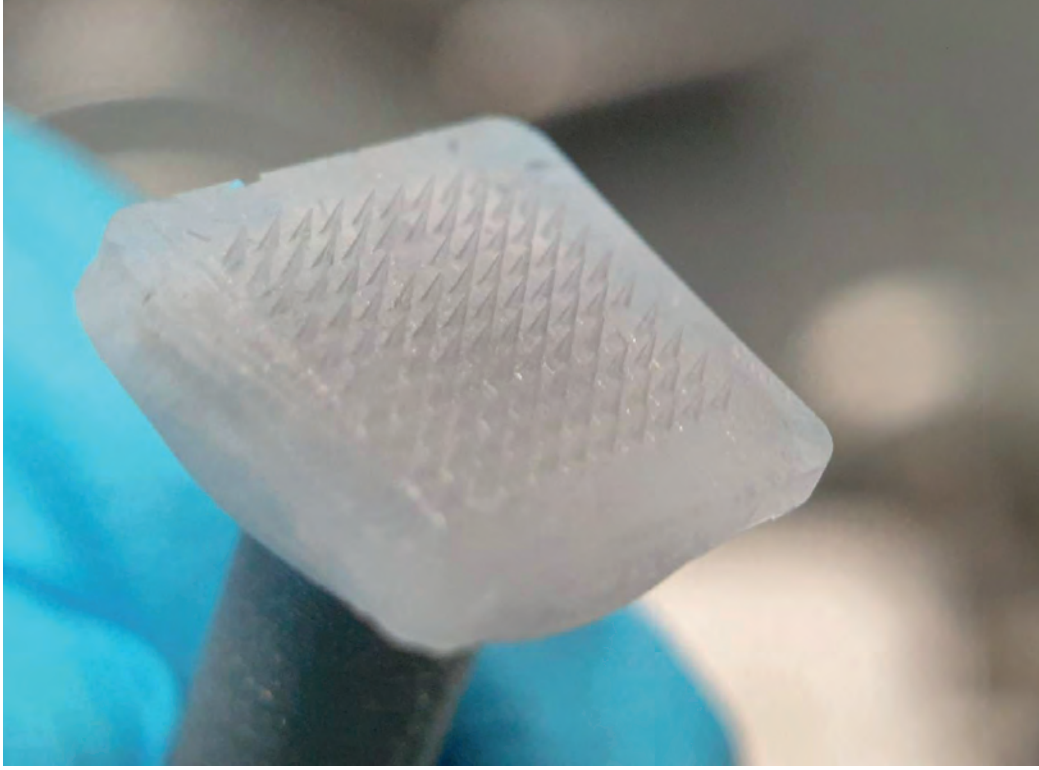
According to the team, changing the size of the threads achieves different release kinetics. Smaller threads can deliver drugs to deep tissues; larger threads administer medicines to subcutaneous tissues. The Riverside researchers expect that their method could help overcome various traditional drug delivery challenges, including the nonspecific distribution of medicines throughout the body.

Reference

1. *T Jariwala et al. ACS Appl. Bio Mater. (2021). DOI: 10.1021/acsabm.1c00232*







Melt Away Delivery

Could frozen microneedles change the way we deliver cell therapies?

Researchers have designed and developed a microneedle technology to allow intradermal delivery of cell therapies for the treatment of skin disorders (1). The team, led by Xu Chenjie, Associate Professor at the Department of Biomedical Engineering at City University of Hong Kong, has produced cryogenic microneedle patches (cryomicroneedles) that melt after delivering the therapeutic payload. Traditional cell delivery methods usually involve hypodermic needles and surgical intervention.

Commenting on the development, Xu says, "The cryomicroneedles are manufactured by micromolding an optimized cryogenic medium and pre-suspended therapeutic living cells at extremely low temperatures (-20 to -196°C). The original process relied on the crystallization of ice, which held the potential to kill the cells used, but the cryogenic medium we developed helped avoid this issue by protecting the cells."

The needles measure less than 1 mm and deliver loaded living cells into the skin.

In healthy mice, cells delivered using the cryomicroneedle patch retained viability and proliferative capability. And in mice with subcutaneous melanoma tumours, the delivery of ovalbumin-pulsed dendritic cells using the cryomicroneedle approach led to higher antigen-specific immune responses and slower tumor growth compared with intravenous and subcutaneous injections of the cells.

Xu believes this approach would help avoid complex processes such as cell harvesting and the preparation of cell-infusing solution during administration of a cell therapy. "Another important design feature is the fact that cells packed into cryomicroneedles can be stored for months, allowing easy transportation and deployment," says Xu.

The cryomicroneedles aren't limited to cell therapy delivery; they can also be used to package, store, and deliver a variety of bioactive therapeutic agents, such as proteins, peptides, and vaccines – potential applications Xu hopes to explore in future studies.

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Time for a Change

How legislation can potentially hinder pharmaceutical progress

A position paper published by an industry coalition cast scrutiny on current EU laws on advanced therapies (1). Under the region's legislation, advanced therapies are subject to genetically modified organism (GMO) laws, which were originally introduced to regulate the production of food and protect the environment. According to the coalition, the laws are also slowing the progress of advanced therapies in clinical development. The opinion has been supported by the European Commission, who agrees that current guidance is hindering the field.

"The European Commission recognized that time was of the essence when lifting GMO requirements for COVID-19 vaccines and treatments," said Paige Bischoff, Alliance for Regenerative Medicine's Senior Vice President of Global Public Affairs, in a statement.

Reference

1. *M Werner et al., Hum Gene Ther (2021). DOI: 10.1089/hum.2021.058*

IMAGE OF THE MONTH

Research Accelerated

An international research coalition is using a new protocol to describe 3D structures of SARS-CoV-2 molecules using nuclear magnetic resonance spectroscopy (NMR). Their NMR approach allows for active compounds that bind to viral proteins to be quickly identified, helping to fuel the next stages of pharmaceutical R&D.
Credit: Uwe Dettmar for Goethe-University Frankfurt, Germany

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QUOTE of the month

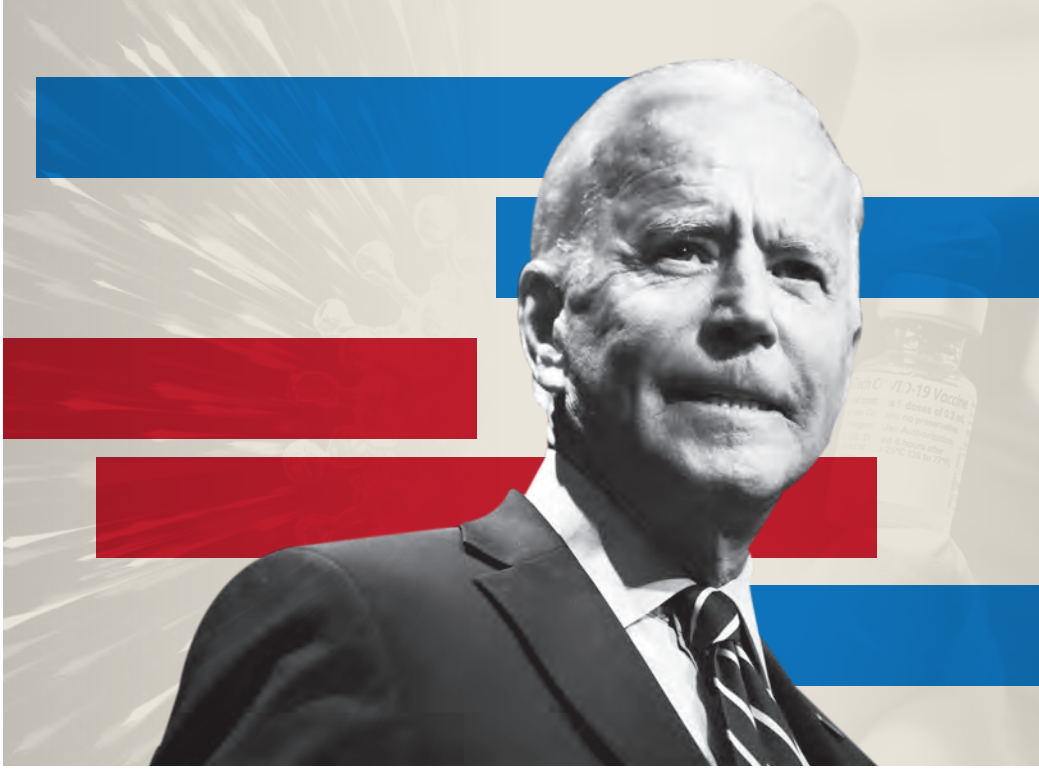
"Over the last few years, we have seen almost limitless opportunities for AI to disrupt all points of the healthcare spectrum – from medical records to drug discovery. But we need to focus on where we can have the most tangible impact now and what to work towards in the long term,"

Brandon Allgood, Chief AI Officer, Valo Health, and Chairperson of The Alliance for Artificial Intelligence in Healthcare. https://bit.ly/3bV1OIW

A Celebration of Design

ACG secures an industry award for its sustainable machinery

ACG has scooped up an iF Design Award for its latest packaging machine, Karton X. The prize, which celebrates innovative product design, was awarded for the instrument's human-machine interface, UX design, and smart connectivity. Though Karlton X was designed to pack blisters, bottles, tubes, vials, and ampoules in secondary packaging, a key focus for ACG was its sustainability. The company produced the system using recyclable materials such as steel, aluminum, and Corian. Karan Singh, Managing Director of ACG, says, "For us, this award is a validation that ACG is addressing the needs of the wide range of pharma manufacturing companies we work with. It acknowledges our drive for innovation and reflects our philosophy of designing and manufacturing high-quality, reliable, and innovative machines."



The Patent Waiver War

Is waiving patents for COVID-19 vaccines the right step forward?

The Biden administration has agreed to support negotiations at the World Trade Organization on waiving patent protections for COVID-19 vaccines – joining over 100 countries who already back the proposal. The hope is that this will address inequities and shortages in vaccine supply. However, there is a clear split in opinions on the matter across the world. Here, we round up a selection of quotes from key stakeholders.

Those for

Biden administration (1): "This is a global health crisis and the extraordinary circumstances of the COVID-19 pandemic call for extraordinary measures. The Administration believes strongly in intellectual property protections but, in service of ending this pandemic, supports the waiver of those protections for COVID-19 vaccines. We will actively participate in text-based negotiations at the World Trade Organization (WTO) needed to make that happen."

MSF (2): "The temporary waiver would apply to certain IP on COVID-19 medical tools and technologies until herd immunity is reached. It was originally proposed by India and South Africa in October 2020 and is now officially backed by 58 sponsoring governments, with around 100 countries supporting the proposal overall. Even after one year of this pandemic and 2.5 million deaths, we still see certain governments denying that removing monopolies on COVID-19 medical tools will help increase people's access to needed treatments, vaccines, and tests going forward. The waiver proposal offers all governments opportunities to take action for better collaboration in development, production, and supply of COVID-19 medical tools without being restricted by private industry's interests and actions and, crucially, would give governments all available tools to ensure global access."

UNAIDS (3): "We are in a race to vaccinate the majority of the world's population to curb death tolls and before more potent variants of COVID-19 emerge, rendering current vaccines ineffective. The faster we can scale up global vaccine supply, the faster we can contain the virus and the less chance we will face a day when variants prove resistant to existing vaccines. As the United Nations Secretary-General Antonio Guterres has said, "No one is safe until everyone is safe." The TRIPS waiver would enable the sharing of technologies, data, know-how, patents, and other intellectual property rights across the world."

WTO (4): "The R&D of drugs is often a joint multi-stakeholder effort benefiting from significant amounts of public taxpayer money. For COVID-19, the search for an effective treatment or vaccine is a global effort involving multiple actors – it is not the result of the pharmaceutical industry's efforts alone. Governments and public funding agencies around the world have poured billions of US dollars of public money to support COVID-19 R&D, especially for drugs and vaccines. However, by and large, no conditions for access or affordability have been included as a precondition to any of that funding. Governments must attach strings to any public money given for COVID-19 medical tools to guarantee that, if they prove safe and effective, they are available to everyone. Today some members have admitted that some conditions had been set on companies, but none of it goes far enough to ensure that IP rights assigned to companies benefiting from taxpayer money do not abuse such rights down the line."

Those against

IFPMA (5): "A waiver is the simple but the wrong answer to what is a complex problem. Waiving patents of COVID-19 vaccines will not increase production nor provide practical solutions needed to battle this global health crisis. On the contrary, it is likely to lead to disruption while distracting from addressing the real challenges in scaling up production and distribution of COVID-19 vaccines globally: namely, elimination of trade barriers, addressing bottlenecks in supply chains and scarcity of raw materials and ingredients in the supply chain, and a willingness by rich countries to start sharing doses with poor countries."

EFPIA (6): "This short-sighted and ineffectual decision by the Biden administration puts the hard-won progress in fighting this terrible disease in jeopardy. While we wholeheartedly agree with the goal of protecting citizens around the world through vaccines, waiving patents will make winning the fight against the coronavirus even harder… Increasing capacity to deliver doses to citizens around the world requires the skills and technical know-how of the vaccine developer to bring on board partner manufacturing organizations. You simply cannot achieve this kind of capacity expansion by waiving patents and hoping that hitherto unknown factories around the world will turn their hand to the complex process of vaccine manufacture. A waiver risks diverting raw materials and supplies away from well-established, effective supply chains to less efficient manufacturing sites where productivity and quality may be an issue. It opens the door to counterfeit vaccines entering the supply chain around the world. Capacity expansion is only achievable through voluntary, collaborative partnerships between the innovators behind each vaccine and expert manufacturing partners. All our focus should be on removing barriers to collaboration, ensuring the free flow of materials around the world and continuing the research effort."

PhRMA (7): "In the midst of a deadly pandemic, the Biden Administration has taken an unprecedented step that will undermine our global response to the pandemic and compromise safety. This decision will sow confusion between public and private partners, further weaken already strained supply chains and foster the proliferation of counterfeit vaccines.

"This change in longstanding American policy will not save lives. It also flies in the face of President Biden's stated policy of building up American infrastructure and creating jobs by handing over American innovations to countries looking to undermine our leadership in biomedical discovery. This decision does nothing to address the real challenges to getting more shots in arms, including last-mile distribution and limited availability of raw materials. These are the real challenges we face that this empty promise ignores.

"In the past few days alone, we've seen more American vaccine exports, increased production targets from manufacturers, new commitments to COVAX and unprecedented aid for India during its devastating COVID-19 surge. Biopharmaceutical manufacturers are fully committed to providing global access to COVID-19 vaccines, and they are collaborating at a scale that was previously unimaginable, including more than 200 manufacturing and other partnerships to date. The biopharmaceutical industry shares the goal to get as many people vaccinated as quickly as possible, and we hope we can all re-focus on that shared objective."

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In My View

Experts from across the world share a single strongly held opinion or key idea.

Navigating the Uncertainty

How collaboration and innovation – bolstered during the COVID-19 pandemic – will guide the future of stem cell transplantation

By Lori Muffly, Hematologist, Stanford Health Care; Assistant Professor of Medicine (Blood and Marrow Transplantation) at Stanford University Medical Center, Stanford, California, USA

More than a year has passed since the start of the COVID-19 pandemic, marking an appropriate milestone to reflect on how the healthcare system has evolved, the difficulties we have faced, and what we have accomplished for patients during this challenging time. For our team of hematology and blood and marrow transplant specialists at Stanford Health Care, the past year has been full of obstacles but – importantly – also innovative solutions.

At the start of the pandemic, we made a crucial decision to continue bringing blood and marrow transplantation (BMT) to patients during COVID-19 as long as we could do it safely. Over the past year, we've learned a great deal. The pandemic forced us to quickly adapt our practices, which has made us more efficient in ways that we anticipate will continue to save lives.

For the past six years, I have worked at Stanford as a physician specializing in BMT. Though I am one of the attending physicians on our team, the full experience of transplanting a patient often requires experts who identify suitable donors, address financial and logistical roadblocks and, in general, make the work that I do possible. In addition to donor search coordinators Jennifer McAtee and Leah Schroer, who work tirelessly every day to oversee and manage the intricate details of patient case progression, one of our strongest collaborators is the National Marrow Donor Program (NMDP)/Be The Match – a nonprofit organization that manages the collection and transport of donor cells through a worldwide network of affiliated organizations. From early-morning emergency meetings to late-night texts with Jenn and Leah to confirm a successful match, my work is part of a delicate process enabled by a collaborative network of people all working toward the same goal: saving lives.

The current pandemic has made the importance of that network even clearer. As new challenges – including a >70 percent reduction in commercial flights

"The past year has been full of obstacles but – importantly – also innovative solutions."

(rendering cell transport extremely difficult) and restrictions on in-person donor and patient appointments – were introduced in spring 2020, our team remained focused on our commitment to patients, most of whom were not in a position to wait for a lifesaving transplant.

Making transplantation possible during a pandemic required looking beyond our standard practices. We expedited new initiatives to streamline donor matching and cell collection, overcome logistical barriers, and prioritize donor and patient safety. NMDP/Be The Match provided essential support within each of these areas.

For example, we knew we needed to expedite HLA confirmatory typing to quickly match donors to patients and speed the path to transplant. Using NMDP/Be The Match's FastTrack Testing service allowed us to do that. Our team helped NMDP/Be the Match pilot the FastTrack program prior to the start of the COVID-19 pandemic – and the benefits of that early partnership were greater than we could have imagined.

Another change made by NMDP/Be the Match in response to travel uncertainty was to collect donor cells farther in advance of a patient's transplant therapy and to have transplant centers cryopreserve donor cells (i.e., freezing cells rather than delivering them fresh) to ensure that they're available on time for patients. This provided certainty but also introduced new logistical challenges, because some of Stanford's cutting-edge cell therapy research requires the use of fresh, unfrozen cells. We carefully reviewed each patient's case to determine who qualified for these clinical trials and whether their donor was close enough to our center to avoid courier travel delays, ensuring that important cancer research could continue despite the pandemic.

Our BMT program also chose to use in-home and remote typing for our related donor transplants through NMDP/Be The Match's Related Donor Services program, which provides financial and logistical support for donors within families (reducing or eliminating the need for family members to travel). Importantly, the NMDP/Be The Match team developed a novel support system to enable related donor collections during the pandemic, including custom workup programs to ease the process of clearing donors for transplant centers like ours. All these changes provide efficiencies that extend beyond the pandemic.

"I like to tell my patients that navigating the steps leading to transplantation is like skiing the bumps – you have to be nimble and flexible throughout the process."

We also worked closely with NMDP/Be The Match to advance their donor optimization efforts, which included the development of a Donor Readiness Score to calculate key components of donor matching and identify the best candidates as quickly and smoothly as possible.

Though the relevance of these initiatives goes beyond the current pandemic, their advancement during this challenging time was critical. Through the support of our program's stellar team and our partnership with NMDP/Be The Match, we not only managed to continue providing transplants during the pandemic, but performed over 400 transplants in 2020 – more than any other year of our program's 30+ year history.

The way I communicate with patients has evolved, too. Although I have always prioritized conversations that allow my patients to feel comfortable, the increased uncertainty introduced by COVID-19 has significantly underscored the benefits of transparent, continuous communication throughout the transplant process. As an avid skier, I like to tell my patients that navigating the steps leading to transplantation is like skiing the bumps – you have to be nimble and flexible throughout the process. As the pandemic has evolved, the team and I learned to anticipate problems sooner and coach patients more smoothly through the bumps, helping them overcome the uncertainty by emphasizing the support systems in place to guide them.

COVID-19 has introduced an unprecedented level of uncertainty and challenge to the transplant field, but it has also led to important positive outcomes for researchers, physicians, and patients. Our collaborative work with NMDP/Be The Match has helped us advance the field of stem cell transplant in ways that will have an impact far beyond COVID-19. Collectively, we are stronger and smarter than we were a year ago – and, through every change, our focus on patients has endured. As our knowledge evolves, we will continue to prioritize sharing our insights with the broader transplant community and encouraging others to share their own experiences as we create space for continued innovation in the years to come.

Making Good Vaccines Better

Mighty mRNA molecules have won the COVID-19 vaccine race, but there is room for improvement when it comes to effectiveness, if not efficacy

By Nigel Theobald, CEO at N4 Pharma, UK

Now that several vaccines have reached the market and many others are in development, I feel it's a good time to take stock of where we are – and, more importantly, where we are going. And I think it is also important to make the distinction between efficacy (reduction of disease) and effectiveness (ability to achieve immunity in the mass population) of the vaccines that are available and being developed. We must also consider what lessons can be learnt as we plan the future management of this (and other) contagious disease outbreaks.

The potential for DNA/RNA vaccines has been explored for many years. Out of necessity, and early in the pandemic, the clinical development of this type of vaccine has been accelerated in an unprecedented manner. There are no other examples in drug development where approval has been gained in such a short time. It is also noteworthy that, by working together, individual companies and regulatory agencies have defined a pathway to authorization and delivered the necessary data to allow expedited review. It will be interesting to observe in the coming years if such a process can be applied to more conventional pharmaceutical products.

Efficacy of nucleic acids for COVID-19 vaccines has now been proven, but effectiveness is becoming more critical as we plan the future management of this disease. Demonstrating effectiveness needs to focus on:

- Ensuring vaccines can be easily stored, transported, and used
- Ensuring production can be scaled up to the volumes required in a pandemic in an efficient and cost-effective way
- Further optimization of delivery systems to increase safe release of nucleic acids into target cells.

A key feature of a good vaccination strategy, whether in response to a pandemic or to endemic disease, is to have multiple versions/types of vaccine readily available that can respond quickly to natural mutation in the virus. Current sequencing technology allows ready identification of novel variants, which may alter the binding characteristics of, for example, the SARS-CoV-2 Spike protein. By using that sequence, mRNA can be constructed and delivered to pharma manufacturers for incorporation into their proprietary delivery systems.

An equally important point is that several delivery systems should be available to alleviate the potential for shortage in any one key component/technology. For example, it has been reported that lipid nanoparticle (LNP) supply is restricted due to shortage in both lipid components and assembly technology at scale.

"Recent developments are making it possible for nanoparticulate silica to be re-engineered to bind oligonucleotides of varying sizes, including DNA, RNA and SiRNA, to the functionalized surface of the particle."

When it comes to delivery systems or strategies, the new COVID-19 vaccines rely on either LNPs, which, as noted above, may be subject to supply constraints, as well as having drawbacks in terms of possible toxicity and sub-optimal cellular penetration; or viral vectors, which can cause side-effects. However, silica nanoparticles could help to overcome some of these issues. Silica is "Generally Recognized As Safe" by the FDA and mesoporous silica nanoparticles (MSNs) – silica-based

nanostructured materials with strong biocompatibility and chemical stability – have been used in many successful drug formulations already. They do, however, have significant limitations for nucleic acid delivery. While inert and safe, most silica systems tested to date have been smooth mesoporous particles, meaning the nucleic acid is attached to the side of the particle, limiting the amount that would be successfully delivered into the cell. An alternative, effective, non-lipid delivery solution that protects the nucleic acid, delivers enough of it into the cell for the required immune response, and ensures safety and immunogenicity was, therefore, required.

Recent developments are making it possible for nanoparticulate silica to be re-engineered to bind oligonucleotides of varying sizes, including DNA, RNA and SiRNA, to the functionalized surface of the particle. By functionalizing silica to alter its topography, researchers are now demonstrating how it can be considered a viable delivery system for nucleic acids. In a comparative study, scientists at the University of Queensland (UQ) investigated how the topography of SNPs impacts their performance as a nucleic acid delivery system (1). SNPs with spiky-, raspberry- and flower-like morphologies were constructed with spike, hemisphere and bowl type subunits, respectively. Scientists at UQ found that the spiky-type subunits exhibited stronger binding affinity towards pDNA molecules and allowed effective protection against nuclease degradation when compared with the other morphologies and a commercial transfection agent. Out of the three, the spiky nanoparticles were shown to best facilitate efficient cellular uptake, endosomal escape and delivery of pDNA to the nucleus, leading to successful intracellular gene expression and the highest transfection rate.

Given initial findings into the ability of silica nanoparticles to also offer enzymatic protection to oligonucleotides and provide formulation stability, I believe there is a strong role for silica to play in the vaccine field over the next five years.

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Powering Discovery with Digitalization

Inventory management tools, Internet of Things, automated replenishment, AI… there are myriad opportunities to use digital tech to improve lab efficiency

By Tola Olorunnisola, President of Innovation, Marketing and Digital at Avantor, Radnor, Pennsylvania, USA

Scientists are on a mission to make the world a better place. But to drive discovery and innovation, companies must maximize laboratory productivity in an increasingly costly – and fast-paced – research environment. Though non-core scientific tasks such as lab operations are critical, they take teams away from the vital work that drives innovative new treatments and therapies. Digitalization can optimize these non-core tasks and give scientists more time for discovery.

Lack of real-time visibility into basic resources is a core challenge for many labs. From the number of centrifuges on the shelf to whether equipment should be repaired or discarded, labs without accurate, instantaneous data must often wait weeks or months to identify trends, react to evolving situations, or make decisions.

Though many labs have already taken steps toward digitalization to operate more efficiently and prevent costly downtime, the COVID-19 pandemic further highlighted the need for real-time information. As labs sought to quickly develop safe and effective treatments and vaccines, they needed visibility into their processes and workflows. Organizations that already had robust digital solutions were better positioned to tap into the transparency needed to quickly pivot in response to global events. As we move into a post-COVID landscape, it will be more critical than ever for labs to have actionable intelligence that helps them get treatments to market faster.

In my view, lab digitalization can help manage a wide range of needs, from day-to-day operations to regulatory compliance. For example, inventory management tools such as smart shelves and point-of-use sensors bring Internet of Things (IoT)-based technology into the lab by providing real-time usage information and automated replenishment. This reduces the number of human interventions using sensor-triggered demand signals instead of physical time interval checks. In addition, moving from lab automation to analyzing data on what scientists are doing and which protocols they are working on produces predictive analytics that are based on past trends and habits.

"Lack of real-time visibility into basic resources is a core challenge for many labs."

Digitalization can also significantly enhance transparency into laboratory chemical management. Often, overstocked inventory, lost chemicals, and potentially expired substances are not uncovered until an audit is performed. Digitalization tools can help reduce this waste. For example, RFID can help locate and monitor chemical stock and provide real-time usage data. This allows laboratories to monitor chemicals, ensure proper handling and storage, and help determine the proper time for disposal and replacement.

Laboratories can also use digitalization tools to manage equipment over its full life cycle. Lack of visibility into equipment, from flasks to freezers, can lead to unplanned downtime, research delays, and noncompliant documentation. Labs can more efficiently manage the complexity of equipment lifecycle management with tools such as a digital repository that makes it easy to record audits or real-time data that indicates it is time to decommission. Likewise, digitalization can help labs navigate the evolving clinical trials landscape. As clinical trial sponsors increasingly embrace global multisite trials and decentralized trials, the implementation of sample management and technology, such as RFID-based tracking and tracing, can

help researchers ensure supply chain transparency and trial integrity.

Although knowing what will happen, when it will happen, and why is valuable, companies can further leverage digitalization capabilities to move into prescriptive analytics that make recommendations and indicate their potential outcomes. This can be done by connecting the right systems and tapping into existing data. For example, in a laboratory that uses methylene chloride (HPLC) solvent for chromatography, researchers need information about the molecules, the conditions, and the resins. As more data points are connected, AI technology can analyze the data and make recommendations for more effective, more environmentally friendly solvents – and, most importantly, provide information on any parameters that might need to be adjusted. In another example, this technology could analyze a cell culture growing in a flask, suggesting better flask options if available and identifying what other condition settings are required to optimize the experiment.

To get treatments to market faster, laboratories must maximize productivity. Whether a lab manages digitalization in-house or works with an outsourcing services partner, these advanced technologies can provide the visibility researchers need to optimize the lab environment so they can focus on what matters most: discovery and innovation.

Roadmapping Future Technology

How do we mitigate the risks and costs of choosing inappropriate technologies for the short and long term?

By Mark Thomas Smith, Staff Engineer in Bioprocess Technology Development at Thermo Fisher Scientific, Logan, Utah, USA

Bioproduction – the process of manufacturing biopharmaceuticals or their precursors – has experienced persistent, yet discontinuous technological progress ever since the release of the first blockbuster biologics. Major technological advances have taken place in various aspects of bioproduction, from cell biology and gene integration to bioprocess media and chromatographic technologies.

However, due to regulatory, cost, and other risk factors, it can be difficult to implement new bioprocess technologies. New technologies are typically introduced early in a new product development lifecycle and can take months or even years to be implemented for manufacturing's benefit. Even in the earliest stages of a new product development cycle, there is a propensity to design bioprocesses strictly on well-known technologies, which is sometimes heralded as a "platform process" – in a sense, "if it ain't broke, don't fix it."

With such potential difficulties integrating new bioproduction technologies into existing processes, it behooves development teams and decision-makers to carefully consider their technology selections with the entire potential product lifecycle in mind. Aspects under consideration might include scale-up and scale-down performance, the physical operations and space required, the number of processes to which the technology can be applied, and how the selection might limit or expand future processing platforms. One might also consider market aspects, such as assurance of supply and delivery lead times, possible alternative and replacement technologies and, perhaps most important, the costs of implementing those technologies at some later date, if needed.

"New filtration modalities, such as tangential flow filtration, have been (re) introduced."

Let us consider the narrow example of selecting technologies for cell culture harvest and clarification. Traditionally, for vessels above 10,000 L, harvest was performed with stainless-steel disc stack centrifuges and post-centrifugal depth filters (1). As cell biology and culture technologies improved, product titers also improved. Increased titers, combined with flexibility and regulatory considerations, helped drive a shift in bioprocesses from large CIP/SIP stainless steel to smaller single-use equipment, particularly for bioreactors. At smaller volumes and moderate titers and cell densities, the stainless steel centrifuges could be replaced with single-use depth filters, reducing the facility engineering capital and operations.

But adopters of single-use depth filtration now face a rising challenge: upstream culture technologies have continued to intensify and single-use reactors are available in larger sizes (e.g., 5,000 L). These improvements portend the end of some large stainless steel bioreactors, promising to be more flexible and cost-effective than massive stainless steel vessels for multi-product facilities addressing smaller indication populations. However, the cell culture volumes and intensities are beginning to stretch the capabilities of single-use depth filtration to the edge of being tenable in performance, economics, or both.

Although some processes are locked into traditional single-use depth filters, there are alternatives available at varying levels of maturity and impact. For example, several companies have developed filters to be paired with flocculants, enabling harvest of relatively high-density cultures; a potential tradeoff is that the addition of flocculants may cause additional purification and development burdens, as well as potentially result in lower product yields. Alternatively, new filtration modalities, such as tangential flow filtration, have been (re)introduced. These have considerable implications in the residual of the bioprocess, potentially requiring development work across multiple bioprocess unit operations (e.g., moving to perfusion-based upstream). These and other technologies are available, but each one comes with additional risks, challenges, or burdens. These would become less daunting if the technology's necessity was realized from the start.

"How do we, as an industry, mitigate the risks and costs of choosing inappropriate technologies for the short and long term without exhaustive, expensive research efforts?"

This brief example of selecting harvest technology, though trite, highlights that there are numerous risks and challenges in adopting new technologies. Effort should be made at the time of initial selection to consider the long-term ramifications. A technology, once known, is subject to an endowment effect in which its perceived value and ease are exaggerated and the relative value and ease of unknown technologies are downplayed.

How do we, as an industry, mitigate the risks and costs of choosing inappropriate technologies for the short and long term without exhaustive, expensive research efforts? One avenue is through industrial forums, such as the BioPhorum Group (BPOG), the International Society of Pharmaceutical Engineers (ISPE), and the Bio-Process System Alliance (BPSA). Technology roadmapping plays a heavy part in these forums, helping end-users to identify future technological bottlenecks and allowing vendors to collaboratively tune in. Overall, a level of transparency and communication between vendors and users is established, creating a more efficient marketplace for new technologies to arise in a timely fashion.

But having technologies is not the same as implementing technologies. Beyond roadmapping needed technologies, it is also critical to collaboratively consider other hurdles. In particular, the obstacles to regulatory implementation need to be addressed. By working hand-in-hand, vendors, users, and regulators can leverage forums and other collaborations to establish best practices that satisfy regulations while shaping the future of regulatory requirements. If we can become more efficient, informed, and decisive about planning and implementing the right new technology today as we look toward the future, the industry, the product, and – most importantly – the patient will be better for it.

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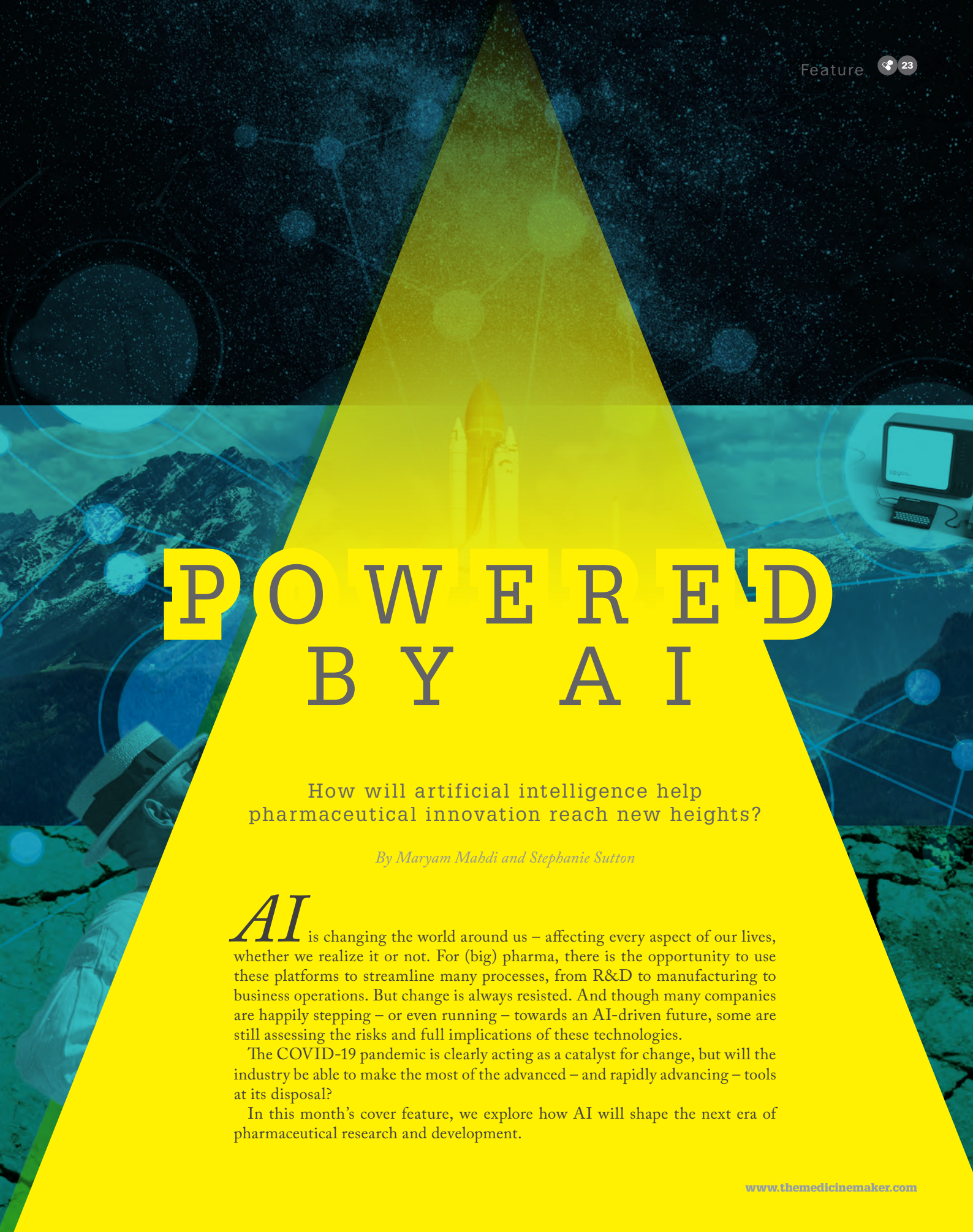


POWERED BY AI

How will artificial intelligence help pharmaceutical innovation reach new heights?

By Maryam Mahdi and Stephanie Sutton

AI is changing the world around us – affecting every aspect of our lives, whether we realize it or not. For (big) pharma, there is the opportunity to use these platforms to streamline many processes, from R&D to manufacturing to business operations. But change is always resisted. And though many companies are happily stepping – or even running – towards an AI-driven future, some are still assessing the risks and full implications of these technologies.

The COVID-19 pandemic is clearly acting as a catalyst for change, but will the industry be able to make the most of the advanced – and rapidly advancing – tools at its disposal?

In this month's cover feature, we explore how AI will shape the next era of pharmaceutical research and development.

BEYOND DRUG DEVELOPMENT

AI opens up new opportunities in R&D – and also provides pharma companies with new ways to connect with patients for better outcomes

Combining cutting-edge computing power and AI algorithms can significantly accelerate drug discovery by giving scientists a vast chemical space to test hypotheses and identify more effective molecules. Roger Palframan, Head External Innovation and US Discovery at UCB, tells us how AI is making a difference to both the company and patients.

Why is artificial intelligence so important for the pharma industry?

At UCB, we see artificial intelligence as one type of enabling advanced analytics tool that helps our people make better – and faster – decisions. It can benefit research scientists, clinical scientists, and other different parts of the business.

We tend to talk about AI in three different areas. First, we use it to understand the patient and their condition as deeply as possible; how does the disease impact the patient population and individual patients? It's important to understand the unmet need so we can really create value for patients. And that includes gaining a better understanding of pathophysiology. This takes us to the second area that is the search for better targets; we want to increase the probability that, by perturbing or modulating a certain target, we can improve the right clinical outcomes for the patient. And the third area is all about getting to the right therapeutic candidates faster, whether a small molecule, biologic, or gene therapy. We want approaches that can accelerate decision making, help us prioritize, and shorten our to-do list on the road to potential therapeutics!

When did UCB first become interested in AI?

I wouldn't say there was a specific time UCB pivoted towards AI. Over time, there has been a convergence of computing power and data availability that has significantly accelerated its adoption. Many of the AI algorithms are not new; rather, we needed a way to make the data ready at scale for analysis using these algorithms, as well as the necessary computing power to perform the analytics process. And it all had to be affordable. The convergence of these factors has been very important and has led to projects like the COVID Moonshot crowdsourcing initiative. We brought algorithms and approaches to the Moonshot that we had already developed in our computer-aided drug design group. Our approaches make use of the Microsoft Azure cloud, which allows us to perform tasks that would take months with UCB's computing capabilities in just a few days. The ability to harness enormous computing power has had a huge impact on what the industry can now do with AI.

The COVID Moonshot has been exciting for all concerned. They have the output from 2020 and are approaching the candidate stage. And I really hope we see some great results. For UCB, the COVID Moonshot has helped us see directly how rapid access to large-scale computing capabilities can really transform medicines discovery. UCB is not a leader in infectious disease R&D, but the same approach can help us speed up discovery stage programs – regardless of therapeutic area. And we have plans to deploy the technology on a number of interesting projects.

How did you get involved with Microsoft?

Like many companies, we had a long-standing relationship with Microsoft at the enterprise level. When we decided we wanted to work on the COVID Moonshot, we approached them through their "AI for Health" program to access the cloud platform. We've now expanded our collaboration with Microsoft to combine their computational services, cloud, and AI with our drug discovery and development capabilities. A lot of drug discovery activities require the analysis of high-dimensional data sets or multi-modal unstructured information; here, computing power is crucial. We're also going to be using a new Microsoft platform to deploy AI across the enterprise.

How have UCB scientists reacted to AI technology?

Many people in the company were already using AI before we increased our focus in this area; our data scientists and computational chemists were already using AI day to day, and we also use AI in other parts of the business, including non-scientific roles and support functions. But we really want to see AI in the hands of as many scientists as possible, and I think that's what the Microsoft collaboration can really enable us to do.

For our scientists, AI has had a huge impact in drug discovery. We have programs where a target was previously thought to be undruggable, but we have used computational design approaches to find a way forward by identifying molecules that can be combined to modulate the function of a particular protein. In fact, there are many exciting targets with really strong causal links to disease that have proved to be very difficult to address, particularly with small molecule drugs.

As another example (which isn't strictly AI, but probably would be seen as a type of AI today): our investigational humanized monoclonal IgG1 antibody bimekizumab was optimized to selectively and directly inhibit both IL-17A and IL-17F, two key cytokines driving inflammatory processes, by superimposing two binding specificities into a single binding site. This advance

COVID MOONSHOT

The COVID Moonshot is an open group of researchers – including biopharma, academia, technology companies, chemical vendors, and individuals – who are working under no IP constraints on new compounds and solutions to tackle COVID-19. The initiative has crowdsourced over 17,000 chemical designs for antivirals from chemists around the world. Volunteers can also help by sharing their computer power for molecular simulations.

The project is led by PostEra, which specializes in medicinal chemistry and machine learning. UCB has contributed employee time in the areas of medicinal chemistry, CADD, and IT to contribute drug design ideas and prioritize crowdsourced submissions (more than 13,000 so far).

Find out more at https://covid.postera.ai/covid

MEET ROGER PALFRAMAN

My background is in life science, pharmacology, and immunology. I did my undergraduate studies at King's College London, and PhD at Imperial College London, before doing a postdoctoral research fellowship, under the Wellcome Trust, at Harvard Medical School. My move to industry was spurred by my desire to apply science to therapeutics discovery. I joined Celltech, which became part of UCB in 2004, and I've had a number of opportunities to gain experience since – leading groups in discovery research, working on significant clinical development programs, and feeding into strategy.

In 2015, I came to Boston to enable UCB to tap into the life sciences hub here and across the US. We've always had a presence in the US, but not in terms of research – despite collaborations with leading universities and biopharma. We started in an office at the Cambridge Innovation Center and we've now established our own research capabilities in the US – started by the acquisition of Beryllium Discovery and Element Genomics – and accelerated with the acquisition of Ra Pharmaceuticals in Cambridge in 2020.

was made possible through proprietary computational antibody design – and we demonstrated that the result had superior clinical benefit to IL-17A-only antibodies. Such discovery capability is core to what we do at UCB.

We are also using AI to better understand disease, because it's very good at pattern recognition. We are collaborating with an academic partner to help us identify subpopulations in epilepsy. We've used AI to analyze over 100 million closed datasets alongside a smaller subset (around three million) of detailed electronic medical records. And we've identified 40 previously uncategorized subpopulations with epilepsy. We're considered a leader in the epilepsy field so it's important for us to understand these phenotypic clusters so that we can better help those patients get the care they need, either with existing therapeutics or with new therapeutics that we have yet to discover.

How do you think AI will shape the future of healthcare?

One of the biggest challenges in healthcare overall is allowing patients to access the right medicine as quickly and effortlessly as possible. Using AI and digital technologies to help patients is something we are very passionate about. We recently announced the launch of Nile AI – an independent digital health platform that improves the delivery of epilepsy care by shortening the path to optimal treatment. The platform consists of a patient app and healthcare provider portal. The portal shows the status of patients at a glance, and virtually informs and supports patients in between appointments, and, crucially, it also allows data-driven care-related decisions. We hope it will benefit both patients and healthcare providers.

Being a pharma company isn't just about developing therapeutics. It's important to be working on solutions that help the patient holistically.

A MORE INTELLIGENT APPROACH

Has AI been a savior in the battle against COVID-19?

AI has helped inform pharma's COVID-19 response. But how? We take a deep dive into the industry's growing reliance on AI systems by speaking with The Pistoia Alliance President, Steve Arlington.

What challenges have been highlighted by the pandemic?

The pandemic has exposed long-standing industry issues, including difficulties accessing data outside of the lab and the lack of ways for organizations to collaborate virtually both internally and externally. These problems have the potential to lead to duplication of work. And with more scientists working remotely than ever before, the pandemic has shown us the true value of digital tools in helping overcome these problems. The search for COVID-19 treatments has also reiterated the vast amount and variety of data produced by the pharmaceutical industry as well as the need for technology that makes the management and sharing of this data more straightforward. The last year has proven that collaboration leads to faster breakthroughs; we must continue to cultivate this cooperative attitude to research, and support scientists by implementing the right technologies.

"We hope this security advantage can improve patient trust and encourage more knowledge sharing across the life science community."

What role can AI play in addressing these issues?

AI can aid the management and sharing of scientific data. It improves the success rates of drug discovery by sifting through huge existing data sets and using them to answer new questions – as we saw with the rapid development of COVID-19 vaccines. AI can also make searching for and finding insights from data much more efficient, letting researchers use existing knowledge and avoid overlapping results.

Why are some companies still hesitant to adopt AI?

The skills gap is the biggest recurring barrier preventing successful AI implementation. There is no room for error when it comes to these systems, and we need specialist data experts to collaborate with scientists to meet this particular challenge. Another barrier is the lack of clear data standards. When data is disorganized and siloed it is not machine-readable, which has the potential to create bias in AI's outputs; in other words, the information that it is using to "train" its algorithm is limited.

The Pistoia Alliance has developed a toolkit called FAIR (Findable, Accessible, Interoperable, and Reusable) that aims to address this algorithmic bias when companies are setting up new data sets (See Technical Support). The resources are free for companies to access and should enable a smoother transition towards increased use of AI systems.

And what about cybersecurity?

As with any new technology, security is an important factor but arguably even more so when dealing with sensitive patient data. Ensuring AI is explainable and removing the "black box" can help to diminish security concerns. When AI is transparent and the source of the data (and decisions it makes) can be easily traced and understood, it is easier for tampering to be uncovered. Other technologies, such as blockchain, also have the potential to increase security because of its trusted, disintermediated system of record. We hope this security advantage can improve patient trust and encourage more knowledge sharing across the life science community.

Any emerging tech still requires us to work together to put the right standards, governance, and guidelines in place to minimize security risks.

How can pharma prepare itself for future pandemics?

COVID-19 presented the life sciences with a complex challenge, but it has also been a catalyst for biopharma organizations to work together in new ways with technology companies, governments, charities, and regulators. From repurposed drugs to new mRNA vaccines, R&D has been accelerated during the pandemic. Technologies such as AI have facilitated this, but ultimately it is collaboration that will drive scientific breakthroughs during any future public health threats.

TECHNICAL SUPPORT

The Pistoia Alliance is involved in projects that allow industry partners to share best practices and discuss ways of overcoming common challenges experienced in the use of AI.

FAIR Toolkit

Motivated by the industry's increasing reliance on data-driven solutions, the Pistoia Alliance set up FAIR. The project, which first began in 2016, published its first set of guidelines in Scientific Data to help companies find, use (and reuse) the data most relevant to them in an ever-growing virtual sea of information. Now the project helps companies gain access to free tools, training, and change management programs. Over 50 data experts and 18 companies are associated with FAIR – helping to enhance clinical trial data management for future drug development.

AI Centre of Excellence (CoE)

The Pistoia Alliance launched its CoE in 2017. The project aims to explore the ethics of AI use and suggest model management for both AI and machine learning. It also regularly hosts webinars to better acquaint its members with the changing AI landscape. The Alliance also encourages international collaboration through the center. Its virtual co-working spaces allow companies across different regions to share ideas and collaborate on the implementation of AI within their organizational structures.

Through the AI CoE, they have also published a list of best practices that can be found online https://osf.io/eqm9j.

THE DREAM WORKS

Perspectives on AI are rapidly changing. In 2015, there were only 20 collaborations between pharmaceutical companies and AI startups. Today, the landscape looks very different. But what impact are these smaller tech companies having on drug discovery and development? Here, we round up just a snapshot of the projects underway.

Insilico Medicine

Insilico Medicine has made huge strides in the use of AI for drug development in recent months. Using its AI platform, the company discovered and developed a drug to treat idiopathic pulmonary fibrosis in the space of 18 months. Their work has helped demonstrate the power of AI for rapid R&D and has attracted several partners who are using their proprietary platform, Pandomics Discovery, for its ability to provide relevant real-world evidence for the development of new drugs and treatments. Some of their better-known collaborators include Pfizer, Boehringer Ingelheim, and Actoris.

Exscientia

Exscientia is also turning heads in the pharmaceutical sector. The AI company recently extended its Bristol-Myers-Squibb partnership with a view to expand its portfolio of small molecule drugs for a variety of indications including oncology and immunology. "Exscientia's application of AI technologies is proving capable of reducing discovery times. Rapid discovery of molecules that can enter the clinic in a timely manner could positively impact our work in discovering treatments for areas of unmet medical need," said Rupert Vessey, President of Research & Early Development at Bristol Myers Squibb in a statement.

Microsoft

The tech giant is playing a large role in the drug development space, using its AI prowess to support a variety of companies with its proprietary cloud-based computing platform, Azure. In the world of pharma, Azure allows for the storage and streamlining of large immunotherapy datasets and ultimately offers the company the ability to efficiently explore clinical data insights.

Microsoft is also working closely with big pharma companies. For example, it recently signed a multi-year deal in 2019 that enabled Novartis to set up its AI innovation lab to support staff in the drug development process. In a statement, Novartis' CEO Vas Narasimhan said, "As Novartis continues evolving into a focused medicines company powered by advanced therapy platforms and data science, alliances like this will help us deliver on our purpose to reimagine medicine to improve and extend lives."

BenevolentAI

In January, AstraZeneca announced that it had partnered with BenevolentAI to launch its first AI-generated target for chronic kidney disease. However, this isn't the tech company's first foray into big pharma; they joined forces with Novartis almost two years ago to support its oncology program. The deal saw BenevolentAI using its deep learning platform to screen Novartis' current pipeline to identify drugs that could be repurposed for other indications.

CULTURE SHOCK

Do pharma organizations have the right mindset when it comes to adopting and implementing AI more widely?

By Alan Kalton

AI is constantly evolving. In the early 1990s, basic AI systems were used to apply best practice logic to help track complex scenarios. Now, AI systems are more powerful than ever and can be used in various ways across the life sciences industry. In addition to drug discovery, pharmaceutical companies can leverage AI to explore the major trends that drive performance and affect sales and marketing, as well as the minute details of consumer behavior to help improve the patient experience. Most commonly, AI uncovers customer preferences – such as preferred channel, preferred time to engage, preferred type of information – so commercial teams can enhance engagement with healthcare professionals (HCPs). Further, AI quickly derives insights from mountains of data to guide marketing teams in developing materials that better meet the specific needs of HCPs and their patients. AI allows personalized interactions like never before – it replaces mass marketing with tailored, relevant communications.

Although the uptake of AI is on the rise, management must shift its mindset to ensure that the systems are used efficiently. In my experience, large companies often have different attitudes towards these systems versus small and medium-sized companies. Although large companies will have the capital and resources to pursue ambitious projects, they can sometimes be entrenched in decades of protocol, process, and tradition. Therefore, understanding how AI can best be implemented – and rolling it out – can seem daunting. The functional silos that often exist in these organizations can hinder the use of AI at scale. Without the ability to make effective decisions across departments, progress can be slow and the success both locally and internationally can be affected.

In contrast, the smaller, more agile companies are leading the charge and engaging with AI. They are willing to explore how products can be launched within an entirely digital framework and how AI can impact commercial success worldwide. They ask tough questions to ensure that the structure of their processes benefit their operations and their investments are effectively used.

When COVID-19 hit, these rapidly growing biopharma companies had to abruptly adapt to a new commercial reality. Antares Pharma, for example, sought innovative ways to continue engaging with customers and turned to AI technology to help bolster internal analytics capabilities and provide critical execution support. Leveraging a modular AI approach, commercial teams can easily configure a right-size solution for quickly identifying the right commercial targets, predicting the ideal timing and content for maximum HCP engagement, and prioritizing next best actions that users are most likely to adopt.

There are several emerging biotechs that are leveraging AI in really fundamentally new ways – and that is largely because they are not stuck in the quicksand of investment that large companies have made in their field forces, marketing automation systems, processes, and more. They can start fresh. One customer is building its commercial team anew using AI as the engine to power and coordinate a digital-only engagement model. They are essentially 'bucking the system' of investing first in the field organization. Post COVID-19, it's like a phoenix rising from the ashes and zeroing in on digital engagement directed by AI intelligence.

Another customer is building its commercial team based on data – a total break from tradition. The company is investing in data technology that integrates all engagement data into a consistent framework as a baseline for driving an AI-first agenda and data-driven approach to commercialization. This move will accelerate their AI journey faster than other companies.

But a challenge for any business when initially considering AI implementation is what AI truly means and how it can positively shape their futures.

Understanding AI

You can ask 20 different sales or marketing professionals from the industry what AI is – and receive as many answers. The fact of the matter is that for pharma to agree on a consistent definition, the industry as a whole must be able to identify the types of problems it is trying to solve using these AI platforms. For example, when extracting relevant information from large datasets, I've heard the terms "multichannel" (an information-centered approach), "omnichannel" (customer-centered approach), and "digital" all used interchangeably within the same company to refer to the analysis of the same products with AI. No wonder there is so much confusion about AI!

There is also a lack of real-world and direct experience with AI for professionals and their companies to draw from and build upon. This is, in part, due to the closed nature of the pharmaceutical industry – although professionals will move to and impart their knowledge on different companies within the sector, the voices of skilled individuals from other industries are often missing from the equation – especially when it comes to the execution of commercial models. Pharma has tried to recruit digital technology innovators from outside of the industry but they quickly grow frustrated by the rigidity of the

traditional commercial model and unique regulatory processes in pharma. The initiatives that they try to develop fail to go beyond the pilot stage and these leaders move on. Essentially, there is a skills gap when it comes to using AI for intelligent customer engagement in pharma.

The good news is that this paradigm is finally starting to change. As the life sciences industry has accepted the need for AI to be more ubiquitous, AI skillsets are in demand and the industry is primed for the requisite changes that must take place. Pharma companies will still need help taking AI innovation to scale but the mindset is beginning to evolve – some might say by necessity because of the lingering impact of COVID-19.

AI can act as a catalyst for strategic change (and many companies are introducing it into their practices), but its dynamic nature has yet to be fully explored on a broad scale. Companies should be able to use the data available to them to move away from quarterly plans and annual reviews, and execute strategies on areas like patient engagement on an ad hoc basis – potentially as frequently as the market changes. Recent events, including the COVID-19 pandemic, have further emphasized how important it is for the industry to consistently and rapidly address issues that can negatively impact the patient experience.

"If we look back at the last 18 months, we can clearly see how the pandemic has changed attitudes in pharma"

The COVID-19 impact

If we look back at the last 18 months, we can clearly see how the pandemic has changed attitudes in pharma. It has brought into question how companies were allocating resources across the entire commercial spectrum and beyond individual business concerns; we've all had to consider the macroeconomic consequences that came along with the uncertainty of the crisis. We didn't have a clear picture of how it would affect the industry as a whole on a long-term basis.

These challenges have meant that we're now seeing greater levels of innovation in areas of AI use that were previously underfunded, such as for omnichannel engagement in commercial. AI has also transitioned from a toy for companies to "play" with, to an essential tool as it became increasingly apparent that we would have to quickly respond to arising issues and ensure that commercial and strategic models allowed us to compete in the marketplace. COVID-19 made the need for digital and AI's application to enable smart digital engagement with customers crystal clear. It has also helped us to think more critically about the customer experience and how it can be improved.

Now, the potential for AI beyond transactional excellence is about driving a dynamic relationship between strategy and tactics. For example, AI allows pharmaceutical companies to transition away from an annual planning cycle to a continuous, in-real-time cycle. Using rules-based AI, companies can quickly pivot to address a significant change such as a new indication for a drug, a new competitive entry, a safety issue, or a regulatory change. This is the holy grail of what AI can do for the life sciences industry and represents a fundamental shift in strategic operations from the executive level on down.

In short, there is a lot to unpack when it comes to "true transformation" for pharma's use of AI in customer engagement. Throughout my time spent in industry, I've seen the phrase used many times and have also experienced the intransigence of the pharmaceutical commercial model. Though pharma has had over 100 years of success, it hasn't fully assessed the limitations of current strategic models. COVID-19 has offered us all a real chance for transformation and is inspiring a behavioral change in companies of all sizes. It's phenomenally exciting. I hope this enthusiasm and shift in mindset won't be lost; we have now a golden opportunity to connect AI to an improved patient experience.

Alan Kalton is vice president and general manager, EMEA at Aktana.

IS THERE GOLD IN THEM AI HILLS?

What opportunities await pharma as it begins to redirect its focus away from the pandemic?

In 2020, we spoke to Peter Richardson, Vice President of Pharmacology at BenevolentAI, about the role the company's AI system had played in its pandemic response. Like many other companies in the industry, they put their machine learning platform to use and found that a drug owned by Eli Lilly, baricitinib, could be repurposed to treat the symptoms of COVID-19.

And although AI has played a significant role in the industry's rapid drug development program through the crisis, stakeholders in the industry are now looking ahead to determine the role it will play in a post-COVID-19 world. To examine the topic further, we caught up with Jackie Hunter, a board director at the company and a member of The Medicine Maker 2021 Power List, who shared her views on the future applications of AI in pharma with us.

How will industry conversations change in a post-pandemic environment?

Last year, the company identified baricitinib as a treatment for COVID-19, which later won FDA approval for use in hospitalized patients. Post-pandemic, we should expect industry conversations to revolve around how we use AI to improve future health systems and revolutionize the drug discovery process. Another topic that will dominate the industry post-COVID is how we improve and unblock approval processes for future therapies and vaccines. We have seen how approvals can be expedited with rolling data reviews and large data trials in the pandemic, and, as a result, we have witnessed huge scientific leaps in vaccine development.

Lastly, the unprecedented way in which data has been shared so rapidly and freely during the pandemic has raised important questions about what data is proprietary and the possibilities of pre-competitive sharing. We will need to see discussions about the standardization of data capture, how we increase diversity in data, and ensure patients have greater feedback on how their data is being used.

How can we accelerate drug development projects of the future?

BenevolentAI and other industry pioneers have demonstrated the power of AI, combined with human intelligence, to generate new hypotheses for serious diseases and identify targets faster and more cost-effectively. However, to change the drug discovery and development process worldwide, we need to see substantial organizational change and significant effort on the part of pharma companies. For example, increasing the use of remote monitoring and standardization of image analysis to reduce the number of patients needed in trials.

Industry challenges can also be solved through productive pharma-innovator partnerships, for example, we partnered with AstraZeneca to uncover novel treatments for idiopathic pulmonary fibrosis and chronic kidney disease. And that led to AstraZeneca selecting the first-ever novel AI-generated target to enter its drug portfolio. However, these types of partnerships are only truly successful if both sides are willing to learn from one another and adapt their ways of working to combine the expertise of traditional pharma with new AI and machine learning approaches. In the case of Benevolent and AstraZeneca, this led to AstraZeneca selecting their first-ever novel AI-generated target from the partnership to enter their drug portfolio.

What technologies will drive the future of pharma?

Clearly, AI and machine learning will impact every aspect of the pharma value chain, and 2020 saw the field make impressive progress on some of the world's most complex scientific challenges, such as AlphaFold (a program developed by GoogleAI offshoot Deepmind for accurate 3D predictions on protein folding) or MIT's work in antibiotic discovery. I think this closer convergence of new technologies with scientific expertise will help the industry be more successful, efficient, and cost-effective as it moves forward.

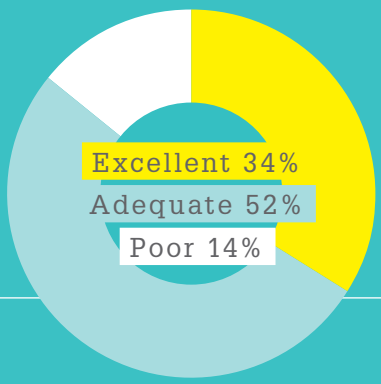
I also hope to see other exciting technologies; for example, blockchain to help patients track how their data is used and smart manufacturing technologies, such as 3D printing, to enable a more personalized approach to medicine.

GROWING INTELLIGENCE

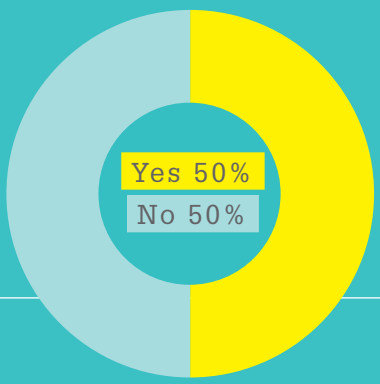
Distribution of AI companies for drug discovery by region

US – 54.4%
Canada – 6.7%
UK – 14.2%
EU – 13.4%
China – 2.5%
Rest of Asia – 8.4%
Australia – 0.4%

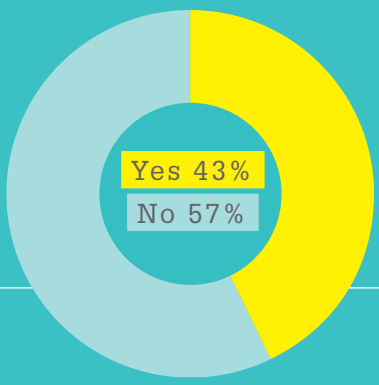
Is there a strong digital culture in pharma?



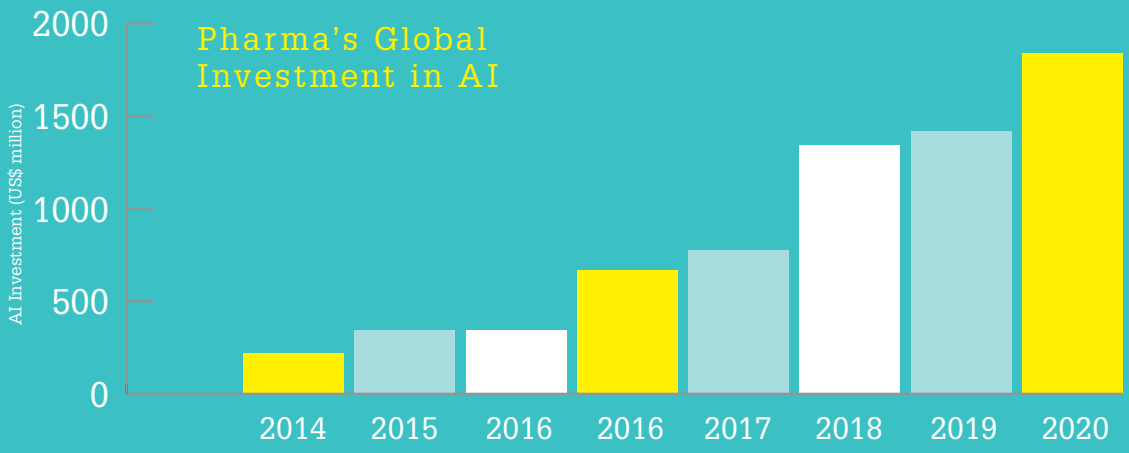
Can AI help drugs get to market faster and eliminate conventional challenges?



Will failure to adopt AI result in financial consequences?



Pharma's Global Investment in AI



Sources: MIT Technology Review (2021). https://bit.ly/2RJq7QK Deep Pharma Intelligence (2021). https://bit.ly/3bNYK2F Aspen Tech (2021). https://bit.ly/34cO99k.

Global Support for Faster Formulation Development

Driven by innovation and the desire to meet new treatment options, pharmaceutical companies worldwide are looking to accelerate time to market for their products. Experts from Colorcon explain how the company's investments in facilities and new technologies are helping the pharma sector reach its goals.

The View From the US

What are the biggest challenges faced by your customers?

CC: Speed of development is a major concern across the pharma industry. We're operating in a climate where companies need to have ready access to reliable and trusted partners that can accelerate processes, but still provide robust formulations. Though companies may want faster development, they also need to ensure that the best formulations – with the most appropriate dosage forms – make it to market.

As a result of the pandemic, on-site staff numbers have been lowered in many pharma companies – and so too has the amount of time spent in the lab and research facilities. During this period, we've heard of companies taking longer to achieve their project goals simply because of challenges with resources. And that's where we have been able to help. In many cases, we have conducted formulation and coating trials for our customers. Their product development teams relied on us to provide resources through our labs when they didn't have full access to their own. We've had our learning curve too as we adopted more digital and virtual technologies to meet customers' needs, but we've managed to navigate through the situation successfully.

Tell us about your US expansion...

CC: We recently extended our technical service capabilities in our global HQ in Harleysville, PA, USA with a new containment suite. Many of our customers work with very small quantities of active ingredients, which can have unknown safety profiles, and be extremely costly and limited in availability. Our investment in the best equipment enables us to produce tablets and capsules with milligrams of active product in the safest of conditions.

Increasingly, pharma companies want to work with partners who have continuous manufacturing capabilities because of the flexibility of the technology and other benefits. We've invested in continuous coating and continuous powder feeding equipment so we can stay abreast of the changing pharmaceutical manufacturing landscape. As a result of our commitment, we can now go from the API all the way to a finished coated dosage form within our facilities and provide prototypes ready for customer evaluation.

Why is your global support network so important?

CC: Many of our customers work in multinational companies with locations across the world. With our network of 22 technical service labs, we are close to our customers – allowing us to provide tailored and consistent support, wherever they are. We recently conducted trials in our California lab and had virtual attendance by our North American team, as well as our clients who were troubleshooting a process issue at their manufacturing site in Asia. Such interaction is only possible when you invest in global expertise and digital technology. The Colorcon team are equipped to provide the same level of support wherever they are based in the world.

What emerging trends are impacting customer's needs?

CC: There is increasing demand for product authentication driven by the tremendous growth of the drug counterfeiting industry; especially with the proliferation of online pharmacies. This issue isn't just economic, it places an immeasurable number of lives at risk. We've developed on-dose authentication technologies that enable drug products to be instantly verified with track and trace across the entire supply chain, down to the individual pill.

Patient compliance is an important area for the industry to improve. With larger fixed or combination doses, some patients find it challenging to swallow their medication due to size. Even single dosages can be challenging for elderly and pediatric populations. Colorcon has addressed this through the development of easy-to-swallow coatings that improve the patient experience, making it easier to take medication and adhere to treatment regimens.

The demand for clean label products continues to increase with consumers wanting wholesome ingredients they can understand, know, and trust. For many consumers, the term "label friendly" means the elimination of a long chemical ingredient list and includes those that are familiar with consumers and are naturally derived minimally processed sustainable

Meet the Experts

Charlie Cunningham, Technical Director North America, Colorcon

"In addition to the products that we formulate, manufacture, and sell, we also provide hands-on specialist technical support to our customers – whether that be in their labs or within one of our facilities. Our network of technical managers provides expert assistance to support our customers through the entire product lifecycle; from formulation development through to scale-up and manufacture. Alongside our teams, we make sure that our labs are top-notch and that our people have the latest digital and virtual technologies to conduct formulation and coating trials with our customers."

Jason Teckoe, Technical Director EMEA, Colorcon

"I manage and support our team of technical managers across the EMEA region – sharing best practices, helping our customers with product selection, development and troubleshooting. Through working closely with the professionals in our laboratories, where our samples are made and trials conducted, we ensure that our customers receive best-in-class services and products in a timely way. As part of a wider global team, we are all charged with ensuring that our innovative products, new initiatives and applications data are implemented around the region. I love the variety that comes with this role. No two days – or customers – are the same!"

ingredients. With our most recent launch of Nutrafinish®, Label Friendly Coatings, Colorcon now provides best-in-class coatings to meet consumer needs for simple ingredients and a clean label.

The EMEA Perspective

What do your clients need for development support?

JT: Alongside big pharma, there are a growing number of virtual or small companies developing drug products that don't necessarily have their own lab capabilities or resources to progress their products into the clinic. These companies often work with consultants and CROs to help convert their drug substance into a drug product suitable for clinical supply and trials. With our understanding of excipients and coatings, we can support early phase screening activity, providing these virtual or small companies access to our formulators, equipment and services as well as generating non-GMP prototypes of the dosage form for subsequent clinical supply.

To expand our capability to meet customer needs, we've invested in flexible isolators for our Technical Centre at our Dartford, UK site, so that we have the ability to handle more potent APIs, and added small scale characterization equipment to evaluate flow, granulation, compression and encapsulation behaviour. The more insights that we can provide to customers during the early phases of their product development, the better!

How do you accelerate formulation development?

JT: HyperStart® is a digital tool that jumpstarts formulation development. The complimentary service allows clients to share details of their ideal dosage form, API, and desired release profile with us, so that our technical team can determine the best starting formulation. In essence, HyperStart references a broad spectrum of formulation data to help reduce complexity and make the development process as efficient as possible.

How else are you helping customers reduce their timelines?

JT: The great wealth of knowledge and experience in our team can help accelerate development in myriad ways. We provide regulatory insight and documentation to support smooth submissions for new products and supplementary filings. Companies don't want to encounter regulatory hurdles in any region that they intend to market in, so we're always on hand to provide insight and guidance.

Our tablet design service, BEST®, also helps ensure that our customers' products stand out from the competition and are designed with the patient in mind. Consulting with Colorcon's experts, the color, size, and shape of tablets can all be selected to create market-leading products. Simply put, our services cover a broad spectrum of needs, ultimately helping speed up time-to-market, particularly for customers who don't have their own facilities.

What about the scale-up step to manufacturing?

JT: . Essentially, scale-up comes down to good process understanding and access to suitable equipment. We have technical experts and equipment available across the EMEA region to help customers in both the early and the latter stages of product development and can support standard pharmaceutical processes such as compression, granulation, and coating. This is also important for early phase development, when companies may not have the right equipment or capacity to progress trials.

Why is it so important for Colorcon to continue to invest to support clients?

JT: The pharma industry is constantly changing and evolving. We are investing to keep ahead of demand and help our customers to deliver their business goals. Our investment in technology, new capabilities, and professional expertise means that we can help our customers through the challenges of today and in the years ahead.

When the Chips Are Down

Looking for human-relevant information on an early drug candidate? Organ-on-chip technology can offer new insights.

By Stephanie Sutton

Organ-on-a-chip is considered an important emerging technology for research and development because it can show how a candidate drug might react in human tissue structures – as opposed to traditional animal models – long before it enters the clinic. Here, we speak with Lorna Ewart, Executive Vice President, Science of Emulate, to learn more.

How do organ-on-chip platforms accurately mimic human organs?

Organ-on-a chip technologies use microscale engineering technologies combined with cultured living human cells to create an experimental platform that recapitulates the physiological and mechanical microenvironment of whole living organs. These microphysiological systems (MPS) enable the study of complex human physiology and pathology in an organ-specific context. These specialized in vitro human disease models can revolutionize drug discovery and development by helping researchers better predict human responses to medicines, including safety and efficacy.

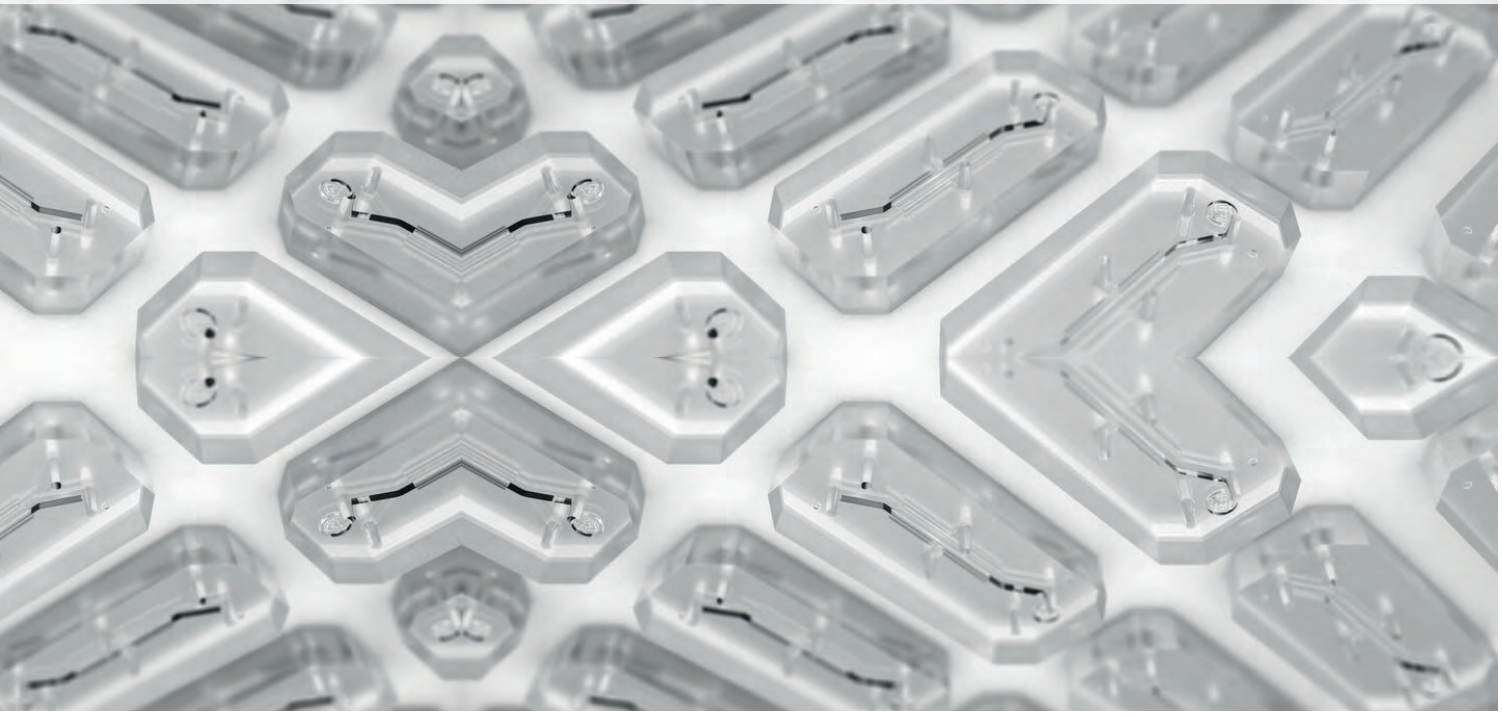
Organ-on-a-chip technology can be designed to fully recreate the complex, dynamic state in which living cells function within a human organ – a so-called "home away from home" for human cells. Such an environment involves modelling complex interactions, often in three dimensions. This starts with the extracellular matrix (ECM), which is optimized for organ-relevant composition, stiffness, and cell attachment. Homotypic and heterotypic cell-cell interactions are recreated. And finally, the model seeks to create oxygen, nutrient, and chemical gradients that provide the complete set of cues cells need to behave and function accurately – just as they would in the human body.

As an example, Emulate Organ-Chips are composed of a transparent, flexible silicone polymer (polydimethylsiloxane (PDMS)) about the size of an AA battery. Each chip has two parallel, fluidically independent channels separated by a flexible membrane, with pores seven microns in diameter. The membrane is coated with an optimized ECM before the channels are lined by living human epithelial cells on the upper channel and living human organ-specific endothelial cells on the lower channel. Such an arrangement recreates the essential tissue-to-tissue interface found in every organ. The channels are flanked by vacuum channels that can provide tissue-relevant mechanical forces for organs to mimic processes such as breathing in the lung.

How well used is organ-on-a-chip technology in drug discovery and the pharma industry today?

We're working with around 19 of the top 25 pharmaceutical companies as defined by their R&D spend. In my view, the industry should always be considering the adoption of new technologies that can reduce the long, costly drug discovery and development process, or improve confidence in how a medicine will perform in human trials.

Organ-on-a-chip technology can develop human-relevant data for drug candidates and also offer a sustainable, ethical research model by relying less on animal models – which are frequently



shown to poorly recreate the human pathophysiological phenotype.

Organ-on-a-chip technology is barely a decade old, so the pharma industry is still in the testing and evaluation phase. Around 23 pharmaceutical companies have established an MPS affiliate under the IQ Consortium – which aims to advance innovation and quality in the biopharmaceutical industry. The goal of this MPS affiliate is to define the criteria of use for new, sophisticated in vitro models, such as organ-on-chip and, to this end, a series of organotypic manuscripts have been published to guide technology innovators, such as ourselves, toward building organ-models to address the key safety- or ADME-related questions relevant in drug development (1). The affiliate is also closely aligned with the FDA, thereby ensuring consistency of direction and approach for advancing this new technology.

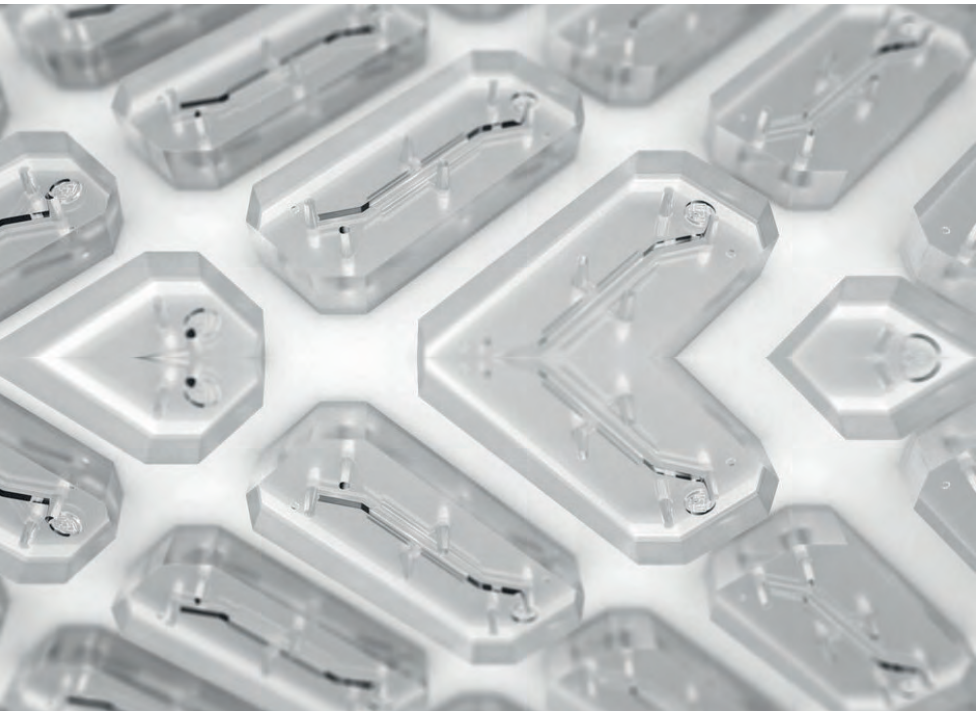
In my experience, customers are really interested in using organ-on-a-chip technology for internal decision-making purposes within the preclinical safety testing or target validation stages of the drug discovery and development process. One notable example is the human Blood Vessel-Chip developed by Emulate in collaboration with Janssen Pharmaceuticals, which was able to recreate the thrombotic toxicities of a monoclonal antibody drug that led to its failure in human clinical trials (2). The ultimate goal of some pharma companies is to include organ-on-a-chip data within their regulatory filings for new drugs, to augment the results from animal data or to strengthen a weight-of-evidence argument.

What is necessary to promote greater uptake?

Promoting greater adoption of organ-on-a-chip technology is likely to result from progress in several areas. These have been discussed in greater detail by in Nature Reviews Drug Discovery (3).

First, adoption will be driven by a move toward technology standardization. Because this is still a developing field, there are multiple MPS platforms and approaches. As leading technologies are further industrialized, they will become standardized, enabling broader inter-laboratory comparisons, technology adoption for key applications, and more widespread use.

Second, regulatory acceptance will trigger technology adoption, especially relating to robustness and reproducibility (both inter- and intra-laboratory) of the technology. This is a central component of the Cooperative Research and Development Agreement (CRADA) between Emulate and the FDA. For example, if organ-on-a-chip technology is proposed to replace an existing approach, regulators will want to see concordance of data between the organ-on-a-chip model and the animal model that it intends to replace. In other cases, if the use is related to a greater understanding of mechanism of action, the user needs to articulate which regulatory question is being answered. A good example of this could be explaining species differences with respect to toxicological outcome, as has been nicely described in a paper where the Emulate Liver-Chip was used to understand drug toxicity (4).



Third, significant progress is underway in demonstrating confidence in new organ-on-a-chip models, as well as translational qualification. Importantly, the work of the IQ_MPS affiliate is designed to articulate new roadmaps that are sound and relevant for enabling organ-on-a-chip innovators to navigate towards faster development and broader adoption. Essential criteria to be fulfilled include the ability to reproduce functionality within and across laboratories, execute with good experimental design, knowledge of model stability over time and donor variability, and qualification of supporting analytical methods.

Lastly, successful proliferation of organ-on-a-chip technology – and the experimental results they produce – within pharmaceutical organizational hierarchies and cultures will lead to the continuing growth trajectory of adoption.

What can you tell us about the new CRADA with the FDA?

The first FDA-Emulate CRADA was in 2017 and was focused on toxicology. Our new multi-year CRADA expands beyond toxicology and is agency-wide, meaning that divisions throughout the FDA will be able to use Emulate products for programs that address some of the most challenging areas, including Alzheimer's disease, the intestinal microbiome, liver toxicity, and, importantly, COVID-19 (5).

Toxicology leaders at the FDA have been involved in collaborative research with our technology since before we commercialized it – back in 2010 when it was in development at the Wyss Institute for Biologically Inspired Engineering at Harvard University. In 2017, after years of being connected with our technology, the FDA established an initial CRADA focused on using Emulate Organ-Chips for toxicology applications within the regulatory process. It was designed so the FDA could gain first-hand experience with our Human Emulation System, working alongside our scientists to generate data together. It is beneficial for the FDA to have a Human Emulation System in their laboratories, and it will pave the way for qualifying the use of our technology and integrating it within the existing regulatory framework for product testing.

The FDA seeks to engage with alternative methods not only to reduce the risk of products reaching the market with toxicological consequences, but also to ensure that regulated products reach the market faster and with improved efficacy (6).

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In what ways can organ-on-a-chip technology be used in the fight against COVID-19?

The COVID-19 pandemic has required scientists to improve the predictive nature of preclinical models to accelerate therapeutics and vaccines entering the clinic. Species differences – including differences in viral pathogenesis, immune response and immune system interactions, inflammatory response, pharmacokinetics, and drug action – are known to impact successful translation of preclinical data to the clinic. More human-relevant alternatives, such as organ-on-a-chip technology can be adopted to accelerate discovery and development efforts in COVID-19 (7).

Historically, animal alternatives for studying respiratory viruses have involved conventional in vitro models that use cell lines (such as Vero, A549, or MDCK cells.) These approaches are poor predictors of human outcomes, most likely due to the simple culture conditions that lack the in vivo relevance and biological complexity required to model viral pathogenesis. In contrast, Emulate Lung-Chips can more faithfully recreate human biology and pathophysiology observed in vivo, including mucociliary clearance, lung inflammation, immune cell recruitment, cytokine production, viral infection, and pulmonary edema (4, 8, 9, 10, 11, 12).

Emulate Lung-Chips have been shown to support key hallmarks of the cytopathology and inflammatory responses observed in human airways after viral infection with human rhinovirus, influenza, and SARS-CoV-2 viral particles that express the SARS-CoV-2 spike protein, as well as relevant levels of angiotensin converting enzyme-2 (ACE-2) and TMPRSS2 protease. Emerging evidence also suggests that the endothelial tissue plays a critical role in SARS-CoV-2 pathogenesis (13) – and some organ-on-a-chip products can incorporate this cell layer. Overall, Emulate Organ-Chips can enable more rapid insights into COVID-19 and other human diseases – and precisely predict human response to vaccines and drug candidates.

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Fifty Functional Cures

Gene therapy's "single most remarkable achievement," CARs for solid tumors and plenty of new collaborations… What's new from the Cell + Gene Curator?

By James Strachan

There have been some big moments for the gene therapy field – China's approval of Gendicine in 2003, uniQure's European approval in 2012, and Lexturna in 2018... But it would be difficult to top the moment that kicked everything off: at 12:52pm, September 14, 1990, Ashanti DeSilva became the first person in the world to receive a gene therapy (1). DeSilva was then four years old and had been diagnosed with adenosine deaminase (ADA) deficiency, a form of severe combined immunodeficiency disease (SCID).

Over the first six months following treatment, DeSilva T-cell count increased and she quickly tested at normal levels. Her health took a remarkable uptick over the following two years. But with no selective advantage, the small number of transfected T cells were unable to form a stable population and eventually died. However, DeSilva exhibited no noteworthy side effects and grew up normally into adulthood. The trial showed that gene therapy could be safe and effective – though, in this case, not curative.

In May, scientific attention returned to the ADA-SCID field with what Fyodor Urnov, Professor and CRISPR researcher at the University of California, described as "The single most remarkable achievement of the gene therapy field since it started in 1989" (2). Donald B. Kohn and colleagues treated 50 patients with ADA-SCID with an investigational gene therapy composed of autologous CD34+ HSPCs transduced ex vivo with a lentiviral vector encoding human ADA (3). Overall survival was 100 percent up to 24 and 36 months. And of the 50 children, 48 are no longer showing symptoms of ADA-SCID.

Bravo to everyone involved in the work! And special congratulations to Kohn, who this week was awarded the ISCT Career Achievement Award in Cell & Gene Therapy (4) – the Society's highest honor.

"He developed the first successful hematopoietic stem cell gene therapy, for children with 'bubble baby disease' – ADA deficiency – and has now functionally cured over 50 children," said Jan Nolta, UC Davis. "The entire field seeks to build upon his success in these trials and he is highly deserving of this award."

And from clinical successes to, hopefully, a glimpse into the future… a gene therapy has prevented learning and memory loss in a mouse model of Alzheimer's disease (AD), according to research from the University of California San Diego School of Medicine (5). The researchers used a viral vector to introduce synapsin-Caveolin-1 cDNA into the hippocampus region of three-month-old transgenic AD mice. Caveolin-1 is a scaffolding protein that builds cell membranes; when it decays, it causes cell dysfunction and neurodegeneration.

"These results suggest SynCav1 gene therapy is an attractive approach to restore brain plasticity and improve brain function in AD and potentially in other forms of neurodegeneration caused by unknown etiology," wrote the authors (6).

Cracking solid tumors

Many people have spoken about the shift, following the first CAR-T approvals in 2017, from questions of scientific efficacy to manufacturing and

Credit: Matt Beardsley/UCSF (PRNewsfoto/ Thermo Fisher Scientific)

Meet The Curator

How did the Cell + Gene Curator come about?

I joined Texere Publishing and The Medicine Maker magazine around five years ago. Back then, we were thinking in terms of small molecules and biologicals, which included cell and gene therapies. Now, given the rise of CGT, we see the pharma industry as a triad: small molecules, large molecules, and advanced therapies. We realized when looking for content for our Upfront news section that there were more CGT-related stories – be it new facilities being built, clinical updates, early-stage research or new collaborations – than we knew what to do with. I remember someone asking the question: wouldn't it be useful if someone just collated – or curated – all the most interesting stories each week? This was the genesis of The Cell + Gene Curator.

So, what exactly is The Cell + Gene Curator?

The idea behind The Curator is to deliver the week's cell and gene therapy news – the latest discoveries, process innovations, and business deals – into a five-minute read. It's aimed at professionals working in the cell and gene therapy sector. But we also want the Curator to be a hub for the community – somewhere to share ideas and opinions in addition to curating all the business and scientific updates. So I'm always keen to shine a light on the big issues facing the field, as well as reaching out to the individuals behind the news of a new manufacturing facility or new class of CAR T-cell therapy.

How do you keep up with all the developments in cell and gene therapy?

It's easier said than done! I have a long list of sources that I check throughout the week – filing away anything that sounds interesting before whittling the stories down to the top 15 or so that make it into The Curator. But I find the easiest way to keep up with all the developments is to speak with people. I spend a lot of time reaching out to my network in the field to make sure I've got my ear to the ground. And we're frequently developing longer-form CGT-related pieces for The Medicine Maker, which are usually based on interviews – and that's an excellent way to keep up with what the experts and pioneers in the field are thinking (or worried!) about.

commercialization – how do you scale a personalized, autologous, cell therapy? Will the industry shift to a more decentralized manufacturing model? And how will payers afford the often very expensive one-off costs? Several years later, many of these questions remain unanswered. But it seems we're witnessing a return to questions of scientific efficacy – specifically, how can we crack solid tumors?

Last year, University of Pennsylvania researchers genetically engineered macrophages to kill solid tumors in both mouse models and human samples (7). Then, in March, Carisma Therapeutics, a company founded by researchers at the University of Pennsylvania, announced that it had dosed its first human participant in a phase I clinical study assessing the safety of CAR macrophages (8). A review of recent developments in CAR-macrophage-based treatments for solid tumors from Anhui Medical University, China, researchers cited "great potential" – with issues around cell proliferation and migration (9).

In April, the University of California San Francisco published two papers on their "SynNotch" system. In the first paper, they found that SynNotch-CAR-T cells could completely clear human patient-derived tumors from the brains of mice – safely and without recurrence (10). In a second paper, another set of researchers showed how components of the system can be switched out to target other cancers, such as ovarian and lung (11).

The new approach has two-steps. The first step uses synNotch to give CAR-Ts the ability to carefully "judge" if they are in a tumor or not; the second step uses a different set of synNotch sensors to ensure a strong tumor-killing response. "These findings address all critical challenges that have been in the way of developing immunotherapies for patients who suffer from these cancers," said Hideho Okada, co-author of the first paper. "This science is ready to move towards clinical trials."

Collaboration is key

A cross-industry alliance between Astellas, bluebird bio, Bristol Myers Squibb, Kite (a Gilead company) and Novartis called

the Cell and Gene Collective launched in May. Their (collective) aim is to increase awareness and understanding of cell and gene therapies in the UK. Earlier this year, we spoke with Roudie Shafie, Director at OVID Health (which is acting as secretariat and coordinating the efforts of the Collective) about the project (12). And we spoke with Anita Ralli, Chair of the Collective and Associate Director Government Affairs at Gilead Sciences, to find out why collaboration is so important for cell and gene therapy.

"To date, the UK has been pioneering in adopting cell and gene therapies to transform the lives of people with devastating diseases, such as end stage cancer," she said. "However, as the science develops and these technologies are applied to a greater number of conditions, new models of care will need to be developed and potentially new ways of accessing value established. Through sharing our experience across companies, we hope to be constructive partners to the NHS and other stakeholders in helping ensure people in the UK continue to be among the first to access the innovation these therapies represent."

In further collaboration news, Thermo Fisher Scientific and the University of California, San Francisco are working together on a cell therapy manufacturing and collaboration center. Set to open in 2022, the 44,000-square-foot facility will be located on UCSF's Mission Bay campus (13). We reached out to Mark Stevenson, Executive Vice President and Chief Operating Officer of Thermo Fisher Scientific, to find out more.

"Emerging biotech companies are doing a great deal of innovation in the cell-based therapies space, but they often face challenging timelines and milestones to support their programs," he said. "Cell-based therapy developers will also have the opportunity to integrate high-quality materials, instruments and pre-configured workflows designed to scale up development and accelerate commercialization and manufacturing. Ultimately, this new facility will help more cell therapies progress through the pipeline to deliver transformative medicines to patients."

R&D Eye Alliance. BlueRock, FUJIFILM, and Opsis also entered into a strategic R&D alliance in May to discover cell therapies for eye diseases (14). The companies have their sights set on off-the-shelf iPS cell therapies for age-related macular degeneration and inherited retinal diseases. Under this agreement, BlueRock has the option to exclusively license three retinal cell therapies currently in pre-clinical development from both parties.

Finally, we return to solid tumors: MD Anderson and Refuge Biotechnologies are working together on engineered TILs and CAR T-cell therapies for solid tumors (15). MD Anderson will apply Refuge's cell engineering platform to its TIL programs, and the companies will co-develop Refuge's RB-340, a HER-2 targeted CAR T.

"It is my belief that TILs are poised for a significant impact in the field of cancer therapy, and engineering improved TILs is a vital part of advancing this modality," said Jason Bock, Vice President of Therapeutics Discovery and Head of Biologics Development at MD Anderson.

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How to Plug the Skills Gap

Experts from the BIA got together to discuss how the UK's biotechnology industry can capitalize on recent investment and post-COVID-19 public appreciation to attract and train more people

By James Strachan

The UK's biotech sector is booming. According to the Bioindustry Association (BIA)'s recent report of UK biotech financing, there has been a 1,000 percent increase in biotech investments since 2012 (1) – and the UK is up there with San Francisco and Boston as one of the world's leading life science clusters. The sector has also been seen as a shining light in the fight against COVID-19, with several UK-based companies and institutions playing key roles in developing and manufacturing vaccines quickly. However, despite the positivity and momentum within the sector, there is a lack of skills in certain areas – threatening the industry's potential growth.

The scale of the problem

To characterize the scale of the skills challenge and offer suggestions for plugging the gap, the BIA hosted a panel discussion entitled, "How to develop the skills needed for a thriving biotech sector."

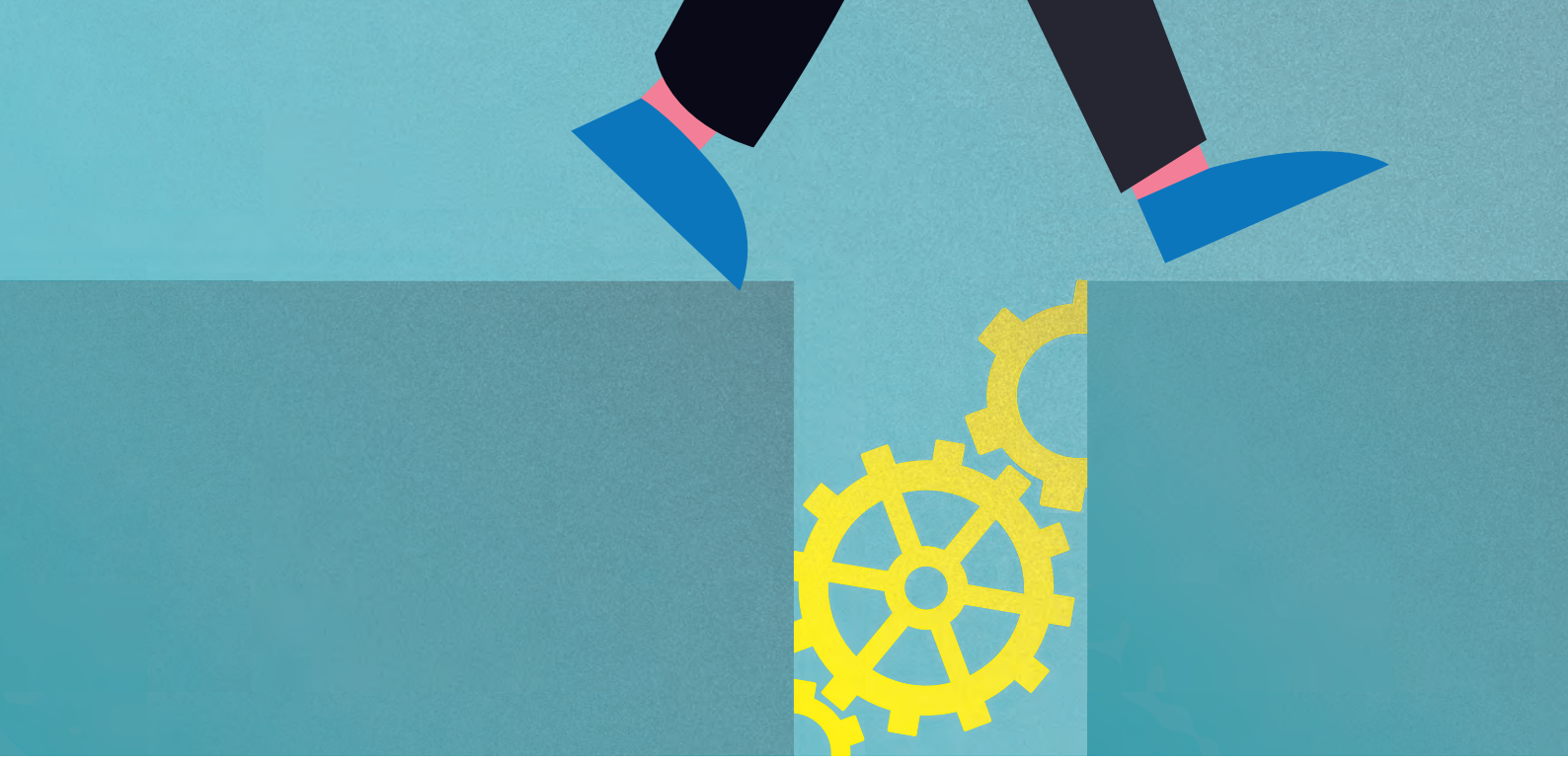
Will Milligan, Chair of the BIA's LeaP Alumni Group and Process Development Lead at eXmoor Pharma Concepts, set the scene by citing the BIA and the ABPI's Life Sciences 2030 Skills Strategy report (2). Their research found that the UK will need 133,000 skilled scientists by 2030 to support the industry's growth. "That's a crazy number," he said. But it's not just science and manufacturing skills; there's also a need for managers, leaders, software developers, commercial and financial skills, regulatory, personal development, and more. "We really need to think about how to fill these gaps."

The panel also discussed the challenges facing specific sectors within the life sciences, beginning with cell and gene therapy. The UK Cell and Gene Therapy Catapult's Skills Demand Survey 2019 found that 83 percent of ATMP and vaccine manufacturing companies raised concerns that the recruitment and retention of skilled talent would slow down or delay their forecasted manufacturing expansions (3). And the problem isn't limited to the UK. For example, the International Society for Cell and Gene Therapy (ISCT) has put together a range of proposals to help address the global talent gap in advanced medicine, including mentoring programs, training courses, and public education programs, which The Medicine Maker covered in its Cell and Gene Therapy Supplement (4).

Reporting on findings from the BIA Cell and Gene Therapy Advisory Committee (which she chairs), Helen Delahaye, Consulting Chief Operating Officer at Azellon, highlighted a lack of trained people in process development, manufacturing, data handling, and software architecture, as well as specialists in commercialization. She also noted that cross-movement of staff from company to company is leading to continuity gaps and rising salaries.

"This makes the UK less attractive to investors wanting to set up new cell and gene therapy companies," she said. Delahaye also spoke about the challenges universities have faced during the pandemic and how those could exacerbate the problem. "Universities have not been able to offer much lab time for students going through undergraduate courses during the pandemic and that could add to the skills gap," she said. "It's a bit of a bleak picture."

The panel identified genomics as another field with positions to fill. Adrian Ibrahim, Chair of the BIA Genomics Advisory Committee and Head of Technology Transfer and Business Development at the Wellcome Sanger Institute, believes genomic data is only going to get bigger and more complex. "As that data grows, we need smarter ways of aggregating, analyzing or visualizing [it]," he said. "There is a massive and already unmet need for high-quality data scientists and high-quality software engineers. Not wishing



to sound negative, but we talked about this stuff five, six, seven, eight years ago – it wasn't difficult to predict. We have some initiatives that we put in place, but not enough to keep pace with genomics."

The third sector discussed by the panel was engineering biology – the design and construction of novel genes, pathways, and organisms. It brings together a range of disciplines and skills from biology to chemistry, engineering to bioinformatics and computing – and that means competing with other, often lucrative, sectors for prospective employees. Tim Brears, CEO of Evonetix, used his company as an example. "We're developing a platform for DNA synthesis and most of the people within our company are physical scientists; we have electronics engineers, software engineers, chemists, biologists – a wide range of disciplines," he said. "If you contrast that to the traditional drug discovery company, where you might find medicinal chemists, biologists, and so forth, the skill sets we need are much broader. We're competing with the likes of Google and Microsoft."

How can we close the gap?

Coming back to cell and gene therapy, Helen Delahaye spoke about the importance of apprenticeship schemes – of which there are several in the UK. Responding to the recommendations of the Advanced Therapies Manufacturing Taskforce, the UK Cell and Gene Therapy Catapult was awarded £1.5 million by the UK government's Industrial Strategy Challenge Fund to establish the Advanced Therapies Apprenticeship Community (ATAC). The purpose of the community is to create a ready supply of skilled talent ranging from manufacturing operatives to technical experts and researchers. Each Friday, ATAC hosts a "lunch-and-learn" meeting for employers who already have apprentices or who are thinking of taking apprentices on. "That's one great initiative that's helping to bridge the skills gap in cell and gene therapy," said Delahaye, who also noted that there are currently around 137 apprentices working in six companies, half of which are SMEs. "But that's still a small number compared with the 33,000 scientists needed."

Another piece to the puzzle is the Advanced Therapies Skills Training Network (ATSTN), which is backed by £4.7 million in funding from the Department for Business, Energy & Industrial Strategy and Innovate UK. Over the past year, ATSTN announced two of an initial three new National Training Centres, which will deliver on-site advanced therapies and vaccine manufacturing training – both practical and digital. In March, the National Horizons Centre, Darlington, was confirmed as the first National Training Centre (5); and in May, RoslinCT, Edinburgh, was selected as the second (6).

Delahaye also discussed a number of training videos and webinars that have been created in partnership with the NHS. "These have become very popular, attracting up to 1,800 attendees," she said. The group also hosts a series of e-learning modules, which are free to NHS staff and can be part of their individual professional development as certified courses.

For students looking to get into the industry, there are now postgraduate courses in cell and gene therapy in the UK – notably at the University of Manchester, the University of Sheffield, and University College London. And, in the US, Delahaye noted that some companies have collaborated with community colleges to set up vocational degrees that train technicians in manufacturing and process development for cell and gene therapies. "This is something that could be considered in the UK," she said.

Reaching further back, Delahaye noted that a "cell and gene therapy explainer"

has been well received in schools. "It was actually written for politicians," she said. "We need to be thinking about our school leavers at 16 and 18. Where are they headed? Are they aware of the industry?"

When asked what could be done to help academia and industry build their skills in the genomics sector, Adrian Ibrahim cited the need for pre-competitive knowledge sharing. The Wellcome Genome Campus set up an initiative six years ago to identify targets based on strong genetic associations underlying disease. Industry partners and academics are involved – and everyone involved has a veto on the specific programs. "Companies support the program because they can influence which programs are taken while also accessing genomics infrastructure – of which there may be one or two in the world at that scale, and certainly only one in Europe," he said. "This has exposed hundreds of scientists to quite a large number of pharma companies. There are some of the finest minds in the world working with each other, sharing knowledge and building."

Ibrahim remembered speaking to the head of cancer programs when he first arrived at the Welcome Institute in 2012. "He said, 'Some of our biologists will arrive without coding skills, but nobody will leave without coding skills,' and that's how it should be across the board. We have lots and lots of smart people; we just need to create the opportunities."

LeaPing forward

Will Milligan spoke about the LeaP Alumni Group as an example of a way to inspire people to advance in their careers and, potentially, become leaders. The program brings together 12 people per cohort from different companies within the biotech sector. "It's an incredibly valuable and unique opportunity," said Milligan. The program lasts two years and, every couple of months, each member of the program takes turns inviting the others into their company to share best practice from their sites. It gives participants a chance to network with others and draw upon different experiences and backgrounds. "How often do people from supply chain manufacturing or regulatory backgrounds get together and talk across sectors and across companies?" he asked. Milligan previously participated in the program while working for a 30-person company and had the chance to visit sites like GSK, Allergan, and Fujifilm.

"It really opened my eyes to what else goes on in the industry," he said. "There were some really inspirational moments during the program. For example, we were visiting Fujifilm and Steve Bagshaw, who was CEO at the time, walked in and chatted to us for 30 minutes about his career and what he'd done in the industry. And it was a fascinating story and those kinds of moments kind of stick with you and inspire you going forward." The program was so successful that the BIA doubled its size after two years – there are two parallel cohorts now. "The key thing it does is inspire."

The discussion closed with the panelists sharing their final thoughts on how to close the skills gap within UK biotech. "When we're asking the question, we're thinking 10 years from now, but my feeling is that we need to start looking earlier," said Charlotte Casebourne, Vice-Chair of the BIA People, Skills and Talent Working Group and Co-Founder & CEO of Theolytics, echoing Delahaye's earlier point. "We need to be asking: at what stage can the BIA start to inspire people to start thinking about what their path to the industry might look like?"

Delahaye noted that there are many British people working abroad in the cell and gene therapy area. "How can we bring them back to the UK to decrease our skills gap?" she asked. "Perhaps that's something we can take forward."

"We have lots of small wins, but big wins only come from national-scale programs," said Ibrahim. "We need to start funding academies and specialist centers for large-scale, cross-disciplinary work."

We also reached out to Oliver Hardwick from Cytiva, and Chair of the BIA Skills Network, who summed things up by painting a positive picture for the future of the sector. "This past year, the UK Life Sciences sector has demonstrated its capabilities to the world. And with appropriate commitment from government, we are likely to see rapid growth in the biotech sector over the next 10 years – with the UK positioned alongside the world's leading biotech regions," he says.

"At the core of that growth will be the skills and talent development across all aspects of our industry – from bioinformatics and cGMP operations, to entrepreneurial and business management skills. Continued focus on skills is required to ensure we build on a position of strength and capitalise on investment to propel the UK life science sector forward to the overall benefit of patients globally."

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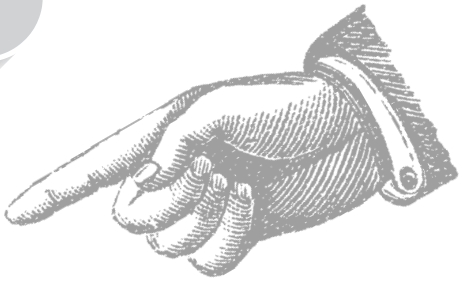


Powering on Through the Pandemic

We ask members of our Power List to share their views on how the industry is coping with the pandemic – and what needs to change for the future

We recently celebrated the publication of The Medicine Maker 2021 Power List, which presented the top 20 most inspirational medicine makers in three different categories – Small Molecules, Biopharmaceuticals, and Advanced Medicine – as nominated by readers and selected by a judging panel. The full list is available at https://themedicinemaker.com/power-list/2021.

Here, we ask a selection of Power Listers for their thoughts on the COVID-19 pandemic…

Gil Roth

Gil Roth founded the Pharma & Biopharma Outsourcing Association in 2014 to give a voice to the CDMO sector in regulatory, legislative, and business matters. During the pandemic, he helped connect the federal government and other parties with CDMOs to develop and manufacture treatments and vaccines.

Post-pandemic, the industry – and governments across the world – will have to answer major questions about pharma supply chains. Our members have risen to the challenge of helping develop and manufacture vaccines and therapeutics for COVID-19 while maintaining supply of their clients' non-COVID-19 products, but it remains to be seen how manufacturing infrastructure will change to accommodate the potential for more global vaccination programs. This will mean hard decisions about building – and paying for – excess capacity into the supply chain, even before the drug substance stage. Government interventions to reallocate resources to particular manufactures may help boost production in the short term, but can create cascading disruptions of other critical, life-saving products. Avoiding those unintended consequences, stemming national or regional blockades, and ensuring equitable access to vaccines: those may be "beyond our pay grade" as CDMOs, but the pandemic has raised the awareness of the outsourcing sector and we've made sure our voice is heard in these conversations.

Beyond that, the pandemic has created changes to every aspect of our lives and work and it remains to be seen what changes will prove long-lasting. The FDA, for example, has had to make major changes in its inspection practices when in-person inspections were off the board. We've had conversations with them and other regulators about how to incorporate some of their changes – more records requests, use of virtual technologies, greater reliance on mutual recognition of inspections – into the post-pandemic world. Greater flexibility and more harmonization among regulators should improve facility assessments.

COVID-19 slowed down clinical trials for many candidates, but we continue to see huge promise in the development of cell and gene therapies. From a CDMO perspective, that's reflected in the billions of dollars our members have invested in that space. These can be transformational modalities for patients, and given the expertise and capital necessary to manufacture them, it's clear that CDMOs will be critical in bringing that vision into reality.

Kiran Mazumdar-Shaw

Kiran Mazumdar-Shaw is Executive Chairperson at Biocon and Biocon Biologics. She is seen as a pioneering biotech entrepreneur, a healthcare visionary, a global influencer, and a philanthropist.

A positive outcome of the pandemic is the global commitment to collective surveillance and pandemic prevention and preparedness. At long last, healthcare investment is likely to see a sharp increase across the world. Moreover, the crisis has brought to the fore a host of complex issues around drug pricing and distribution, as well as a number of social and other inequalities that are now demanding close attention.

Governments worldwide will be forced

Future Perspectives

In 10 years, how will the industry look back on COVID-19?

Edward Haeggström, Chief Executive Officer at Nanoform

"COVID-19 has marked a turning point in the pharmaceutical industry, sparking one of the most efficient and collaborative global responses ever seen with the development and rollout of vaccines. I hope that, in 10 years' time, we will look back on this pandemic as the start of a new era in the industry and a trigger to the acceleration of future developments. It showed that the impossible can be done: vaccines to the market from scratch on a global scale and in a single year."

Andrew Moore, General Manager at Pfizer CentreOne

"The industry will view this historic period as the catalyst that propelled us to do things differently and collaborate in ways not seen before. We found ways to be more innovative because we worked closely together to find solutions faster and overcome challenges at a time of unprecedented need. This was often achieved despite working remotely and conducting meetings virtually. There are many lessons learned throughout this experience, some of which we haven't even realized today."

Kelly Chibale, Neville Isdell Chair in African-Centric Drug Discovery & Development and South Africa Research Chair in Drug Discovery

"COVID-19 has reminded us of the importance of investing in infectious disease R&D and also provided a blueprint for global collaborations toward efficiently delivering products to address unmet medical needs for the benefit of patients."

Andrew Moore

Ross Burn, CEO at CatSci

"The pharmaceutical industry will look back at this time as a catalyst for change in terms of realizing the power of collaboration, digital transformation, and redefining how quickly new vaccines and medicines can and will be developed. I hope that the incumbent mass screening capabilities that have proven key for many countries during the pandemic will be repurposed for other diseases, giving a better outlook for patients by boosting prevention and early detection."

Will Downie, CEO of Vectura

"Often, out of a crisis, great things happen. This is clearly a moment in time where the world has faced one of its biggest challenges, with the pharmaceutical industry playing a central role in fighting the pandemic. I truly believe we will look back on COVID-19 as a seminal moment; a time where the impossible was made possible. Drugs that would normally take 10 years to bring to market were developed in less than a year. It may be the point where a seismic shift in pharmaceutical development changed forever. I hope so."

to explore innovative partnerships with the private sector to address essential healthcare infrastructure, create viable healthcare contingency plans, and build strategic reserves of key supplies. There is likely to be a reprogramming of national economic priorities toward universal healthcare and providing social safety nets for the most vulnerable sections of society. I sincerely believe that the COVID-19 experience will encourage governments to engage and collectively endeavor to deliver universal healthcare on a platform of access and affordability.

Despite its disruption, COVID-19 has also had a positive impact on medical innovation and global collaboration in drug development. We are witnessing one of the most frenetic and promising periods of medical invention and innovation in history. Though scientists are currently focusing on COVID-19 vaccines and therapies, the research and development efforts are likely to lead to a host of other discoveries, many of which will yield significant and sustainable benefits to mankind.

Scientists around the world are sharing information like never before and pharmaceutical companies are collaborating in unprecedented ways. This kind of close collaboration across borders is helping science leapfrog, leading to an acceleration in drug development projects.

Governments worldwide will have to strike a better balance between regulation and innovation in the interest of public health. Now that our priorities have radically changed, our regulatory frameworks need to change, too. If the world can take a risk-based approach to COVID-19-related treatments and vaccines, it can extend the same approach to other diseases. If the "lab to market" journey of any therapy can be compressed like it has been for vaccines against COVID-19, then many unmet healthcare needs can be addressed – and rapidly. Regulatory agencies should pivot to basing their decisions to approve or not approve a drug on the basis of real-world evidence pertaining to the safety and efficacy, rather than data from clinical studies conducted under a controlled setting.

John Chiminski

John Chiminski is Chair and CEO at Catalent Pharma Solutions. In the more than 20 years he has spent at Catalent, he has overseen the company's strategy to help accelerate the small molecule development process and improve clinical outcomes.

The vertically integrated pharmaceutical industry of 20+ years ago would have

been challenged to mobilize capacity and capabilities at the scale and speed required to respond to the pandemic in the way we have, and we have seen a whole new level of industry collaboration. I think we have proven that CDMOs are important and our customers are including us in all manner of initiatives – for example, in COVID-19 response best practice sharing forums. This demonstration of integration and collaboration has helped the industry solve problems and avoid many supply chain issues, and we will do all we can to continue in this way. Regulators have also been flexible and available, even adopting remote/on-site hybrid inspections to support essential products.

We also learned that we can act quickly in our industry, where timelines have previously been measured in years and decades. From contracts being put in place to secure capacity, from initial discussion to signed agreements in weeks, not months... In one case, we went from tech transfer to a released batch for a high-profile therapeutic in just 10 days.

Rick Bright

Rick Bright joined The Rockefeller Foundation in March 2021 as Senior Vice President, Pandemic Prevention & Response, Health Initiative. He will lead the development of the Foundation's pandemic data and action platform, which will help prevent future pandemics by identifying and responding to the earliest alerts of a disease outbreak and stopping it in the first 100 days.

During the COVID-19 response, the industry has shown tremendous innovation in technologies developed for rapid diagnostics and vaccines, and also in new ways of partnering for surge capacity, both domestically and globally. We have also learned a lot about the global nature of supply chains.

I think many post-COVID-19 discussions in industry will center on sustainability of newly established capacity, ways to integrate technologies – particularly new diagnostics – into daily life, and a split discussion about strengthening global partnering and supply chains versus how much domestic capacity a company may plan to build within a few countries.

It will be critical to leverage the regulatory and clinical trial efficiency we have observed in evaluating drugs and vaccines for the COVID-19 response. There are many examples around the world of significant improvements to reduce the development time using novel clinical trial designs and improving efficiency in the regulatory review process. There is also the ability to incorporate artificial intelligence into in silico processes that can reduce the time for new molecule discovery or synthesis. This can reduce risk of candidate failure – again regaining valuable time in the development timeline.

Emmanuel Ligner

Ligner is President and CEO at Cytiva and Group Executive at Danaher Biotechnology Group. He has been the President and CEO of Cytiva since July 2017, when it was known as GE Healthcare Life Sciences.

The post-pandemic conversation will revolve around the power of collaboration, mRNA technology, and the regionalization/localization of the supply chain. The collaboration between industry and government created the environment needed to accelerate vaccine development. We "cracked the code" on new tools that will have an enormous impact on global health. We will also be discussing in-region, for-region supply chains. Though the "Center of Excellence" model and one global hub worked before, the pandemic created a need for more regional supply chains.

This past year proved we can accelerate drug development and find ways to solve the world's greatest health challenge when financial risk is minimized and regulatory pathways are accelerated. We must bring these lessons learned with us into the post-pandemic world. Historically, phases of a clinical trial take place in sequential order but, with the COVID-19 vaccines, they were done in parallel. Drug developers also planned for commercial manufacturing early in the process. Accelerating drug development will require parallel planning all the way through commercial manufacturing.

I'm excited about the development of new modalities. It's amazing to see years of research and development come to fruition with mRNA technologies and cell therapies finally reaching patients. We must continue investing in automation and digital technologies that will help accelerate the development and manufacture of these novel therapeutics so we can reach as many patients as possible.


Miguel Forte

The Advanced Medicine View

How might the industry's success in developing and rolling out COVID-19 vaccines be applied to cell and gene therapy development?

Miguel Forte, CEO at Bone Therapeutics
"Development of vaccines for COVID-19 came about at lightning speed because of the alignment of a global need, regulatory support, and political will! Extensive scientific collaboration and focus to address a significant unmet medical need is an important lesson to extrapolate to the field of C&GT, where it is key to collaborate and combine emerging technologies to deliver what we know is bringing enormous value to patients with still unmanageable conditions."

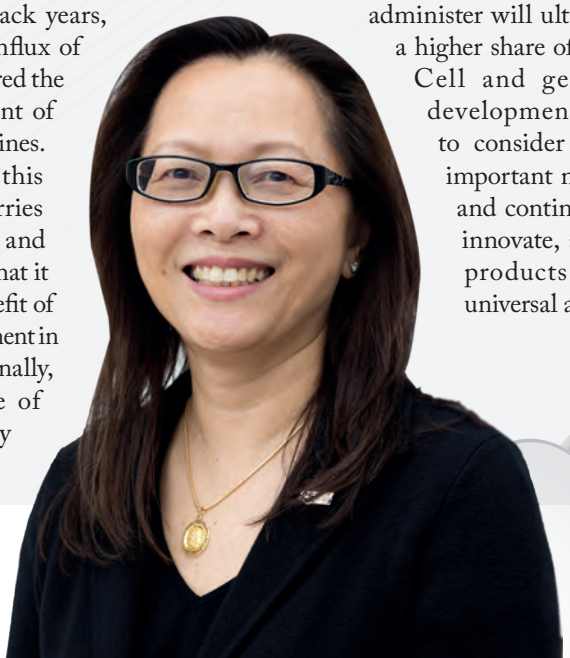
Catherine Bollard, Director at the Children's National Research Institute and Professor of Pediatrics at George Washington University
"The success of the mRNA vaccine technology for COVID-19, I believe, has huge implications for the cancer vaccine field and ultimately for combination vaccine and cell therapy approaches for cancer and viral infections."

Evelina Vågesjö, Co-Founder and CEO at Ilya Pharma
"Cell and gene therapies are aiming to cure and/or solve unmet medical needs currently not solved by the traditional small molecules and biologics. The industry and regulators have proven that, with collaboration and dedication, it is possible to deliver safe vaccines when needed. I hope that this level of collaboration to accelerate development of cell and gene therapy products becomes the new normal because there are still many urgent unmet medical needs."

Fabian Gerlinghaus, Co-Founder and CEO Cellares
"Like many, I have been fascinated by the speed with which vaccine manufacturing facilities can be brought online. Processes for manufacturing vaccines were transitioned from one facility to another. Readying facilities to manufacture products occurred with epic velocity. Cellares is working to accelerate time to market for cell therapies in a similar way."

Bruce Levine, Barbara and Edward Netter Professor in Cancer Gene Therapy at the University of Pennsylvania
"Government support of vaccine research dates back years, and the recent influx of funding has spurred the rapid development of COVID-19 vaccines. The success of this development carries lessons for cell and gene therapy in that it validates the benefit of long-term investment in research. Additionally, the importance of a robust supply chain has gained wide acceptance during mass vaccination campaigns. In particular, the investment and knowledge gained implementing large-scale cold chain logistics will carry lasting benefits for future delivery of cell and gene therapies."

Queenie Jang, CEO at ISCT
"Looking at the variety of vaccines in use, this has provided a wealth of real-world data to explore how differing storage, handling, and logistics requirements directly affect adoption. This has been especially apparent in evaluating the cold chain requirements for various vaccine candidates. Although technically possible, restrictive cold chain and product characteristics (ie., ultra-low temperature storage, stability) will ultimately impact universal adoption. Worldwide, vaccines that are easiest to transport, store and administer will ultimately have a higher share of the market. Cell and gene therapy development will need to consider these same important market forces and continue to invest, innovate, and improve products to achieve universal adoption."


Queenie Jang

Ushering in New Technology – and the Next Generation

Sitting Down With… Maik Jornitz, President and CEO of G-CON

What did you initially have planned for your career?

Something totally different; I was actually always interested in interior design! But in those days (at least in Germany) nobody hired interior designers, so it wouldn't have been a good career choice! I was also very interested in biology and engineering, but I didn't know exactly how to combine the two. And then I spoke to a friend of mine who suggested bioengineering. I didn't even know this existed! For me, it was a match made in heaven.

How has uptake changed for 'podular' cleanroom tech?

The early days were definitely very hard because we had to convince a very conservative industry that this is a beneficial tool in the toolbox. But nobody wants to be the first to try something new; everybody wants to be the fastest second. Adoption is becoming more rapid now – comparable to a chain reaction. We saw the same effect with single use technology adoption. It took a long time to trigger, but today the majority of applications are running with single-use process technologies. We're seeing rapid adoption of podular cleanrooms – and the COVID-19 vaccine capacity needs certainly created additional realization of its benefits.

Outside of G-CON, you are involved with many industry societies and associations. Why do you find this so rewarding?

There are two points to this answer. The first reason could be considered selfish: I enjoy learning. I learn a tremendous amount from the network and peers, as well as from the organization's activities. I believe that you should never stop learning. You should always be intrigued by something new to improve the industry and yourself. You need to give your input and point of view, but also listen to differing views from your peers.

The second reason is a reflection of the first: over the years, I've gained a great deal of know-how and experience, and I feel I have an obligation to train the next generation – after all, at some point, we'll all retire! We need a solid base of next generation experts coming up through the ranks to take our places. I was lucky to have an excellent mentor in sterile filtration. It is a highly critical process step. My mentor trained me and introduced me to other people – and that allowed me to learn more and more. I want to share that knowledge with the next generation to build up other sterile filtration experts or people who are passionate about the industry and, ultimately, patient. I do this in many ways. I still write a lot of papers; some may be provocative, but this is necessary to encourage interaction and discussions. I also write books, and I give a lot of talks at conferences. Even throughout the pandemic, I have been pre-recording presentations for virtual conferences and taking part in Q&A sessions.

What are the most surprising changes you've seen in biopharma manufacturing over the years?

When you look at the changes, they are not surprising – other than the fact they have happened really slowly! A friend of mine always says that he has spent 40 years in the industry and what surprises him the most is that there have been no changes! I think we have so much great technology out there, but it's implemented at such a slow pace. When you look at other industries, like the semiconductor industry or the computer industry, they are much faster. We need to be much faster and visionary to be able to serve the patient better.

One good surprise is the progress in cell and gene therapy. This field has become really dear to my heart and many G-CON projects involve cell and gene therapy. We now have targeted therapies against some cancers and rare diseases. For me, it is a real glimmer of hope. Rather than throwing a nuclear bomb at cancers, we are using a sharpshooting approach. Overall, if we look at the kind of treatments that are out there today, it's clear that we are living in a much more promising era. Another fascinating bit of rapid progress can be found in COVID-19 vaccine development. We saw the industry come together and step out on thin ice by developing vaccines at great financial risk. I praise these vaccine developers; it's fantastic to see how fast they've found a solution.

If you could change one thing about the industry, what would it be?

You can probably guess from my earlier answer about change, but the one thing I would like to change is the adoption rate of new technology. If the industry adopted new technology much faster, it would definitely benefit patients.

Having said that, I can also understand why the industry is cautious – just consider the long and tedious process of post-approval changes. Indeed, it can take three or four years to have a global change implemented. I think we need an evolution – perhaps revolution – in the relationship between suppliers, industry, and regulators. If new technologies lead to higher safety for the product and the patient, why does it still take so long to implement the change? We need to find a way to get more technology into the industry. Just think: if the semiconductor industry had not adapted, we would not have smartphones...

What inspires you?

The patient, saving patients' lives! I don't work directly on the production of therapeutics, but I'm a wheel in the clock work. And the products we create are important for production. We are still saving lives. In this industry, whatever function and whatever you do, you ultimately still work for the patient. And that is inspiring.

This interview is available as a video at https://bit.ly/350uJot

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