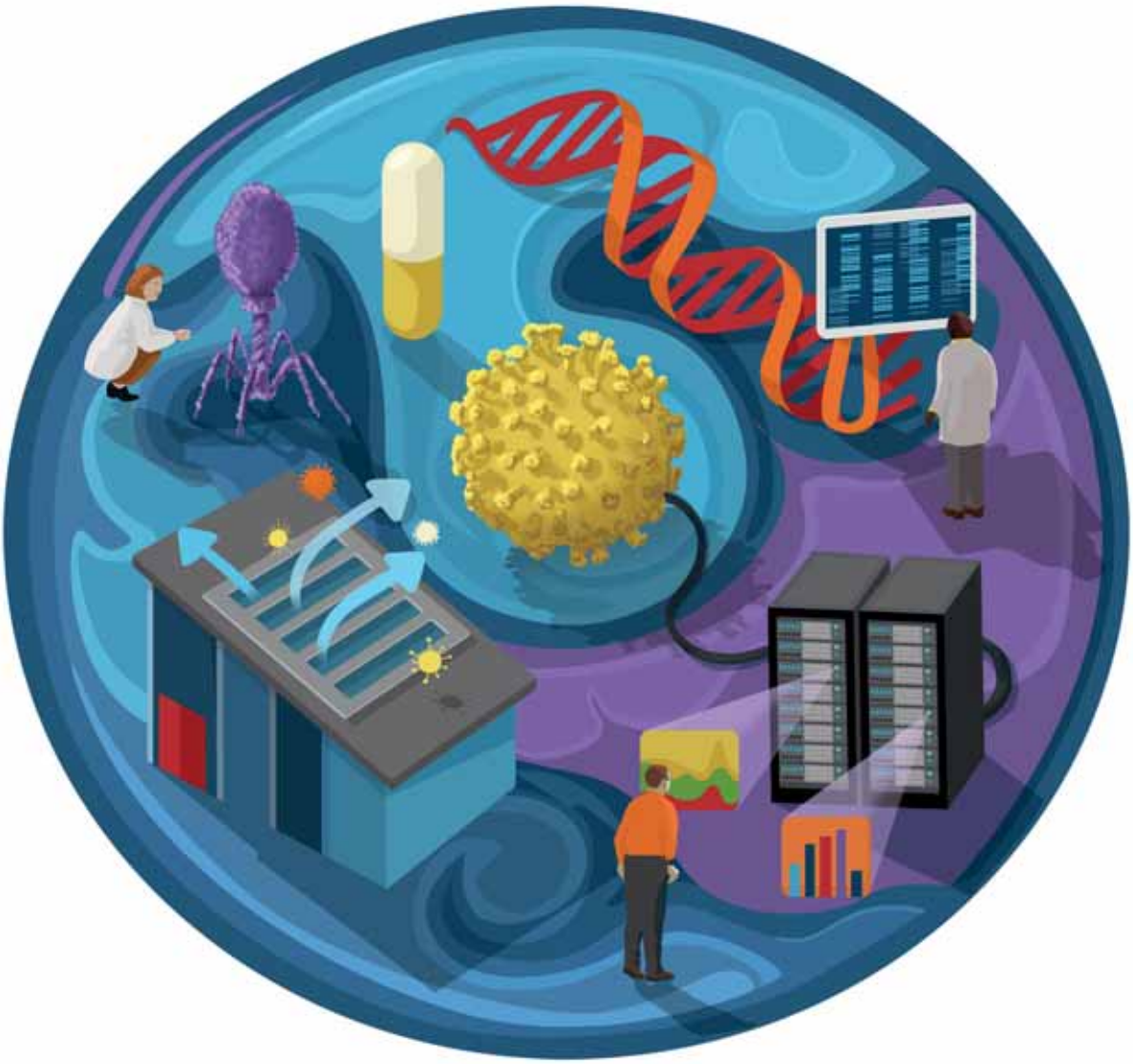
NewStatesman

Spotlight

BIOTECHNOLOGY: THE BREAKTHROUGH SECTOR

James Bethell / Chi Onwurah / Sharon Peacock / Samira Asma

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The promise of biotechnology

Biotech is booming. The past year and a half has proven to be a catalyst that has taken a respected but still somewhat obscure sector from labs and auditoriums to the front pages of newspapers – and to the top of many portfolios. Reports are replete with biomanufacturers securing record investments, planning new research centres, and calling on bright young talent to choose bio-engineering over mechanical engineering, medicine and many other disciplines.

Small wonder, then, that the government is talking up biotech as a key part of building back the UK economy bigger and better in the wake of both the pandemic and Brexit. The UK is indeed in an excellent position to do so, evident in the instrumental role UK scientists played in the sequencing of the Covid-19 genome and the breathtaking speed with which domestic vaccine manufacturing was scaled up throughout this year.

This is not, however, a fait accompli – and there are many challenges to be addressed to keep this momentum going. One is industry-specific: across biotech, managers and researchers alike complain that the different constituent disciplines are still too siloed and are not cross-pollinating each other nearly as much as they could be. Another is the risk of the government's policies getting in the way of its aspirations: post-Brexit deregulation might be an appealing prospect to some, and might indeed engender a short-lived boom in research and investment, but bonfires of regulations are hardly a sustainable fuel source, and many of the most promising applications of biotech rely on stern regulatory guidance to facilitate their entry into the market. Likewise with immigration: if the UK wants to be a world leader in biotech it needs to bring the world into the UK biotech sector, ensuring gifted researchers and engineers have every incentive and freedom to come to the UK – the entire economy will benefit from it.

Above all, biotech growth requires a steady hand. It cannot be a fad, and it shouldn't take another disaster to attract investment. The UK was able to adjust its research and manufacturing to the current crisis because of foundations laid over decades by governments past, both Labour and Conservative. It is imperative that foundations are laid now to shore up infrastructure across the sector, to allow the UK to reap benefits for many decades to come.

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Innovation is hampered by a lack of long-term focus and strategy. By Chi Onwurah, Shadow Minister for Science, Research and Digital

We need ongoing investment in life sciences

The pandemic has demonstrated Britain's strengths in life sciences to the world and, equally importantly, to Britain. The development, manufacture and delivery of the vaccine into so many arms did not happen by accident. It was thanks to sustained long-term investment under the previous Labour government, which set up the Office for Life Sciences and invested in successful institutes like the Centre for Process Innovation in the north-east, combined with attention and focus from the current government. Now I hope we will learn the lessons of that success and apply them more broadly to our biotech sector.

My background is in telecoms – I entered that sector as a graduate engineer in 1987 and I have seen it grow and become the basis for our global economy and our cultural, social and, often, educational lives. The pandemic has accelerated the migration online and we are all digital citizens now.

Today, the next big thing is often seen as being artificial intelligence (AI). It will impact how we live and work – for the better, I hope. But the real innovation may happen at the intersection of AI and other sectors, particularly biotech. The UK is fortunate in having great strengths in both. This could help us pioneer new ways to speed up the development of drugs, such as the Deepmind AI scientists who have cracked protein folding, which will make the development of antibody therapies easier, or the researchers who help us address climate change by modelling new biofuels.

Although the government certainly talks up science, and has committed to doubling science spend by the end of this parliament (after cutting it significantly from 2010 to 2015), its warm words on science have seldom been matched by deeds and the sector is hampered by a lack of long-term attention and focus.

The cuts by the government to overseas aid hit core science programmes, which benefit the globe, and the chaotically negotiated UK-EU Trade and Cooperation Agreement disrupted scientific collaboration and raised costs to science-based businesses, increasing red tape, especially for Northern Ireland. The incredible truth is that many critical science bodies did not know their funding for this year until a few days before it started. Science needs long-term funding commitments but the government refuses to provide it.

The Industrial Strategy seems to have been shelved, with decisions on science made piecemeal rather than strategically. Indeed, the government only recently announced a Science Council to give the direction to funding one would have hoped was already coming. So while

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Labour would spend 3 per cent of GDP on R&D

I welcome the recently announced ten-year plan for the sector, I note that, critically, it is unfunded and follows two sector deals, an (abandoned) industrial strategy, various missions, and challenge funds. The government needs to stop making policy by press announcement and instead deliver on real change – like actually meeting its commitment to double dementia research, or ensuring that Covid-19 tests offered to NHS staff are manufactured in the UK.

Before the pandemic I visited pioneering biotechnology company Newcells Biotech, based in my Newcastle upon Tyne Central constituency and spun out from the University of Newcastle. It was great to meet a local start-up company with brilliant scientists working to address some very important health challenges with innovative bio techniques to transform the drug discovery process and reduce animal testing. Newcells was supported by local venture capital.

Labour wants to enable more successes like that. We would build on the UK's science successes and ensure we continue to be an innovation nation, by spending 3 per cent of GDP on research and development. This target includes private sector investment "crowded in" by public money – Labour long understands the importance of policies that encourage this and it is why Gordon Brown introduced SME research and development tax credits.

This is a no-brainer for the economy. The Campaign for Science and Engineering found that for every £1 invested by the government on research and development we get back 20p-30p each and every year. Research from King's College London and Brunel University also showed that for every £1 invested in medical research we get back 25p to the economy each and every year.

The Labour Party would also champion universities as engines of regional progress, strengthening regional economies by strengthening research and development investment. Despite the government's "levelling-up" pledge, compared with the south of England the north receives less than half of the life science investment per head, although it has great teaching hospitals and significant health inequalities.

Labour would also encourage continuous life-long learning and reskilling. This must be key to the Knowledge Exchange Framework (an important element of Research England's benchmarking of universities) and will help ensure the transition to a green economy supports job creation and retention.

We should be proud that the Oxford AstraZeneca vaccine is being distributed around the world at cost. But the Covid-19 crisis highlights that we need to do more to enhance capacity for developing and manufacturing medicines and improving global equitable access to affordable medicines, medical tools, diagnostics, treatments and vaccines to protect public health here and abroad.

The UK BioIndustry Association has pointed out that the lack of UK-based investors in larger funding rounds weakens the incentive for UK firms to remain and grow in the country, meaning jobs and economic activity are lost and UK science is commercialised elsewhere. Labour would work to make more investment available across our country. The Labour Party wants to ensure more is made, built and sold in the UK. Biotech is an important part of enabling that.

Putting patients first

The NICE review is a golden opportunity to expand patients' access to new therapies, says **Gordon Lundie**, senior director of market access and pricing at Gilead Sciences

Over the past two decades, the National Institute for Health and Care Excellence (NICE) has been responsible for deciding who is able to access new medicines, making cost-benefit appraisals of their roll-out and determining the price the NHS will pay for these treatments. Along with Brexit, and the opportunities afforded to the UK by leaving the regulatory orbit of the European Medicines Agency, the current review of NICE procedures – the biggest since the body was established in 1999 – provides a chance to modernise and optimise the process by which medicines and treatments are approved and prices are set.

Since the NHS is such a huge consumer of pharmaceuticals, and has NICE acting as the gatekeeper into a national market of almost 60 million patients in England and Wales, the UK pays some of the most competitive prices for medicines in Europe, providing excellent overall value for money for our healthcare system. However, the model, as it currently stands, has its drawbacks. The UK may have some of the lowest unit costs for medicines in Europe, but patients often have to wait longer for treatment than you see in Germany, Italy, Spain and France. In simple terms, this means patients are often unable to get the treatments they need, resulting in untold human tragedy.

With our life science ecosystem and NHS expertise, the UK remains one of the best, most attractive places in the world for research and medical innovation. With the NHS's integrated service and partnerships, a host of biotech and pharmaceutical companies like Gilead, as well as top universities, the UK is at the forefront of the global industry. During the Covid-19 pandemic we've seen how essential these partnerships have been. The rapid development, manufacture and roll-out of vaccines was only made possible by "triple helix" cooperation between the public sector, academia and the private sector. This kind of rapid scale-up of cutting-edge medical technology and the breaking down of industry silos is clearly a model of best practice that we should look to emulate in the future, and the UK is one of the best-placed countries to do that. In turn, Brexit looks likely to speed up the

The UK is at the forefront of the global industry

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process by which new medicines are approved by replacing the costly, time-consuming regulatory approval process in the EU with a more streamlined, pragmatic approach.

We are, however, falling behind in other areas. As a biopharmaceutical company, Gilead invests huge amounts in new research and drug development. When these new medicines are developed – many of which have the potential to extend people's lives and greatly improve quality of life – the value to the people who take them may not be fully captured by the method NICE uses to calculate the cost and benefits of new treatments. The ongoing review, with recommendations expected in the coming months, provides the opportunity to consider serious reform.

We want to make sure the price we get for these treatments reflects the value they bring to patients and their families. To give a good example, rheumatoid arthritis can be a debilitating illness, but there are drugs called TNF inhibitors that help prevent the kind of inflammation you see with that condition. Although these drugs have been around for a number of years, NICE is only now changing its guidance to allow their use for people with moderate disease. This is despite them being used for these patients in France, Germany, Italy and Spain for a number of years. Until now, NHS patients have had to wait for their condition to deteriorate and become severe before they were able to access TNF inhibitors.

It happens due to current NICE methodology that calculates that it is cheaper for the NHS to treat people who are already disabled than it is to prevent people from becoming disabled. This is a totally false economy. By evolving NICE's approach to be more flexible, more future-oriented, and more focused on prevention, patients and the NHS will see the benefit.

We've got a real chance now, with this NICE review, for the UK to catch up with other European countries in terms of drugs access and pricing. A key area to be addressed is the discount rate. Currently, Gilead offers an innovative, individualised medicine for people with certain blood cancers, known as CAR T-cell therapy. The NHS could see any benefits well into the future, but they pay for the treatment up front. In order to factor in that future effect, NICE applies discount rates to reduce the value of those future years gained. However, this is calculated at a very high rate, so that the 20th life year gained will only be counted as half as valuable as the first – a discount rate that far outweighs the rate applied to other government investments in physical infrastructure, for example. We'd like to see the discount rate equalised, so it's consistent between the NHS and the rest of what Treasury guidance stipulates, and so people's future years of life gained through innovative new treatments are properly valued.

Another area that requires reform are modifiers. NICE only has one – the "end of life" modifier. This stipulates that if a new treatment comes along that gives at least an extra three months of life for people with terminal cancer, for example, then because that time is really valuable for people, we are willing to pay more for that than we pay for other things. There are a lot of other instances, though, when patients gain an awful lot from a medicine, not just "end of life". Current thinking places little value on medicines in comparison with how patients truly benefit from them and this is an area where NICE needs to enhance its understanding and appreciation.

Events of the past 18 months have shone a light on British healthcare innovation that's come from industry, the NHS and academia working in collaboration. At the heart of that work has been the patient. As we emerge from the pandemic, both Brexit and the NICE review give us an amazing opportunity to build upon this enhanced partnership of industry, the NHS and academia, and evolve the existing methodology to embrace the new ways of working to heighten the value medicines bring to patients. Let's grab this opportunity to strengthen the NHS for future generations.

A vaccine centre in Mysuru, India. The Oxford-AstraZeneca vaccine was developed in the UK but is being produced and distributed at relatively low cost around the world

"The UK has a deep heritage in biotech"

The health and economic benefits of the life sciences sector will help the UK build back better. By James Bethell, Minister for Innovation

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We are a world leader in this space

The biotechnology industry has played a crucial role in our response to Covid-19. Whether it's the development of the Oxford-AstraZeneca vaccine, genomic sequencing of the virus to track new variants, or the Recovery trial identifying safe and effective therapeutics, biotechnology has never played such an important role in ensuring the health and wealth of our nation. We have been able to respond rapidly to the threat posed by Covid-19 thanks to our world-leading science and research infrastructure, and genomic and health data capabilities.

Both government and the sector have made significant investments in diagnostic and vaccine R&D and manufacturing capacity. NHS Test and Trace will have created the capacity to manufacture two million lateral flow devices per day by autumn 2021 and the UK's vaccines taskforce has invested £350m to increase vaccine manufacturing capacity on our shores.

These investments open up significant opportunities for improving healthcare beyond the pandemic. By increasing the UK's diagnostic capabilities we will be able to provide patients with the right tests, at the right time, in the right place. This means treating people earlier with more precise diagnostics to prevent as well as diagnose illness, while giving patients more control over their own health by encouraging self-monitoring. Using diagnostics earlier and more effectively will help us move away from a model of get sick, get tested, get treated and towards a model of get tested, get treated.

We will pursue these opportunities by continuing to develop our strengths in R&D in biotechnology. Clinical research is the backbone of healthcare innovation and thanks to the UK government's ongoing investment and the expertise of the National Institute for Health Research, we are a world leader in this space. These capabilities have placed us at the forefront of Covid-19 research, with the first global participants in the Janssen and Novavax trials recruited in Dundee and Blackpool.

We also have the opportunity to drive the next generation of biotechnology discoveries through investing and developing our expertise in genomics and health data. In response to the pandemic, the government and Wellcome Trust rapidly funded the Covid-19 Genomics UK (COG-UK) consortium, which has taken a leading role in sequencing and analysing viral genomes. Experts from across all four nations have sequenced more than half a million genomes since the pandemic began and around a third of all genomes submitted to the global database have been from the UK. We will build on this incredible progress to support the growth and development of innovative genomics-focussed firms.

The health benefits of a thriving bio-industry are clear, but this sector also delivers important economic opportunities. The UK has a deep heritage in biotechnology providing high-quality jobs across the country. From medtech in Yorkshire and Humber to Liverpool's reputation as a leading centre for infection and immunology research, our priority is to make sure the sector has the support to build on this heritage and grow, attracting investment and creating jobs around the UK, working in close partnership with academia and government.

Biotechnology has been crucial in tackling Covid-19 and will help us develop new tools to improve how we approach research, diagnosis and treatment. Our recently launched Life Sciences Vision sets out our continued ambition to ensure the UK is the leading global location for the life sciences to innovate, grow and deliver breakthroughs to patients and the public. This is key to making sure we can gain from the health and economic benefits generated by the life sciences sector, helping us build back better and level up across the UK.

FUJIFILM Diosynth acts as a "partner for life"

Spotlight sat down with **Andy Topping**, chief scientific officer at FUJIFILM Diosynth Biotechnologies, for a conversation about biotechnology, innovation and partnerships

FUJIFILM Diosynth Biotechnologies (FDB) is a contract development and manufacturing organisation (CDMO) providing services to companies that develop complex new medicines and require biological systems for their manufacture. This includes the likes of antibody drugs, enzymes and gene-therapy products. All of these require particular skills and expertise to develop and manufacture.

If you're a biotech start-up, your focus is on the discovery of new products rather than manufacturing. So outsourcing functions such as process and analytical development, then leaving manufacturing to a CDMO such as FDB, allows for rapid progress of products to the clinic and eventually to the market. FDB works with more than 100 companies each year to provide the services that help get products to market.

How did you get started in this field and what has been your career path?

Andy Topping: I have had an unusual career path in that I started with ICI and stayed there as it changed through takeovers or mergers and became FUJIFILM Diosynth Biotechnologies. I started as a microbial molecular biologist and early on we were looking a lot at industrial products, but the focus of the company from the mid-1990s has very much been on biologics (protein-based therapeutics). At the same time, the third-party service provision we specialise in was opening up in the US when regulations changed to allow companies to outsource these functions. Now I mainly work in process design and development pathways, along with looking after 500 scientists, plus our external partnerships with universities, as well as our corporate research arm.

FDB has been involved in the fight against the Covid-19 pandemic. Can you tell us a bit about its role?

We have been involved in supporting the manufacturing of Covid-19 vaccines in three of our sites (two in the US and one in UK). It is interesting and rewarding work. FUJIFILM's expertise is with protein-based products, so we are working with companies to produce these in particular.

What does innovation mean for a service provider like FDB?

We at FUJIFILM Diosynth try to add value to what can be quite a

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traditional arrangement by lending our equipment and manufacturing expertise to customers. Providing support around development, formulation and analytic services all adds to the value of that relationship and makes it more innovative. We are the experts in being able to make products inside and out, and we have the processes to do that. We have the experience because we have worked with hundreds of molecules for 30 years. Our customers have a deep understanding in a very focused area of work because that is their business.

One of the challenges of manufacturing and working on a broad range of products is we need to ensure the innovation and science is really broad too. We need to be flexible in order to deliver all of those different products that might each require very specific processes. Our equipment and facilities need to meet those broad needs and to interoperate. We did a gap analysis, and designed and built a system called SymphonX – a single-use rig which can operate multiple unit operations. It also allows processes to be much more compact by optimising the use of water. This single unit is able to operate several steps in the process, connect them together and interchange between them. Logistically, it also means: we deal with fewer vendors, [we have] fewer issues around parts for the equipment, streamlined training, and it allows us to build more flexible processes.

Can we expect more innovation in the future?

Our parent organisation supports our science-led approach to everything we do, and that means they provide the investment to make that happen. It is about making sure we can respond to new types of products as they emerge, such as viral vectors, cell therapy, microbiomes, and in vitro and synthetic methods. Much of that would have been unthinkable 20 years ago but the technology has moved on and our customers want help with those products.

Can you say more about your collaborative work with universities?

As an organisation we look at the things we need for the future, building the knowledge together with external collaborators. We are working on a long-term project, a Centre of Excellence in Bioprocessing with the Universities of Edinburgh, Manchester and York, supporting around 20 PhD students this year. That collaboration is going to be strengthened through a "Prosperity Partnership" that is being supported by two UK research councils. This will be a five-year programme worth around £8m in funding. The universities really can provide that underlying knowledge and platform that allows us to build products. It is a similar story in the US, where we work with groups like AMBIC [Advanced Mammalian Biomanufacturing Innovation Center] and BPOG [BioPhorum Operations Group] and the universities near to our sites there.

Can you talk about the business expanding in the UK?

FUJIFILM Corporation is making the investment in the UK because the demand from the UK and Europe has increased and, together with the supply chain challenges from Covid-19, we wanted to be able to increase our capacity to meet those customer needs.

Your core purpose as an organisation is to be a "partner for life". What does that mean for you?

I like to be able to solve not just the immediate problem, but to set our customers up for success in the future so that they choose to come back to us to work together again.

From tracking deaths to lockdown adherence, data analysis has been a vital weapon in the fight against Covid-19. Experts discuss where it could be heading. By Sarah Dawood

Can big data help tackle the next pandemic?

Data analysis has become a crucial tool in healthcare. From helping doctors spot cancer and sepsis early to calculating bed capacity in hospitals, interrogating large data sets can enable clinicians to provide more tailored patient care and make headway in understanding diseases overall.

Big data has also played a crucial and remarkable role in the fight against Covid-19. It helped scientists understand the virus's protein structure, enabling them to develop treatments and vaccinations at pace; it allowed clinicians to better manage resources in intensive care units; it even helped researchers discover the optimum temperature for viral transmission.

But many of these applications were reactive rather than preventative, and localised rather than global. In future, could data collection be used to tackle and stop a pandemic before it takes hold?

Use of big data during Covid-19

Some tech in this area already exists – Canada-based AI start-up BlueDot, which scans social media for health trends, predicted there was a new virus days before the World Health Organization (WHO) released its first statement after spotting an unusual cluster of pneumonia cases in Wuhan. Physical tech has also been implemented; water management company Suez deployed a tracking system in Spain that scans waste water for virus traces, predicting where Covid-19 clusters would appear.

But the most prevalent uses of data science throughout the pandemic have been in understanding the virus, in terms of infection, recovery, diagnosis and treatment. The NHS National Covid-19 Chest Imaging Database (NCCID) brought together more than 40,000 CT scans, MRIs and X-rays from 10,000 UK patients, enabling clinicians to spot lung patterns, diagnose patients quickly and predict whether they would end up in a critical condition.

On a larger scale, UK Biobank, a database of health data from 500,000 UK participants, has facilitated several studies, from immunity testing to predicting people's risk of severe illness. Finnish company Nightingale Health used this database to analyse more than 100,000 blood samples, and discovered that people with a particular set of genes – a "molecular signature" – were five to ten times more likely to be hospitalised. The company developed a take-at-home blood test, which Finnish businesses gave to their employees to help them assess their risk and working patterns.

The database was also used to analyse which pre-existing health conditions most increased the risk of death from Covid-19 – a study of nearly 2,500 individuals found that the most common comorbidity was hypertension, followed by cardiovascular disease and cancer. These findings have been used in hospitals to ascertain which patients might need more care.

"By understanding which preconditions facilitate rapid deterioration from Covid-19, we were able to simplify this into a score card, which could help staff on the ground understand who needed more attention," says Aldo Faisal, director of the UK Research and Innovation (UKRI)

Data science has been used to understand Covid-19 in terms of infection, recovery, diagnosis and treatment

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"A rise in symptom searches could be an incredibly powerful signal"

Centre for Doctoral Training in AI for Healthcare at Imperial College London. "For instance, who might suffer from kidney failure and would need dialysis. This is a predictive application of AI."

Data analysis has also been a useful tool in shaping economic decisions and assessing the public's compliance with restrictions, says Olivier Thereaux, head of research and development at the Open Data Institute (ODI). "This is not necessarily AI, just solid data science," he says. "Pretty simple data sets can be used to provide really helpful statistics for policymakers."

One example is the City Intelligence Unit at the Greater London Authority (GLA), which worked with big tech companies including Google and Apple to collate 6,000 sets of mobility data. These were analysed to assess movement and adherence to lockdown. This analysis also helped researchers spot mass gatherings to predict where clusters might appear, and to understand which sectors had seen the biggest drop in footfall, informing decisions around economic re-opening.

Similar examples exist on a global scale. Google Trends, which tracks patterns in people's internet searches, collated a Covid-19 trends page in 2020, demonstrating the most common queries in different countries, from symptoms to food banks. This provided valuable insight into health and economic impact and such tools could be used in future as a warning sign, says Simon Rogers, data editor at Google. "This whole area is rife for proper research but we could certainly see a rise in symptom searches before a rise in cases – it could provide an incredibly powerful signal."

The future in healthcare

Some experts feel that more targeted data, rather than such mass consumer-generated data, could help policymakers make crucial decisions. "If we can gather data from healthcare, transport and financial companies, we could then run AI algorithms, which could find the best policy to minimise deaths," says Faisal. "This could help policymakers better balance health and economy."

The WHO is undertaking a project to improve international data collection

Others feel global collaboration is the key to tackling the next crisis. Samira Asma, assistant director-general for data, analytics and delivery at the WHO, says accurate reporting has been an issue throughout Covid-19. The WHO has calculated death rate from the start but has found that continents such as Africa significantly under-report. The organisation estimates there were more than three million Covid-19-related deaths in 2020 compared to just 1.8 million reported.

There needs to be a renewed focus on health, like there is for climate, Asma says. "Like the World Meteorological Organisation (WMO), we need a global enterprise – a shared resource for data collection," she says. "Similarly to how we can forecast weather or natural disasters such as tsunamis via satellite tracking, we should have a monitoring system for pandemics and epidemics."

The WHO, meanwhile, is undertaking a project that looks to improve international data collection. It has developed the World Health Data Hub, a digital portal where countries can securely deposit anonymised health data about their citizens. This will eventually become a searchable database with country-by-country infographics and reports. The organisation is also pooling wider socio-economic data into what it calls a "data lake", such as information on the healthcare workforce and access to essential services and medicines. Due to launch in 2022, this hub could be vital in highlighting health disparities and enabling a faster, fairer response to future emergencies.

"The aim is to make timely, reliable data accessible for countries in a desegregated fashion," Asma says. "Having data on a national level is not enough – equity is so important." Additionally, the WHO is developing a Health Data Partnership, comprised of 60 global organisations, which will train local workforces on effective data capture.

Instilling data literacy will be essential, says Thereaux, regardless of how intelligent tech becomes. There is no use having a truly predictive system without the individuals to interpret the findings.

"You need medical, epidemiological and data science experts working alongside each other to run these predictive systems," he says. "You can't just build a system and expect it to detect a future pandemic. It's about training data scientists, but also decision-makers, in what data can do."

Another priority is developing global standards, to ensure data is treated ethically and is fully anonymised. Thereaux suggests that the creation of data institutions would help to ensure it is used for the public good. "Institutionalising the stewardship of data would give companies the will to share data for research and development of new medicines," he says. "It would mean no one loses out commercially and smaller organisations do not risk their work being absorbed by big tech, creating a much healthier ecosystem of collaboration and innovation."

Faisal adds that "federated learning" could be explored – an AI "learns" from someone's data without the need to collect or store it in the cloud. "The model travels rather than the data," he says. "A predictive model trains locally on an individual's phone, then travels onwards with what it has learned about the disease. This travelling model can visit millions of phones, constantly improving – you never see individuals' private information."

Tools like this could be used to learn about a virus as it develops – for instance, into variants – and could be coupled with mobility data and physical tools like sewage scanners to create targeted interventions. An area's waterways might show an increase in virus particles; this combined with footfall data could indicate that specific streets need to be locked down rather than a whole city.

For many experts, predicting a pandemic is not the be-all and end-all – rather, it's about using technological advancement to better track a pandemic's path and tailor a response that reduces both loss of life and loss of livelihood. "The question is – is it all about prediction or is it about better disease control?" says Faisal. "Being able to predict the next pandemic would be great but I'm not sure what the level of intervention needed to stop it would be. I think smarter sensing of disease that enables us to manage the response would be better and would allow society to be much more flexible in future."

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Coronavirus and the genome hunters

The work of Professor Sharon Peacock and COG-UK pushes the frontier of biotechnology research.

By Jonny Ball

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The UK's coronavirus record has been mixed at best. But one area in which the country has unquestionably excelled is in the identification of new coronavirus variants. Even one of the government's fiercest critics, former No 10 adviser Dominic Cummings, picked out this kind of virus hunting as an area of science in which the country was "a superpower", when speaking to the science and technology select committee in March.

In April 2020, the start of the UK's first lockdown, the Covid-19 Genomics UK Consortium (COG-UK) was established to sequence and analyse SARS-CoV-2 genomes. The group was made up of a dozen academic institutions, the UK's four public health agencies for England, Scotland, Wales and Northern Ireland, and the Wellcome Sanger Institute, which conducts genome research.

"We were very fortunate to get funding from the government, through Patrick Vallance," Sharon Peacock, professor of public health and microbiology at Cambridge University and director of COG-UK, tells *Spotlight*. The initiative has been a huge success. In January of this year, over one million coronavirus genomes had been shared internationally with the Global Initiative on Sharing Avian Influenza Data (GISAID), the primary tool for scientific data-sharing on Covid-19. Almost half of those, 45 per cent, had been identified in the UK.

The "genomic surveillance" COG-UK is engaged in is crucial in the fight against the coronavirus. It allows researchers to ascertain routes of transmission, look at how different variants behave, monitor the outbreak of immune escape variants, and, crucially, develop vaccines. "There will be a time when we are thinking about this in the same way that we do flu," Peacock explains. "That is, whenever it's required, we'll ask what vaccine will give us the greater coverage for that year, for whatever time frame or region." The key to that is identifying dominant strains and mutations and targeting them with the correctly modified vaccine.

Peacock is also engaged in work with other genomics researchers, trying to unlock the causes behind the massive differential reactions in patients, spanning from symptomless or mild illness to ventilator treatment and death, or to the protracted misery of long Covid. "We're working together with Health Data Research UK and Genomics England," says Peacock. "We're linking the human genome, and the viral genome and detailed health informatics data [for] a much, much deeper analysis."

An extraordinarily difficult year for the country has not precluded astounding success in some areas. The vaccine roll-out has been the fastest of any large nation, and years of publicly funded research into pioneering technology and the life sciences meant the UK was able to quickly develop its own jab, one that will be sold relatively cheaply across the world. The NHS has been heavily stretched, but unlike in other areas of the continent, neither ICU beds nor ventilators reached their full capacity (although this is largely due to a rapid expansion of available critical care spaces and the cancellation of elective treatments that now leaves the service with record waiting lists). And while the UK suffered one of the worst death rates (13th highest in Europe and 18th in the world), and endured many months of lockdown, the link between cases, hospitalisations and deaths seems to have been severely weakened.

Genomics research has been instrumental to a lot of what the UK got right in its fight against the coronavirus. It has sharpened the world's understanding of SARS-CoV-2 in ways that will reverberate through generations, and needs to be nurtured and bolstered for many years to come.

Covid-19 shows collaboration is now essential

Cytiva's Global Biopharma Resilience Index has shed light on a sector critical to the future of public health

The coronavirus quickly emerged last year as the largest peacetime public health crisis in over a century. As Covid-19 spread across continents, governments adopted emergency measures in a desperate attempt to limit both health effects and indirect social and economic costs. The need to enact fast measures sheds light on the importance of the biopharmaceutical industry to the lives of people all over the world.

The biopharma industry is engaged in the research, development and manufacture of naturally synthesised medications – vaccines grown in culture, for example, versus chemically produced or synthetic pharmaceuticals. This innovative field is set to reach a global market value of $535bn by 2027, and the UK is already one of the world leaders in biopharma R&D. The sector employs 60,000 workers in high-productivity jobs requiring specialised skills, with many of these roles in the north-west and other places outside of the traditional south-eastern "Golden Triangle". An additional 50,000 work across a supply chain commanding an annual turnover of over £29bn.

The unprecedented events of the past 18 months, however, have exposed weaknesses within the sector. To identify the biggest risks during this crucial period, Cytiva surveyed more than 1,000 senior executives in the industry to develop a holistic appraisal of the state of biopharma. It then published the findings of this *Global Biopharma Resilience Index* study.

For the recent progress in the industry to continue, Cytiva found there was much to be done. At a time when biopharma's work became more important than ever before, the pandemic exposed stretched and globalised supply chains, skills and talent shortages, unreliable manufacturing capabilities, and governance and regulatory issues.

One bright spot from the pandemic has been the successful and collaborative R&D ecosystem that emerged in the scramble for a coronavirus vaccine. This type of cooperative, cross-sector working will need to continue long after Covid-19 is over. The unprecedented speed at which the industry was able to develop, manufacture, and roll out vaccines will serve as a new target to maintain.

But with the exception of Covid-19 efforts, the *Resilience Index* revealed that research silos are very much a reality. Only 34 per cent of biopharma executives agreed there was a widespread culture of cooperation and open innovation in private companies,

versus 32 per cent in academic institutions, and 30 per cent in contract research organisations and think tanks. Partnership remains a challenge, and a lack of collaboration hinders innovation.

Developing a deep pool of specialised talent in manufacturing, digital and R&D is crucial to the future of the industry. It is also the industry's biggest struggle. One-quarter of executives stated it has become increasingly difficult to source a skilled workforce. Only one-fifth said domestic labour regulations supported the recruitment of talent from abroad. The end of free movement within the UK coupled with the decline of international travel could exacerbate this trend. With the UK creating a new points-based system, it is essential that skilled individuals can come and work in this growing sector.

To address the talent struggle, British schools are emphasising science, technology, engineering and mathematics (STEM). The government is also working to promote these subjects, along with an increased focus on technical education. But the skills gap persists, with demand in this burgeoning sector outstripping limited supply, and a lack of affordable talent stunting development in the industry. As it is necessary to construct a collaborative model within R&D, part of the talent solution lies in establishing fruitful partnerships – working with local universities, trade associations and government to set up the right training, create internships, and help people transition into the biopharma industry.

Supply chain constraints are another area of concern for the sector that Cytiva explored through the *Resilience Index*. The findings from the research reflect how the pandemic placed increased pressures on global trade and cross-border production, both central to the industry. China and India have become the centres of generic medication and active pharmaceutical ingredient manufacturing, and 47 per cent of executives surveyed said that their countries were dependent on drug imports. The data that emerged in the study suggests that many key industry players want to boost their resilience by reducing import dependence. The majority surveyed declared the era of automatic outsourcing over, and 67 per cent of respondents said that domestic production was likely to increase over the next three years.

The political impetus behind the re-shoring trend, and the desire to boost resilience, is strong. The embrace of various shades of economic nationalism, protectionism, and industrial strategies that foster investment in domestic manufacturing will likely continue. Stella Kyriakides, the EU's health commissioner, has asked bloc members to work towards "reducing our dependency on other countries".

But building local supply chains from the ground up will not be easy. The prohibitive costs of every country developing the requisite biopharmaceutical facilities will prevent states from retreating entirely inwards and limit autarky and deglobalisation. While elements of the supply chain, like packaging, could benefit from localisation, the pandemic has aptly demonstrated how global collaboration and partnership are the key ingredients to success in the biopharma field.

Over the past decade, the use of biopharmaceutical therapeutics has increased dramatically, but the Covid-19 pandemic has been a wake-up call for the industry. The survey respondents recognise that business models need to adapt – the industry must embrace permanent collaboration and build deep partnerships to boost innovation and quicken the process of taking drugs from laboratory to market. Part of the solution relies on improved supply chains, with an emphasis on fostering talent and working together to embed cutting-edge technologies into our approach. *The Cytiva Biopharma Global Resilience Index* offers a snapshot of what's needed for continued industry success, a key first step towards securing a resilient and innovative biopharmaceutical future for all.

Supporting the UK's transition to net zero

By **Nigel Scrutton**, director, and **Kirk J Malone**, director of commercialisation, of the UK Future Biomanufacturing Research Hub

The pandemic has thrown into sharp relief the power of biotechnology to positively impact global society. It has delivered a pathway that is leading us out of the crisis: by rapidly identifying the Sars-CoV-2 coronavirus, delivering quick and accurate mass public testing, and discovering and manufacturing effective vaccines at record speed. While there is no vaccine for climate change, biomanufacturing promises to provide key technologies to tackle this global environmental emergency.

Industrial biotechnology is the term that describes the application of nature's catalysts (enzymes) and biological systems to synthesise chemicals, materials, food and fuels. Industrial biomanufacturing takes this approach and works to upscale it, creating opportunities to sustainably develop and produce the essential chemicals that underpin modern society. The process provides several benefits: the inherent, exquisite selectivity of enzymes may lead to products with fewer impurities, which in turn can lead to lower manufacturing costs, lower energy consumption, and enable the use of renewable biological and waste resources as feedstock.

The UK government recognised the economic potential of biotechnology in its *Growing the Bioeconomy* report, which set out a national strategy to 2030. The government's aspiration is for the UK to become a global leader in developing bio-based solutions. This is underpinned by four strategic goals that aim to: capitalise on the UK's world-class research, development and innovation base; maximise productivity and potential from existing UK bioeconomy assets; deliver real, measurable benefits for the UK economy; and create the right societal and market conditions to allow innovative bio-based products and services to thrive.

The aim of this strategy is to create a suitable environment to double the size of the UK's bioeconomy from £22bn (2014) to £440bn by 2030. Industrial biomanufacturing is aligned with this goal, and supports all four of the government's Industrial Strategy Grand Challenges:

(1) Clean growth – providing sustainable alternatives to fossil-derived materials, chemicals and fuels.

(2) AI and the data economy – increasing applied biomanufacturing through fusing AI and big data approaches with lab-based techniques.
(3) Ageing society – biomanufacturing novel medicines to help meet the needs of an ageing society.
(4) Future of mobility – supporting advanced bio-derived fuels and bio-inspired lightweight materials.

The UK is recognised as having a world-leading research base that could act as the bedrock to grow the bioeconomy. In 2012, public sector investment in the UK's Synthetic Biology for Growth Programme led to the establishment of six synthetic biology research centres (SBRCs), which have provided new capabilities for the engineering of biology. One of these SBRCs, SYNBIOCHEM, sits within the Manchester Institute of Biotechnology (MIB) and has established innovative and sustainable biological routes to the production of fine and speciality chemicals. The leadership of the MIB in this field and wider industrial biotechnology was recognised by the award of the Queen's Anniversary Prize for Higher and Further Education.

In the same year, the UK Future Biomanufacturing Research Hub was established. Also based at the MIB, the hub is pioneering new bioproduction technologies. Its purpose is to research sustainable biomanufacturing processes through industrial and academic collaborations with major international companies in the energy, chemical, personal care and pharmaceutical sectors, along with a variety of SMEs that are developing innovative technologies.

However strong the UK's academic base is in biotechnology, by its very nature, the research is predominantly focused at lower technology research levels (TRLs) 1–3. In order to accelerate the translation of new biomanufacturing technologies into commercial applications, we need to ensure that fundamental research is well-financed and that we establish the right support to drive innovation through the feasibility stage to pilot-scale demonstration and into products. This support needs to be twofold. Firstly, through infrastructure: we need an expanded network of intermediary-scale fermenters and bioreactors, located in close proximity to the academic base, but open to industrial use, which would better link discovery science with production. Secondly, we need dedicated funding that would allow industry to engage in biotechnology research and development, and de-risk the evaluation of new approaches and stimulate private sector investment in sustainable biomanufacturing.

With the UK hosting the 26th UN Climate Change Conference of the Parties (COP26) in November, now is the time to ensure public investment is in place to seize industrial biomanufacturing's potential to grow the UK's bioeconomy. This would attract wider investment, mobilising international finance to grow the talent pipeline at the frontier of global net zero. There is a risk to the UK economy of not supporting biomanufacturing at higher TRLs. The pharmaceutical, chemicals and materials manufacturing sectors are highly competitive and global in nature. Failure to stimulate sustainable and clean biomanufacturing may have a detrimental effect on our existing companies, as other countries overtake the UK in their competitiveness and technologies. However, with the right support, industrial biomanufacturing offers major opportunities to grow a more circular economy and reach net-zero targets. Its technologies can ensure the optimal use of resources to meet the needs of modern society in terms of health, energy, chemicals and materials, and the environment.

Learn more at: uom.link/biotechnology

The post-Covid building

Ventilation plays a key role in preventing airborne infections like Covid-19, but improving it may come at a cost.
By Samir Jeraj

Even after the Covid-19 restrictions in the UK wind down, the office may never quite return to the old normal. Inside buildings and workplaces, desks have been distanced, plastic barriers placed around receptions, and whole new sets of procedures are now in place to manage the challenges of the pandemic. One of the greatest of these is how to safely and effectively ventilate buildings to prevent airborne infections while keeping the energy cost down.

This is not the first time that people have turned to natural ventilation in order to protect against disease. In the 17th century, following the Great Fire of 1666, the Old Bailey courts in London were rebuilt to be in the "open air" to prevent the spread of typhus, while "miasma" or "bad air" was similarly wrongly identified as the cause of the bubonic plague in the same era. In the early 20th century, steam heating systems designed to circulate fresh air were installed throughout cities in the US – particularly New York – following the Spanish influenza pandemic.

But following the energy crisis in the 1970s, the cost of energy rocketed and buildings started to be sealed up in order to keep costs down. The unintended consequence of that is that the air quality inside buildings became very poor (this was still an era when people routinely smoked in their workplace) leading to what was termed "sick building syndrome". Hence came the move for ventilation to deal with these issues, and since then it has been a balancing act between energy and effectiveness.

"Ventilation has been ignored for a very long time," says Benjamin Jones, an associate professor at the University of Nottingham, but adds the pandemic has prompted a surge of interest in the issue.

Andrew Eddy works on this problem for Verto's new-build Zero-Carbon homes, as head of innovations and sustainability. The homes use mechanical ventilation with a heat recovery system, which works for buildings that have a well-insulated and "fairly airtight" structure – this means relatively little uncontrolled heat loss or air loss, he explains. The system then pumps air from outside into the home through a filter while removing it from other places in the home where moisture gathers and where there is the greatest risk of problems such as mould.

Poor indoor air quality can lead to, at the most dangerous end, health risks such as carbon monoxide, which can kill, or at the other end of the scale, persistent bad smells that make living or working environments unpleasant. "That's the best rule of thumb: if you walk into a room from the outside and it smells bad, it's under-ventilated," says Jones, and that means the infection risks from airborne disease are higher.

Filters can be installed to ventilation systems to screen out airborne virus particles, but it is problematic, Jones explains, because there may not be space for them in the system: "There will be a lot of resistance to airflow, and so if the fan power isn't increased the ventilation rate will fall. It's like breathing through a mask; it's harder." There are also leakage issues if they are installed badly. "Because they resist airflow, the air will take the path of least resistance and will flow around it, negating the benefits of the filter," he says.

Persistent bad ventilation over a lifetime leads to health issues, such as chronic obstructive pulmonary disorder. A report published in 2020 by the Royal College of Paediatrics and Child Health recommended national action to improve indoor air quality to prevent children from developing issues ranging from respiratory and skin conditions to hyperactivity and poor school attainment.

Tuberculosis patients from St Thomas' Hospital rest in the open air beside the River Thames in May 1936

Jones would like to see changes to building regulations to help promote better air quality. While school buildings are really well regulated, he says, homes are still governed by a set of standards that are not fit for purpose. Something as simple as requiring kitchens to have a cooker hood fan installed in new homes and as part of any refit would have a significant impact.

"We've seen a massive increase in requests for natural ventilation during the pandemic," says architect Thomas Jepson, founder of Passion Plans. He feels this demand is as much about concerns around sustainability as well as the impact of Covid-19. When harnessed correctly, natural ventilation can significantly lower heating and cooling bills and ensure the future of the planet.

Each project has its own needs depending on the local climate, Jepson continues. "Beach homes will take advantage of the breeze coming from an onshore direction. Mountain homes will take advantage of the wind rolling downslope," he says. Rooms and even windows can be designed to better promote air quality. However, natural ventilation does have its challenges, he acknowledges, particular in very hot, very cold or humid environments, where ensuring the appropriate temperature, flow of air and protecting against mould all become more difficult with natural ventilation alone.

Some companies and organisations have their sights set on an even more ambitious task than ensuring the safety of the air inside buildings. "It's more than cleaning the air – that next step is making that air healing or healthy," says Jo Pannecoucke, the founder of Take Air, a Netherlands-based company that has developed ventilation technology that uses biology in order to actively improve the quality of air alongside removing airborne dangerous infections. Take Air claims to have solved the problem faced by filtering systems – that the more effective they are, the more energy it takes to push the air through the system and through the filter.

"The missing link for us was biotechnology," says Pannecoucke. The team at Take Air looked at what micro-organisms could be safely part of their technology to accomplish their goal of creating healthy air, making the link with other products that include "healthy bacteria". "At that time if you talked about bacteria everyone was running away!" says Pannecoucke. While traditional filters would see the air pressure drop significantly, Take Air's system produced a negligible fall.

After nearly five years of work to test and develop the technology, Covid-19 shut down the world but also underlined the importance of airborne infections. "We had never heard about Covid – we were working on influenza," Pannecoucke says. The team tested their system on Covid-19 over the next 18 months and came to the conclusion it was effective at stopping it too. "We have been testing and working on a system that on the one side is catching and killing viruses, including Covid, and on the other side is doing what we started to do and rebalancing the air to a healthy microbiome balance," says Pannecoucke.

Previous pandemics prompted massive changes in the built environment, using natural ventilation to open up buildings, towns and cities to encourage fresh air flow. Covid-19 has already forced change in how and where we work. Whether there will be a move back towards natural ventilation and the likely greater energy costs, or new technology will arrive to improve the safety quality of air inside buildings, remains to be seen.

GETTY IMAGES

The future for industry will be circular

Turning waste into high-value products makes sense for the environment and the bottom line

The journey to net zero is already well under way. Consider the countries that have, or are in the process of, committing to net zero by 2050; this is where just under half of the world's gross domestic product (GDP) is generated. But the downside to that scale of economic production is waste: from agriculture, food and municipalities, and in the form of carbon dioxide. A lot of this waste is generated as a result of manufacturing processes being too "linear". And removing this waste without using landfill or incineration is a huge issue. Without taking a new approach to waste – and moving away from a linear processing approach – hitting net zero will be impossible.

One solution is "circularity": recycling and re-using waste streams and products to create a closed-loop system, which minimises resources and the creation of waste, pollution and carbon emissions. As we journey towards net zero, these "circularity" principles are increasingly embedded in the research and design of products.

As a leader in sustainable technologies, Johnson Matthey is striving to help the chemical industry transition. Martin Hayes, biotechnology lead, explains: "More and more companies are starting to move away from linear chemical processes to circular ones – which is definitely a step in the right direction – by looking at how the waste from chemical processes may be the source for biological processes. For example, biological entities, such as enzymes or organisms, can be used to recover precious metals from waste streams, maximising value while reducing waste."

Another example is the use of gas fermentation to upgrade waste products, particularly carbon dioxide and hydrogen, and convert them into chemicals. Hayes adds: "In this instance, by linking biology and chemistry to

Food waste is a large contributor to emissions

The circular economy includes everything from generating renewable energy to reducing waste

get the desired end product without affecting the customer experience, but making the process much cleaner."

As a large contributor to greenhouse gas emissions (GHGs), food waste is another issue. But a circular approach can help here as well. Food waste can be fermented to convert it into something more useful, such as renewable chemicals. "What is valuable about this is that it means that these chemicals are not produced from virgin fossil material," says Hayes.

However, in order to use these technologies efficiently, we need to be clever about how we collect waste streams – for instance, by collecting process waste streams at centralised or distributed sources so that they can be used as fermenter feedstocks. And to realise the potential in these technologies and new businesses, it's important to take a collaborative approach and for multidisciplinary teams to work together. Hayes continues: "We know that getting the biology to the end product requires engineers, chemists, microbiologists, biochemists, different scientists working together with commercial expertise to make a product that is sustainable, has a low environmental footprint and is still profitable. We work collaboratively in partnership because we recognise we need to develop these solutions in ways that reflect the needs of each client and the broader society."

But the scale of the issue shouldn't be underestimated. Scaling up and optimising processes such as fermentation can be resource-intensive and involve large volumes. That type of process intensification needs engineers and chemical engineers to make it smaller and more efficient.

While the UK leads in renewable technologies, it is also important to think in terms of connected systems rather than isolated applications of technology. That broader perspective in a circular system will get us towards net zero.

Regulation can arguably play a role here, to incentivise the use of sustainable alternatives over conventionally produced fuels and chemicals. This may include the introduction of greater penalties for the generation of waste or supports that encourage re-using and upgrading the waste products. Ultimately, the regulatory environment could help to accelerate the transition to net zero.

One way governments can help is by reforming the legislation on the production of chemicals to level the field in favour of more sustainable alternatives to petrol and oil. But incentives will be needed to encourage companies to make this shift. Employing a carrot-and-stick approach could see greater penalties for waste, like a carbon tax, that encourage re-using and upgrading the waste products. If this works well the situation will be reversed and organisations will be paid for their waste – it will completely revolutionise the way we approach waste.

But before legislation is introduced to incentivise a move to the sustainable practices that are needed, there is an opportunity for industry to embrace these technologies and systems now. Hayes concludes: "It requires technologies to make this happen and that is where Johnson Matthey can help. Businesses that are not prepared for that move will find it costly, whereas those who are already on the journey to net zero and the circular economy will reap the benefits."

Solving the healthcare challenges of today and tomorrow

By **Rob Field**, director, Manchester Institute of Biotechnology, The University of Manchester

Over the past 18 months, the Covid-19 pandemic has impacted the health and well-being of societies, businesses and economies across the world. During this period we have witnessed unprecedented levels of innovation and interdisciplinary working between industry, the public sector and academia to deliver solutions. While we are far from clear of this viral threat – which we will need to learn to live with, as we have done successfully with influenza – current scientific and medical advances are helping to speed up our recovery.

The UK's biotechnology community of academic and industry experts has led the way in RNA vaccine development for Covid-19, with the timeline from concept to clinical deployment having been astonishingly short. In addition to tackling the immediate Covid-19 challenge, this development helps us prepare for the future. We are now well placed to rapidly counteract new pathogenic organisms or strain variants as they emerge. Along with the wider potential applications of nucleic acid therapeutics, such as gene therapies, this prompts renewed interest in how these entities may be manufactured efficiently and cheaply at scale. These can be complex and involve challenging chemical processes; harnessing nature's synthetic machinery (enzymes) for biocatalytic processes shows promise and warrants further investment and exploration.

UK biotech has led the way in vaccine development

The Manchester Institute of Biotechnology at the University of Manchester

With the emergence of new Covid-19 variants, ongoing vigilance is paramount. There is real need for rapid new diagnostics for community surveillance and individual diagnoses at the point of care, as well as at home and in the workplace. This remains a challenge and a continuing requirement, not least in connection with early deployment of vaccines and the identification of variants that are resistant to vaccination attempts.

Current and emerging diagnostics solutions make use of a range of biological agents for detection: PCR tests for laboratory-based detection of virus genes; nanopore sequencing of complete virus genomes; and established antibody-based testing in lateral flow devices (now being adapted with newer approaches based on artificial RNA receptors or sugar-binding technologies). The diagnostics community is embracing the full spectrum of what nature offers us, adapting and deploying the components to great effect in ways that nature had not intended.

The acquisition and preparation of samples is instrumental to the transition from diagnostic theory to roll-out for scalable use in the community. The Manchester Institute of Biotechnology (MIB) is heavily engaged in studies that aim to gather diagnostic information from a breath sample or a skin swab, rather than an uncomfortable nasal swab or invasive blood sample. MIB embraces academia-industry-stakeholder collaboration, and the resulting activities, which require integrated thinking that transcends traditional disciplines, are currently seeing development at unprecedented pace.

While we contemplate ways to manage current and future pandemics, we also need to consider the valuable role that antiviral drugs can have. HIV infection rates have plummeted in those parts of the world where antiviral drugs have become routinely available, demonstrating the power of chemistry to tackle this deadly infection. Moving forward, there is a need to identify cheap and sustainable routes to manufacture for antiviral drugs. Specifically, approaches are needed that are suitable for deployment in the developing world, where high-end manufacturing capability and infrastructure may be limited. A key technology that is embraced in other fields worldwide, and has been for millennia, is fermentation (bread making, brewing and fermented foods). Challenges and opportunities lie in harnessing that historic knowledge and capability through adapting the micro-organisms that we use so that they make molecules that nature did not intend them to produce. This goal can be realised through bio-engineering, which offers real scope for sustainable drug manufacture.

While we must ride the Covid-19 wave, we cannot forget that antimicrobial resistance, neurodegenerative diseases, cancer and other pressing healthcare challenges have not gone away. The pandemic has heightened awareness among government and society of the power of contemporary, problem-solving science and the relative investment that is required. Biotechnology lies at the heart of the solution to the myriad of real-world challenges that we face today; our increasing ability to precision-engineer biological systems provides powerful new opportunities for future healthcare.

Find out more about how biotechnology is helping us to understand Covid-19 at: uom.link/covid-prognosis

Is this the end of offshoring for biopharma?

59%

of biopharma executives say that the era of offshoring drug manufacturing to low-cost countries is over

67%

say that the manufacturing of biologics is likely to increase dramatically in their country over the next three years

Dive into the key findings of Cytiva's Global Biopharma Resilience Index at **cytiva.com/resilience**

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Bacteria-eating viruses step up where antibiotics fail

"Phages" could become a more sustainable and effective way to fight infections – but UK regulations are yet to catch up.
By Samir Jeraj

SHUTTERSTOCK

Ella Balasa felt she had no other option. "The intravenous antibiotics weren't working. I was so sick," she says. Balasa has cystic fibrosis, a lung condition that means, among other things, the 29-year-old suffers recurring bacterial infections. Their severity increased over time, necessitating longer stays in hospital and stronger antibiotics as the bacteria became resistant.

In 2019, she developed an infection that stopped responding to treatment altogether. "I was on intravenous antibiotics for five or six weeks and I wasn't having any relief from my symptoms," says Balasa. Her lung function dropped to 18 per cent and she was placed on supplementary oxygen.

A few months earlier, she had been contacted by the makers of a documentary about a cystic fibrosis patient in Texas treated with something called "phage" therapy. As someone who had a background in biology and worked in a lab, Balasa was intrigued. "I had not really heard about phage therapy before," she says. "They showed me the video and immediately I was like: 'I need this.'" She contacted the researchers at Yale working on phage and, after a one-week treatment course, she started to clear the infection, at a much faster rate than before.

Phages are viruses that only attack bacteria, by attaching themselves to the bacteria's receptors. Each phage has a specific bacteria that it attaches to and kills, which means if you can find the right one it can be used to treat an infection resistant to antibiotics. Phages also lack the severe side effects of stronger antibiotics. They're not a new technology: phages were being used to treat infections a century ago, but fell out of favour when antibiotics were discovered.

"The fact that phages are abundant in nature and the fact that they are specific makes them a very good alternative to antibiotics," says Antonia Sagona, an associate professor at the University of Warwick. There is still the possibility that bacteria become resistant to phages, she adds, but the phage viruses themselves evolve and adapt along with the bacteria. They can also be given in a cocktail alongside traditional antibiotics, and genetically modified to help counter resistance.

In the UK, however, regulations only allow phage therapy as a "last resort". Given the treatment is also so specific and personalised, it is difficult to construct large-scale trials. In other countries, Sagona explains, such as Belgium and the Netherlands, authorities are more open to using phages in a broader range of cases. Sagona feels the UK is quite regulated and cautious more generally in medical research, which makes it hard to develop more novel therapies. The UK has also traditionally invested heavily in the discovery of ▶

antibiotics, so there is a legacy there, she adds. "I am hoping that it [phage therapy] will be something that will be easier to approach and easier to approve compared to the situation now," she says. "There is a big effort from the UK side to establish the regulations for phage therapy to be applied here."

One specialist who has carried out phage treatment in the UK is Helen Spencer, the lung transplant lead at Great Ormond Street Hospital. One of her cystic fibrosis patients had the same problem as Balasa – an infection that was resistant to antibiotics and was shutting down their lungs. The infection recurred even after a lung transplant, placing the patient at high risk. "Most of those patients, if you get recurrence of infection, have died following transplant," Spencer explains. "We knew we were in a pretty bad place."

It was the patient's mother who asked about whether phage therapy could be a possible treatment. By coincidence, one of Spencer's colleagues had done his PhD thesis on phage 20 years earlier, and he put her in touch with a researcher in the US.

Graham Hatfull describes himself as a "basic biologist" who has been working away at the science of phages at the University of Pittsburgh since the late 1980s. It was only when Spencer contacted them about her case that they got involved with the clinical side. "It's a pretty dire situation for those patients out there who have got these types of infections for which the physicians really have little or no options," he says. "Often, the idea of using phages therapeutically is the last and only possibility for those patients."

"Behind the scenes, Graham and his team in Pittsburgh were searching for phages and that took a couple of months," Spencer explains. The team screened thousands of phages and, using genetic modification, came up with a cocktail of three to use on the infection. It was just in time: by that point the patient had been sent home for palliative care alongside antibiotics.

Once they had agreed to go ahead, getting the phage across from Pittsburgh and approved for use took another 12 weeks before the patient could come in for treatment. "She tolerated it well," Spencer says. "To see her respond felt pretty miraculous at the time because all my other patients had died from this infection." While her life has been extended, the infection still has not fully cleared and the team at Pittsburgh is continuing to work to find more phages to treat the infection.

Hatfull's lab has since been contacted by around 200 clinicians working on cases where phage therapy might be an option. In each case, his lab tests its phages to see if they will work on the specific bacteria, and it has been able to help in around 20 cases. However, variation in the strains of bacteria means the phage that worked on the Great Ormond Street case is very unlikely to work on any other case. What Hatfull and his team are looking at now is whether it is possible to have a standard off-the-shelf phage treatment and how to get there from the almost personalised treatments that are being administered at present. The team is also yet to find a phage that works on the 40 per cent of strains where colonies of bacteria are "smooth" as opposed to "rough". Encouragingly, however, they are yet to see resistance emerging to phage therapy.

There is no risk of phages mutating to infect humans, assures Hatfull. "Phages have been around for probably around three billion years and we are exposed to them and we have phages in us all the time," he explains. They are so specific that it takes a huge amount of work to get phages to attack a broader set of strains of just one bacteria, so it's highly unlikely it could "jump kingdoms" to even another species of bacteria, let alone humans.

"When Covid emerged people realised the limitations of modern medicine," says Gordon Jamieson. "It's a serious disease that there wasn't a tablet for. The same for antimicrobial resistance. There

Phages eating bacteria in a clinical sample

"To see her respond felt pretty miraculous"

we have a tablet, but the tablet's going to stop working."

Jamieson is chief commercial officer at Fixed Phage, a British company that is essentially a "phage hunter": it looks at a problem – whether an infection or how to extend the shelf life of a salad – looks at which bacteria are at work, identifies the phages that attack that bacteria, and then works to "stabilise" them for use. The shelf life of phages is often quite short, just a few days – not enough time to be transported and used – so Jamieson and his team have been working on extending that to a few months. Similarly, because phages are so specific to each type of bacteria, the company also has to use "cocktails" of phages depending on how accurately the bacteria can be identified.

Jamieson has found regulators "open to discussion" about the use of phages because of the threat from antibiotic-resistant bacteria. However, the team still has to demonstrate safety, quality and effectiveness. "There's a little community of phage scientists and phage companies and what we're all wanting to do is see more phage products out there, because then it creates the pathway," he explains.

While Jamieson acknowledges there are challenges and limitations, he is optimistic about the future of the technology. "It's the same as electric cars or silicon chips – it's one of those technologies you start somewhere and you've got to develop it, and once people get interested you can move mountains," he says.

Balasa still gets infections – it is a chronic part of her condition – and still has to take antibiotics, but feels that phages really worked for her, and believes longer and more frequent courses of treatment may help "beat back" the infections more. She has spoken widely about her experience and is active in pushing for new treatments for infections. "It's the thing that affects my life the most," she says.

SHUTTERSTOCK

What next in the world of bioengineering?

Ellen Simmons of Cambridge Consultants takes a critical look at this crucial branch of science to see what challenges are in store – and how to tackle them

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The world of bioengineering is seeing such dramatic change that it can feel as though science fiction is becoming reality.

Can you envisage a future in which chemotherapy is no longer routinely needed to treat cancer? When, instead, we will manipulate the body's own cells to heal itself? I can. And I feel confident that such treatments will be in regular use within the next five to ten years.

These are exciting times to be working in bioengineering. We are now at the point where our ability to change the physical make-up and behaviour of cells is leading to remarkable innovations in health treatments, food production and so much more. From reprogramming our immune systems to producing kilos of edible meat synthetically, I believe that the interface between biology and engineering is where we will see the most dramatic scientific progress in the next decade.

With such huge opportunities also come a host of ethical questions. Biomedical engineers are on the edge of advances that previous generations of scientists could only have dreamed of. But what do we do about them?

I'm a biomedical engineer for a product development and technology consulting firm. I joined Cambridge Consultants in 2017 as a new graduate, having studied biomedical engineering at the University of Glasgow. Mine was only the third year that the university had offered this subject to undergraduates and there were just 35 of us on my course. This career choice seemed unusual back then but it vividly reflects the evolving situation in life sciences today – the intake now is around 100 students per year, on a par with the numbers studying mechanical engineering. Like a lot of youngsters with good science A levels, I had initially considered a career in medicine. Then I discovered that I could become an engineer working with live products. Once a niche field, bioengineering is now set for centre stage. As my fellow bioengineers look seriously at the prospect of creating a full ecosystem on Mars, I truly believe that this branch of science is the space exploration of the 21st century.

Since I joined Cambridge Consultants four years ago, I have worked on several projects that have opened my eyes to the potential of this field. In one notable project, the company was commissioned by a small start-up to see if it is possible to use DNA as a data storage system akin to flash memory. The science behind this made sense. DNA is tiny but stable – so could it be used to record and store vast amounts of information for industrial systems, or even the average consumer?

I have never forgotten the thrill of seeing the whole of Wikipedia condensed to a few drops of DNA in a test tube. It is fair to say the project has been an outstanding success so far. Its potential is literally life-changing: the world expends a shocking amount of energy on computing and data storage. By engineering the biological potential of DNA to store information, we can make such a difference to all our futures.

Another project we are working on, called PureSentry, is also a game-changer. It is aimed at making gene therapy for conditions like cancer far less expensive and inaccessible. We know that it is now possible to treat cancer by extracting cells from the body's own immune system, altering them to attack the cancer and re-introducing them into the body. However, the cost – up to £500,000 per patient – is prohibitive. A substantial percentage of this expense goes on the difficulties of culturing the cells outside the body, so we worked

in-house on a way to make the process quicker, safer and cleaner. PureSentry is a monitor that combines our engineering knowledge of fluidics, optics and AI to observe cell cultures in real time, spotting contaminants instantly.

In this way, our inexpensive piece of bioengineering kit could make gene therapy far more widely accessible. It is no exaggeration to say that I foresee a time, within the next decade, when cancer patients will not have to go through chemo or radiotherapy in order to be cured of their disease.

Another project, with huge implications for oncology and other serious health conditions, is called CellPreserve. This aims to extend the life of cells in a liquid biopsy so that far better diagnoses can be achieved. Again, this project is centred around the intersection between biology and engineering. The team created a piece of kit that can manipulate a liquid biopsy so that an individual cell could be kept alive and monitored for up to 14 days. This opens the door to earlier and more accurate diagnoses, as well as better treatments, for patients.

As part of my job, I have been encouraged to take part in all sorts of forums that debate the bigger picture around the future of biomedical engineering. I believe that the implications for what we're able to do now aren't just scientific, but also ethical and political. Discussions between policy-makers, teachers, technologists and thought leaders are becoming more commonplace, which has opened my eyes to how I should view my day-to-day work as a bioengineer.

Take agriculture, for example. We now live in a world where it is technically possible to grow a whole kilo of edible meat from a single cubic centimetre of pork. What does that mean for the world's farmers, our environment and our health – not to mention climate change?

I believe it is important for scientists to raise their heads from their microscopes and keep a steady eye on the bigger picture. Bioengineering may soon mean we're able to grow food in space and colonise another planet. But what does that mean for our treatment of the planet we currently occupy?

And with gene and cell therapy already saving lives in the fields of cancer and other rare diseases, where are we going with the genetic manipulation of the human body? Will we soon be growing whole human organs for transplant? Will it become possible to create a designer baby with, say, an immunity to certain illnesses or – more problematically – a world-beating sporting ability? Could wealthy people one day be able to pay to change their own cells to become healthier or more intelligent? During this rapid time of growth in the biotechnology sector, it is crucial that regulatory bodies evolve alongside the furthering of education in bioengineering to allow these technologies to be forged responsibly.

This may all sound like the stuff of science fiction, but these dilemmas are already front and centre in the biotech world. How we address them is one of the biggest questions facing science, and the world in general, today. I am honoured to be a part of that debate, but we cannot assume that technologists alone can provide all the answers.

TOMORROW'S SCIENCE, TODAY'S NHS

Cell and gene therapies aim to transform patients' lives, now let's support the NHS to get ready for the future.

The Cell & Gene Collective is funded by Astellas, bluebird bio, Bristol Myers Squibb, Kite (a Gilead Company) and Novartis.

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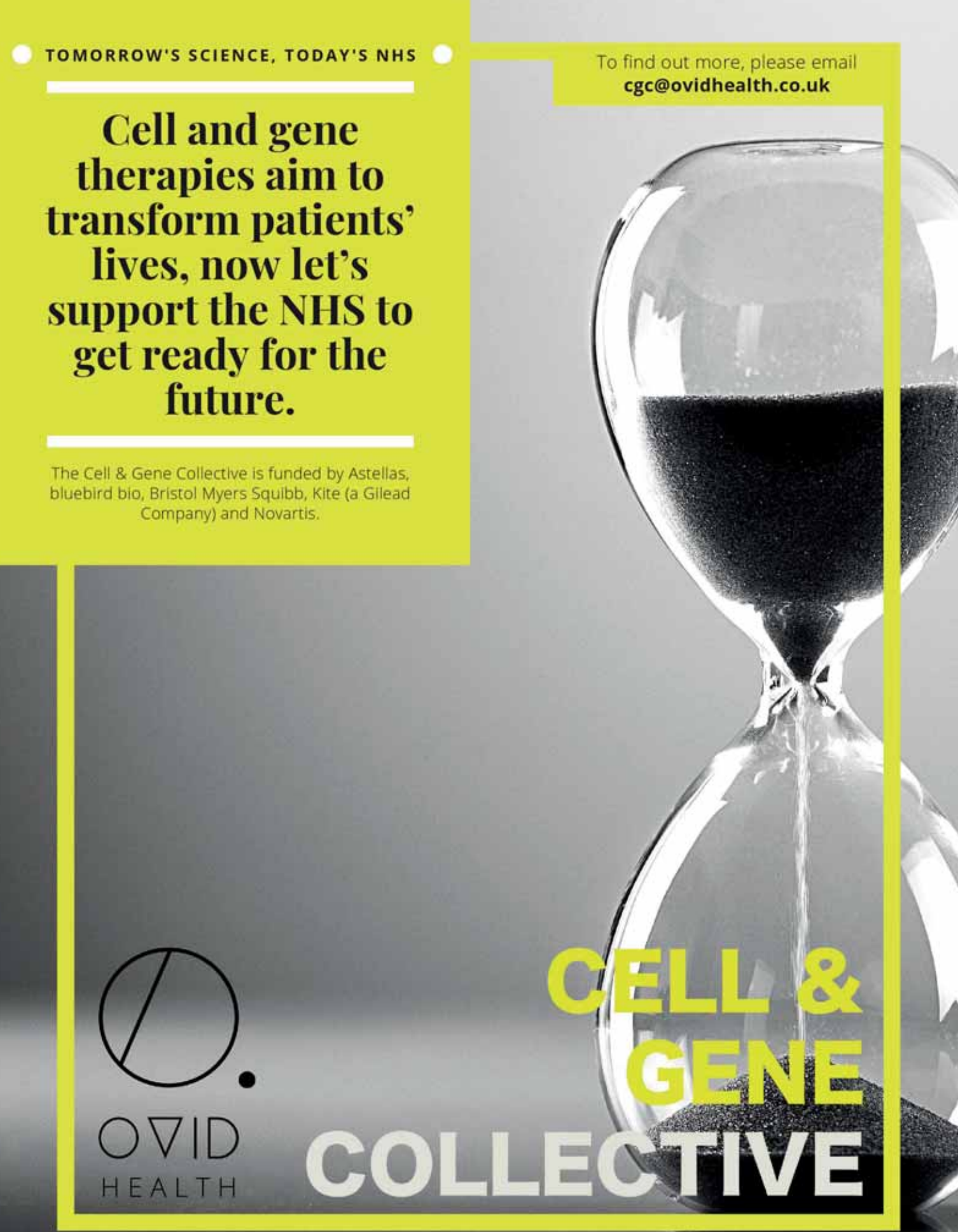

OVID HEALTH

CELL & GENE COLLECTIVE

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