Riyadh Global Medical Biotechnology Summit

Pushing the boundaries of our existing thinking and practices

قمة الرياض العالمية للتقنية الطبية
RIYADH GLOBAL MEDICAL BIOTECHNOLOGY SUMMIT
RGMBS 2021

“What we have to look at philosophically is what the unmet needs of the Kingdom are and how biotechnology can address that. When we can couple the unmet needs with the new technologies, then we can start to imagine a new concept, a new strategy and a new positioning for Riyadh.”

—Elie Haddad, senior advisor and project lead, Riyadh Biotech City, Royal Commission for Riyadh City

A biotechnology oasis

The COVID-19 pandemic, which has brought much of the world to a standstill under lockdowns and caused hardship to millions around the globe, has been a wake-up call to the importance of biotechnology and the promise it holds.

Thanks to recent advances in the field, the world was able to produce vaccines in record time—thus saving millions of lives. Biotechnological breakthroughs have also brought hope to those suffering from diseases that, until less than a decade ago, were thought to be fatal. Today, we are able to bring hope to so many people and allow them to live healthy and prosperous lives.

The Riyadh Global Medical Biotechnology Summit comes at a critical time for the world, but also an important time for the Kingdom of Saudi Arabia. The Saudi National Vision 2030 has identified addressing health and economic challenges, increasing non-oil revenues, and supporting innovation and entrepreneurship as key pillars for the future of the country.

We are proud to have brought together the local, regional and international biotechnology community virtually this year. We are happy and humbled to have had leading researchers, academics and industrial experts from around the world join us and share their expertise, wisdom, and successes and failures.

It is critical that we re-examine our existing approaches and think of innovative models that bring together research in biotechnology, clinical trials and industry to push boundaries and come up with new models.

Together with local and international players in biotech R&D and industry, we have put together the Riyadh Declaration for Biotechnology to accelerate the Kingdom’s vision to become a biotechnology oasis for the region and to attract top talent from around the world.

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Our ultimate goal is to contribute to the well-being of humans all around the world, and to contribute to global biomedical and health R&D and innovation. By learning from our colleagues in other countries, and by tapping into the unique strengths of the Kingdom, I am confident that Saudi Arabia will soon be a leading gateway for biotechnology.

Bandar Al-Knawy
CEO, Ministry of National Guard
Health Affairs

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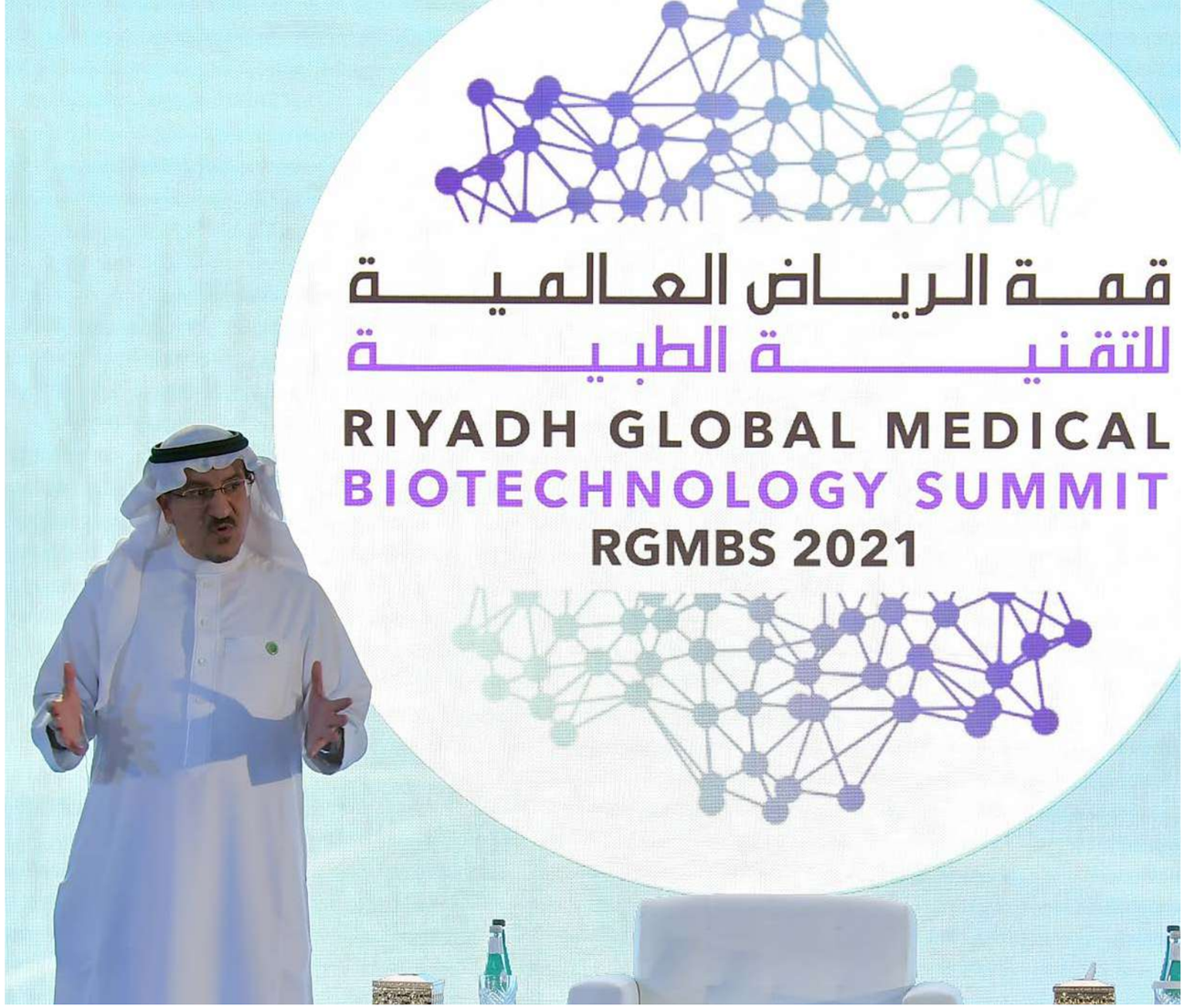
Valuable and versatile tools for Saudi Arabia's future

A conversation with Ahmed Alaskar, executive director of KAIMRC

Ahmed Alaskar is a professor and consultant in haematology and stem cell transplantation, and has been a significant figure at KAIMRC for the past 10 years. He reflects on the blossoming biotechnology industry in Saudi Arabia, its strong links with academia, and how biotechnology will help bring many of the Kingdom's ambitious plans to fruition.



How has medical biotechnology research in Saudi Arabia changed in the last 10 years?

Biotechnology is now a key focus for the Kingdom, in line with Saudi Arabia's Vision 2030. The country aims to move from an oil-based economy towards a sustainable and resilient economy that will enable it to thrive long into the future. To achieve this, our population needs excellent healthcare and medical technologies, and this is where our innovative research and development programmes in medical biotechnology come to the fore.

Vision 2030 encourages academics, industry representatives and scientists from all backgrounds to collaborate on translational research. KAIMRC is a leader in this regard — after years of producing high-quality publications and focusing on basic research in the medical and life sciences, we are now actively pursuing the transformation of that knowledge into tangible, viable products that will boost the Kingdom's healthcare system.

Which biotechnologies are a focus for KAIMRC?

Our ultimate goal is to improve the health of the population, and this means developing novel therapies for multiple conditions. We are building a strong reputation in drug discovery and diagnostics, and are screening thousands of molecules for potential candidates. These discovery pipelines are strongly supported by the artificial intelligence and computational biology units here at KAIMRC, and these technologies have really come into their own during the COVID-19 pandemic.

Our facilities allowed us to sequence the whole genomes of the COVID-19 strains circulating in Saudi Arabia in-house. Our AI specialists were able to match screened molecules to potential viral targets. These results have since been taken forward into drug development and clinical trials, and initial results have just been published. Saudi Arabia has also been dealing with another coronavirus, MERS-CoV. KAIMRC scientists have been working alongside researchers at the University of Oxford since 2015 to develop a MERS-CoV vaccine. The latest clinical trials for this vaccine candidate demonstrate that it has an excellent safety and immunogenicity profile.

How has KAIMRC's biotech strategy changed because of the pandemic?

The COVID-19 pandemic has obviously had hugely negative consequences across the globe, but it has also led to significant gains in the medical and biotechnology fields. We have witnessed an unprecedented acceleration of research and technological development over the past two years. We have learned that it is possible to streamline research that often takes 10 or 20 years into the space of a year. The insights gained from this pandemic will filter out into all manner of other medical advancements, and KAIMRC's research strategies will evolve to keep pace. It has been a true honour for KAIMRC to be a part of the collaborative efforts of scientists across the world. From the moment the first whole genome of the virus was shared publicly, scientists have come together to solve problems and

The COVID-19 pandemic has obviously had hugely negative consequences across the globe, but it has also led to significant gains in the medical and biotechnology fields.

understand the virus more rapidly than at any other time in history. When you bring together all the diverse experiences and capabilities of the world's scientists to focus on one goal, it is astonishing what can be achieved.

How can medical biotechnology help boost recovery from the pandemic?

As researchers, we create the roadmap that we think medicine and clinical healthcare should follow. Our experiences with COVID-19 mean that we are better prepared than ever before for any future novel pathogens that might come our way. But there are also many thousands of existing pathogens — bacteria and viruses — that we know very little about. Once we have the genetic fingerprint for a pathogen, it can provide us with so many details.

We now have the computational abilities to analyse viruses and bacteria rapidly, accurately, and in all their incredible complexity. In this way, we can reduce deaths from many diseases, improve health policies and public education, and above all, boost quality of life.

How will the biotechnology industry evolve in the next 10 years in Saudi Arabia?

Vision 2030 inspires us to achieve several goals, including enhancing the health of the population, improving quality of life and diversifying our economy. Biotechnology hits all these targets. Economy and health are two sides of the same coin. The development of high-quality biotech products not only serves the population, but provides a sustainable source of income for the country. This then improves quality of life — not just for the people of Saudi Arabia, but for populations across the world. Biotechnology development goes hand in hand with improved efficiency and effectiveness, and provides a valuable set of tools for our country's future.

The Riyadh Global Medical Biotechnology Summit

KAIMRC successfully hosted its 12th annual global conference, dedicated this year to medical biotechnology, bioinformatics and biotherapeutics. Running from 14–16th of September, the Riyadh Global Medical Biotechnology Summit (RGMBS) 2021 brought together over fifty-five speakers from the local, regional and international biotechnology community including academic, industrial and governmental organisations to discuss developments in biotechnology in light of the COVID-19 pandemic.

Dr. Bandar Al Knawy
Chief Executive Officer, Ministry of National Guard Health Affairs President, King Saud bin Abdulaziz University for Health Sciences and Summit President

Prof. Ahmed Alaskar
Executive Director, King Abdullah International Medical Research Center and Summit Chairman

Dr. Abdelali Haoudi
Head R&D Strategy and Business Development, Managing Director, Medical Biotechnology Park and Summit Vice Chairman

Introduction to Riyadh Global Medical Biotechnology Summit 2021

Prof. Ahmed Alaskar, Executive Director, King Abdullah International Medical Research Center

Developing a COVID-19 Vaccine for the World at an Unprecedented Pace

Sir Menelas N. Pangalos
Executive Vice President & President BioPharmaceutical R&D, AstraZeneca

Mr. Walter Klemp
Chairman and CEO Moleculin, Inc.

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Chaired by Prof. Ahmed Alaskar, Executive Director, King Abdullah International Medical Research Center

Biotechnology in the Kingdom of Saudi Arabia: Challenges and Opportunities - Towards Better Alignment with the Saudi National Vision 2030

Chaired by Prof. Ahmed Alaskar, Executive Director, King Abdullah International Medical Research Center

Eng. Suliman Almazroua
CEO of the National Industrial Development and Logistics Program

Eng. Nizar Al-Hariri
Chief Executive Officer, National Industrial Development Center

Dr. Ashraf Allam
CEO, Pharmaceutical Investment Company

Dr. Abdulrahman Alnuaim
Professor, physician, healthcare executive and pharmaceutical industry consultant at Ministry of Industry

Dr. Pierre J. Magistrett
Director, KAUST Smart Health Initiative

Dr. Elie Haddad
Senior Advisor & Project Lead, Riyadh Biotech City, Royal Commission for Riyadh City

Dr. Malak AlThagafi
Director of the General Directorate for the National RDI, King Abdulaziz City for Science and Technology

"We have learned that it is possible to streamline research that often takes 10 or 20 years into the space of a year."

—Prof. Ahmed Alaskar
Executive Director, King Abdullah International Medical Research Center and Summit Chairman

SESSION 2: Biotechnology Parks/Clusters: Best Practices and Future Trends

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Senior Advisor to the Ministry of Industry, KSA

The Munich Biotech Cluster: Turning Science into Innovation

Dr. Horst Domdey
Chief Executive Officer, Biotech Cluster Development GmbH

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Dr. Mehmood Khan
Chief Executive Officer, Hevolution Foundation

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Dr. Richard Smith
Chief Operating Officer, Rockland Immunochemicals, Inc. USA

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Dr. Manal Alaamery
Head, Developmental Medicine, Chairman Innovation and Entrepreneurship KAIMRC, KSAU-HS, MNG-HA

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Chairman and CEO, Moleculin Biotech, Inc.

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Chief Executive Officer, Johns Hopkins University, USA

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Dr. Ronald DePinho
Professor and Past President MD Anderson Cancer Center, USA

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Dr. Eric Kmiec
Founder and Director, The Gene Editing Institute, Helen F. Graham Cancer Center & Research Institute, Christiana Care Health System

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Dr. Hitesh Sanganee
Executive Director & Head of Emerging Innovations, AstraZeneca

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Mr. Markus Peterseim
Managing Director, Alvarez & Marsal, Frankfurt, Germany

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Head, KAIMRC- Eastern Region, Deputy Executive Regional Director-Medical Services, MNGHA

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Professor Global Health Systems, Director of Global Health Systems Cluster Harvard University, USA

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Dr. Lynda Chin
President and Chief Executive Officer, Apricity Health LLC, USA

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Senior Director, Strategy and Performance Improvement Alvarez & Marsal Dubai, UAE

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Dr. Fouad Atouf
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Mr. Markus Peterseim
Managing Director, Alvarez & Marsal, Frankfurt, Germany

Dr. Waldemar Radziszewski
Executive Medical Director, Global Clinical Development, AMGEN

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Chaired by Dr. Jamila Louahed, GSK

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Dr. Hani Al Hashmi
Senior Medical Affairs Director, Pfizer, KSA

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Dr. Jamila Louahed
Vice President and Head, Global R&D, GSK

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Dr. Naif Al Harbi
Director, Vaccine Development Unit, Director, Research Quality Management Research Scientist, Infectious Diseases Research Department, KAIMRC

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Dr. Jon Heinrichs
Associate Vice President and Franchise Head, Sanofi Pasteur

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Mr. Sven Frie
General Manager, Commercial Enterprise Solutions, Cytiva

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Dr. Manal Alaamery
Head, Developmental Medicine, Chairman Innovation and Entrepreneurship KAIMRC, KSAU-HS, MNG-HA

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Dr. Paolo Martini
Senior Vice President, Moderna

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Mrs. Bouchra Bensaoud, Danaher

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Mr. Iain Sharp-Paul
Vice President EMEA Marketing, Cepheid

Mr. Sherif Harydi
General Manager, Middle East, Cepheid

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Mr. Perry Frederick
Senior Director, Strategic Research, Europe, Middle East, and Africa GE Healthcare

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Dr. Ahmed AlZahrani
Director of Healthcare Technology Development, Information Technology Department, MNGHA

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Dr. Hicham Fenniri
Professor, Departments of Chemical Engineering, Bioengineering, Chemistry & Chemical Biology, Northeastern University, USA & Chief Scientific Officer, MAScIR Foundation, Morocco

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Dr. Madhuri Hegde
Vice President and Chief Scientific Officer, PerkinElmer, Inc.

Empowering Infectious Disease Surveillance Using Whole-genome Sequencing

Prof. Majed Al Ghoribi
Chairman, Infectious Diseases Research Department, Associate Research Scientist, King Abdullah International Medical Research Center

A triumph for science: Hastening the race toward a COVID-19 vaccine

An unprecedented international response by researchers, funders and regulators made it possible to develop COVID-19 vaccines in record time.

In the opening keynote of the COVID-19 Vaccine Forum hosted by KAIMRC in November 2020, Bali Pulendran of Stanford University declared that he was "in awe" of the rapid pace at which COVID-19 vaccines have been developed. He explained how the many phases of vaccine research, trials, regulatory approval and large-scale manufacturing had often previously taken 10 years or more. But in the case of COVID-19, the first large scale vaccinations began on 8 December 2020, just under a year since the first case of the disease was reported to the World Health Organization.

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At the KAIMRC Forum, Adrian Hill of the University of Oxford summarised the key factors behind the astonishing success of what he called "the grandest global experiment in vaccine technology ever undertaken." He emphasised the unprecedented collaboration involving thousands of different specialists worldwide, all focusing their multidisciplinary attention on one target. They worked at record speed to sequence the viral genome, analyse its structure and explore the options for vaccine development.

Hill then turned to the role of unprecedented levels of funding from governments and other bodies, saying that for the first time in his career almost "unlimited funding" has been available.

He also talked of a new willingness by regulators to work much faster than normal, which he views as one of the major lessons to be learned for vaccine development in the future. Hill explained that there is no single global regulatory body for vaccines, which would simplify the currently cumbersome process of dealing with regulators in different countries who often take different views on the same clinical data.

The crucial basic research itself was accelerated by researchers being well primed by existing work and by the novel nature of the first vaccines. Rather than the traditional approach of administering viral proteins directly, these are based on RNA or DNA that instructs the body's cells to manufacture a key immunogenic part of the viral coat's spike protein.

Researchers working on these vaccines say they could be developed quickly in part because we already had the technology to rapidly and routinely synthesise RNA or DNA of a desired sequence. RNA and DNA vaccines have never previously been licenced for use in humans, although they have been used in veterinary applications and in many laboratory tests on animals.

The Pfizer/BioNTech and Moderna vaccines use synthetic single-stranded messenger RNA (mRNA) molecules that contain the genetic instructions to directly induce the body's cells to make the proteins that stimulate immunity. The Oxford-AstraZeneca vaccine achieves a similar outcome using double-stranded DNA, which is transcribed into mRNA by the normal metabolic activity within a cell.

YOUSSEF KHALIL/ NATURE 2021

A vaccine in a year

Vaccine development timeline

November 2019
Retrospective studies suggest the first confirmed case of Covid-19 came on 17 November, in Wuhan, China

January 2020
Chinese scientists isolate a novel coronavirus (7 January)

May 2020
Human trials of Pfizer/BioNTech vaccine begin, along with trials of many other vaccine candidates

August 2020
Phase 1/2 clinical trial results announced by Pfizer

90%

November 2020
Phase 3 clinical trial results from Pfizer and Moderna indicate effectiveness rates above 90

January 2021
Vaccination programmes with Oxford-AstraZeneca and Moderna vaccines now also underway

December 2019
First cases of the disease that would later become known as Covid-19 revealed by authorities in China (2 December)

March 2020
US NIH begins Phase 1 clinical trial of an experimental vaccine developed in collaboration with Moderna Inc.

July 2020
Phase 1/2 clinical trial results announced by Moderna

October 2020
Submission of trial results data to regulators begins

December 2020
Several countries grant emergency authorizations for Pfizer/BioNTech, Oxford-AstraZeneca and Moderna vaccines to be used

JONNY WEEKS/THE GUARDIAN - POOL/GETTY IMAGES

Robust vaccination drives have meant shorter hospital stays around the world.

The Oxford team point out that DNA is more robust than mRNA and the adenovirus's tough protein coat also helps protect the genetic material inside, which makes their vaccine stable at significantly higher temperatures than mRNA-based vaccines—a significant benefit. The researchers behind the Oxford-AstraZeneca vaccine credit the "head start" they got through their many years of research on DNA vaccines as a key factor behind their rapid response.

Sarah Gilbert, who designed the vaccine, explained to the KAIMRC Forum that the COVID-19 vaccine delivers DNA using a system which had already been developed in their laboratory. A harmless, modified adenovirus carries the DNA in their vaccine.

"We had used this to make many different vaccines in the past," Gilbert said, some of which were already in phase 1 clinical trials.

All that is required to adapt this versatile system to a new disease is to change the DNA sequence being delivered. Together with an intensive research effort, this head start made it possible for the vaccine to move into clinical trials in April 2020, a mere 104 days after the researchers first received the genetic sequence of the SARS-CoV-2 virus responsible for COVID-19.

This feature was also a key factor in accelerating the production of the Pfizer/BioNTech and Moderna vaccines.

Pfizer, which made the first COVID-19 vaccine to get regulatory approval, emphasised the significance of their partnership with German company BioNTech in meeting the challenge so quickly. They say this brought together BioNTech's specialist expertise in developing mRNA vaccines with Pfizer's more broad expertise in vaccine technology, regulatory issues, and manufacturing and distribution.

Most of the researchers placed particular emphasis on the unusually quick efforts of regulatory bodies worldwide to assess the results of fast-tracked clinical trials, in many cases, granting Emergency Use Authorizations for the earliest vaccines. These allow the vaccine to be used based on preliminary data provided that further surveys of efficacy follow as vaccination gets underway.

The phases of vaccine trials normally proceed consecutively and usually take several years. In the case of COVID-19, the massive funding available and the urgency of the situation made it possible to overlap some of the clinical trial phases. The researchers also pointed out that the vast number of infections worldwide made it easier and faster to run trials with many participants in a shorter time while still getting sufficient evidence to demonstrate efficacy.

In the case of COVID-19, the massive funding available and the urgency of the situation made it possible to overlap some of the clinical trial phases.

"Vaccines are good for pandemics, but pandemics are good for vaccines," Hill told the Forum. The fact that COVID-19 rapidly became a pandemic helped get vaccines quickly developed and tested. For example, the Oxford-AstraZeneca team report that their vaccine "will have been tested on almost five times as many volunteers as is usually required for licensing a vaccine."

Hill also calls for regulators worldwide to come together to simplify and accelerate the regulatory process, which currently involves multiple national regulatory bodies and the ensuing complexities. According to him, this is the major change needed to improve vaccine development in the future.

The key players in academia and industry generally agree that the experience of developing COVID-19 vaccines is likely to significantly improve the process in the future. If the new and quicker technology of RNA and DNA vaccines proves effective in the long term, it could accelerate vaccine development overall. The vast funding thrown at the COVID-19 challenge is unlikely to be available again, but the lesson that regulatory bottlenecks can be overcome may also bear fruit.

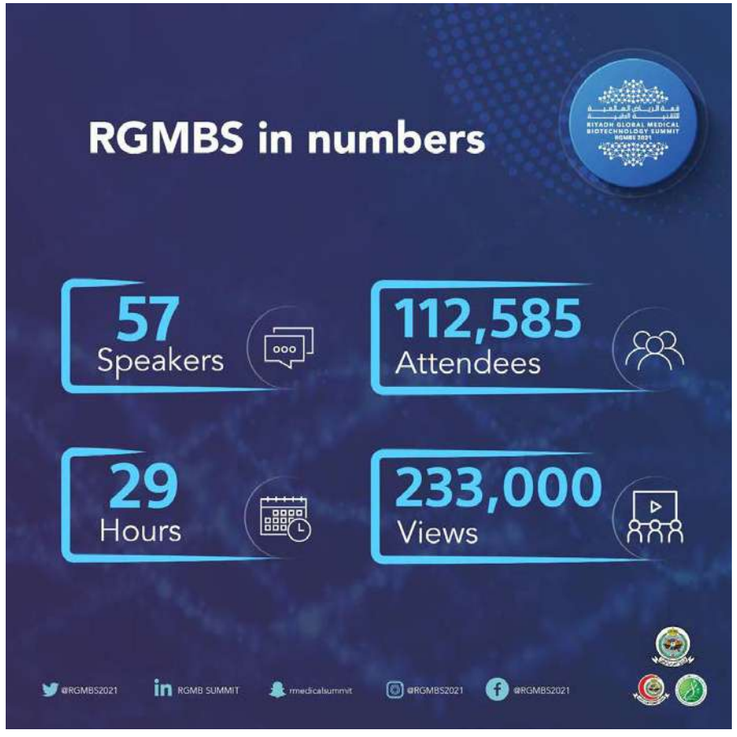
If these lessons are learned, "developing new vaccines in three years instead of 10 years would become a bit more realistic," says Hill.

"Supporting and strengthening innovations and technological development are key strategic areas in the national strategy and transformation programme. RGMBS brings together thought leaders to push the boundaries of our existing thinking and practice, and to propose innovative models."

— Bandar Al Knawy, CEO of the Ministry of National Guard Health Affairs and president of King Saud bin Abdulaziz University for Health Sciences

Kickstarting Saudi Arabia's biotechnology future

A conversation with Abdelali Haoudi, head of R&D Strategy and Business Development, managing director of the Medical Biotechnology Park at KAIMRC, and vice chairman of RGMBS 2021.



The Riyadh Global Medical Biotechnology Summit (RGMBS) 2021 sought to present the latest developments in medical biotechnology, together with potential opportunities for collaboration, to local stakeholders, international partners, and senior government decision-makers. More than 30 international academic and industrial entities from over five countries were represented at the summit from a variety of medical biotechnology research areas. Abdelali Haoudi organised the RGMBS 2021 with colleagues, and here describes how the Kingdom of Saudi Arabia benefits from hosting such a summit during the global COVID-19 pandemic.

What benefits will the summit bring to Saudi Arabia and to the global biotechnology industry?

We do not need to reinvent the wheel for medical biotechnology in Saudi Arabia. However, there are inspiring best practices and successful models out there, and we are motivated by these successful models and want to adopt them to the needs of our country. The best way to achieve this is to partner with successful entities and countries in this field. We are interested in strong science and research and development, as well as best practices for the manufacture of novel medicines, vaccines and medical devices. Another key interest is the commercialisation of these products locally, regionally and globally. Therefore, global partnerships represent a cornerstone in the successful establishment of these activities in the Kingdom. The summit witnessed the signing of six different partnerships in medical biotechnology, with several other partnerships in the planning stages.

What lessons can be learned from the biotech industry's pandemic response?

Medical biotechnology companies have played a significant role in the quick response to the COVID-19 pandemic in terms of vaccine development. Two out of the four major global COVID-19 vaccines were developed by medical

Medical biotechnology companies have played a significant role in the quick response to the COVID-19 pandemic in terms of vaccine development.

biotechnology companies, namely Moderna (USA) and BioNtech (Germany) in partnership with Pfizer. The biotechnology sector has proven to be agile and very responsive to urgent needs. There are lessons to be learned from this successful and fast deployment of vaccine development, manufacturing and commercialisation over a period of a few months, instead of the years or decades it usually takes. Clearly, we have learned that there are quicker and more effective ways to translate research findings into products, to streamline procurement processes, and to establish strategic alliances that move innovative products rapidly to the market.

How will discussions at the summit influence best practice in Saudi Arabia?

We invited leading global experts in different fields of medical biotechnology to the summit. These experts are renowned in their respective fields and therefore represent invaluable reference points at this critical time. We will come up with a clear and actionable plan to enhance the current situation in Saudi Arabia that focuses on improving the pace and dissemination of R&D and innovation from lab to the market with clear economic, health and societal impacts. These recommendations will be shared with senior government officials in the hope that the government adopts them.

What investment strategies does the Kingdom's government have in place for medical biotechnology?

The government recently selected medical biotechnology as a strategic choice for economic diversification and better resource healthcare improvement. As

PHOTO CREDIT

such, a number of investment initiatives are now underway. For instance, the Saudi Public Investment Fund has set up the Pharmaceutical Investment Company to support novel therapeutics and drug development start-ups.

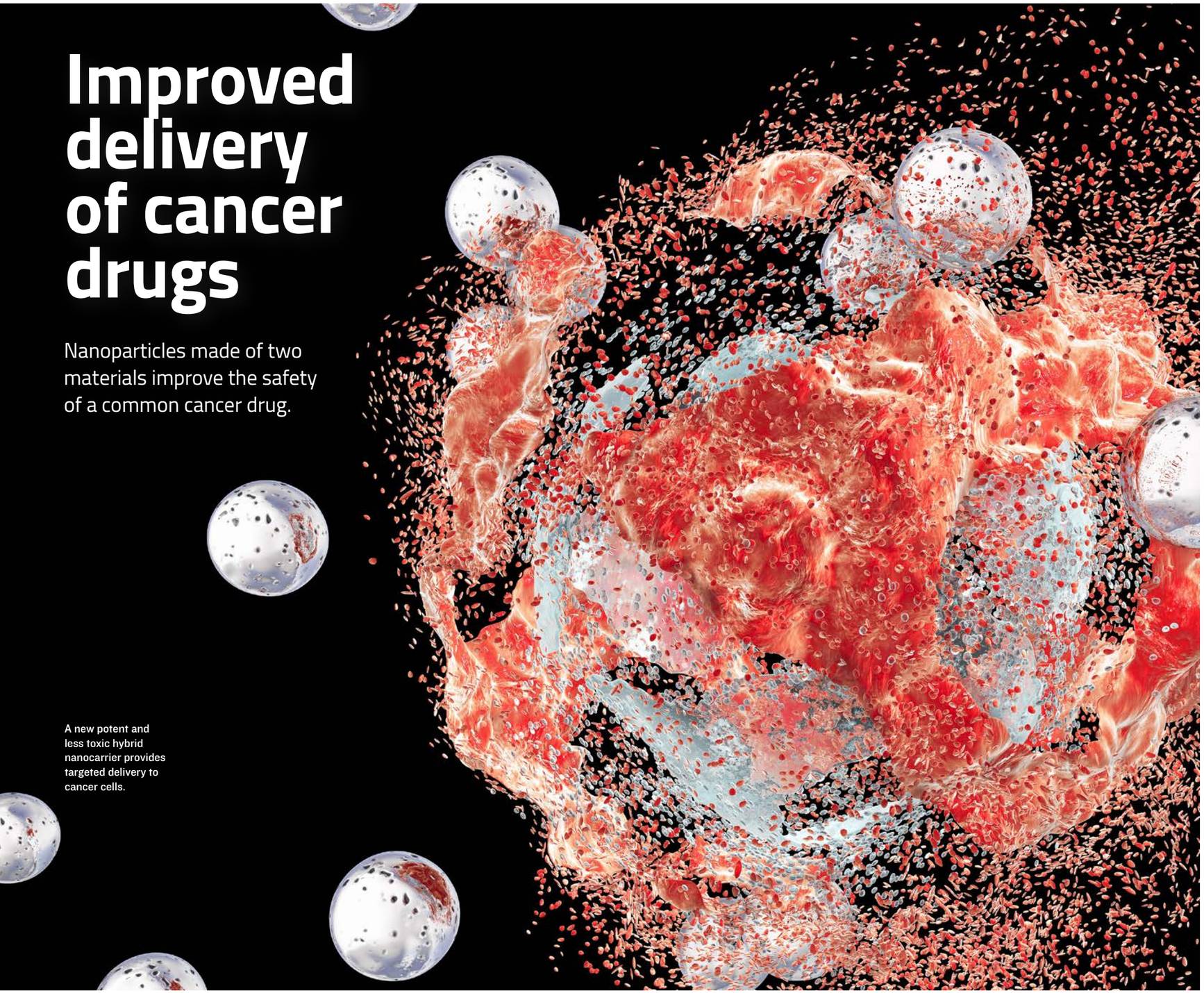
What strategic innovations are needed in the Middle East to improve healthcare access and make the best of new technologies?

Countries in the Middle East must integrate R&D, innovation, and entrepreneurship as a strategic and key priority in their future economic development plans. They must not simply be left as another facet to academic teaching—which is currently the case in certain countries. Additionally, there is an urgent need for enabling policies for procurement and the creation of start-up biotech companies, as well as diverse investment opportunities in this rapidly evolving field.

Furthermore, legislation enabling researchers to embark on biotechnology start-ups is a must, because this will allow researchers to become successful entrepreneurs while remaining in their academic careers as active scientists. It is this blend of capabilities that has fuelled the development of medical biotechnology companies in developed countries, particularly the U.S., and this provides a significant benchmark for the Middle East to aim for.

Improved delivery of cancer drugs

Nanoparticles made of two materials improve the safety of a common cancer drug.



A new potent and less toxic hybrid nanocarrier provides targeted delivery to cancer cells.

KATERYNA KON/SCIENCE PHOTO LIBRARY/ GETTY IMAGES

A new drug delivery platform developed by Saudi scientists could enhance the safety and efficacy of a common therapeutic for breast cancer.

The technology is based on hybrid nanoparticles composed of a biodegradable polymer coated with a layer of fatty molecules known as lipids. This mixed design combines the biological compatibility and cell penetrability of lipids with the enhanced stability and prolonged drug release of polymers.

When loaded with the anti-estrogen drug anastrozole, the hybrid nanocarrier proved stable and effective against breast cancer cells. "This is a novel formulation that provides better safety and biocompatibility than the free-form drug," says Salam Massadeh, leader of the Therapy Development Lab at KAIMRC. "It's more potent, less toxic, and offers targeted delivery to the cancer cells, demonstrating the power of nanotechnology to improve existing therapies and create a new generation of drugs."

Massadeh co-led the study with KAIMRC's Manal Alaamery in collaboration with researchers at King Saud bin Abdulaziz University for Health Sciences. Both Massadeh and Alaamery have a track record of developing nanotechnology-based treatments for breast cancer, having received patents for innovations related to nanoparticle delivery of various drugs over the past few years.

However, the earlier advances were built around nanoparticles consisting entirely of polymers. The incorporation of lipids on the outer surface improves

"It's more potent, less toxic, and offers targeted delivery to the cancer cells, demonstrating the power of nanotechnology to improve existing therapies and create a new generation of drugs."

solubility and helps ensure the drug is fully absorbed into the bloodstream, leading to more stable dosage levels in the body. This not only protects against debilitating side effects such as thrombocytosis, a blood clotting disorder that can result from variable drug concentrations in the body, but also means that patients will need less frequent doses.

The researchers showed that the hybrid nanoparticles had a consistent spherical shape measuring around 200 nanometers in diameter and that around 80% of the nanodrug carriers were successfully filled with anastrozole. The team treated breast cancer cells with their nanotherapeutic and saw a similar level of cell death as in treatments using standard anastrozole.

The KAIMRC team next plans to test the anastrozole-loaded nanoparticles in mice. If the therapy proves safe and effective, trials with patients could follow.

Massadeh, S., Omer, M.E., Alterawi, A., Ali, R., Alanazi, F.H. *et al.* Optimized polyethylene glycolylated polymer–lipid hybrid nanoparticles as a potential breast cancer treatment. *Pharmaceutics* **12**, 666 (2020).

Digital care platform such as Apricity Health's can help improve patient care and capture data to fuel research and development.

Bridging gaps for future healthcare

Building the infrastructure to enable digital medicine will augment healthcare and accelerate biomedical R&D.

"If Saudi Arabia wishes to leapfrog other countries in precision medicine, it should build a digital highway for healthcare data and AI tools as the national infrastructure for digital medicine. This will facilitate the generation, sharing and analysis of patient big data to drive biomedical research, accelerate drug discovery and improve healthcare for all," says Lynda Chin, co-founder and CEO of US-based company Apricity Health, and a leading cancer genomic scientist.

Apricity Health has developed a digital care platform to help improve cancer care and capture data to fuel research and development. It is a small-scale model of how to build an infrastructure to realise the potential of digital medicine, and bring novel treatments and precision medicine directly to cancer patients. The strategy

Creating a technology infrastructure to bring virtual multidisciplinary cancer care to patients everywhere is our mission.

that shapes their approach is threefold: lead with expertise; scale with technology; and empower the oncologists.

In the beginning, the Apricity Health team turned to world-class experts to identify bottlenecks that new technologies can overcome. For example, instead of making phone calls to check in on high-risk patients, remote monitoring via apps on a mobile phone can monitor every patient every day.

The second step was to make sure that the technology can always smoothly augment current practices rather than replace them. "Our goal is to give every healthcare provider the knowledge they need to deliver clinical best practices," says Chin. "We can augment their knowledge base with the most recent medical advances or guidelines using AI and machine learning. We can also integrate and synthesise patient data, so they can provide evidence-based care that is personalised to each patient."

Finally, Chin points out that treating a cancer patient is a team effort. "The patient needs more than the oncologist, but the oncologist must be at the helm, quarterbacking a multidisciplinary team of healthcare professionals, from non-cancer specialists to nutritionists," Chin says. "This provides whole-person integrative care to maximise the treatment outcome of that patient."

In an academic cancer centre with many specialists and care professionals under one roof, multidisciplinary care for a patient is more easily achieved. However, this is not readily available to most people. Even in the US, over 80% of cancer patients are treated in a regional or a community setting. There, an oncologist needs to send patients to different clinics or faraway cities to see different specialists, often with a long lag time to get an appointment. These challenges are further amplified if patients live in an underserved community.

"Creating a technology infrastructure to bring virtual multidisciplinary cancer care to patients everywhere is our mission," says Chin. "We believe our model is a game changer in terms of making access to specialty experts and care more equitable."

The digital infrastructure developed by Apricity will also capture high-resolution longitudinal patient data, which builds a comprehensive health record for the patient. This can drive genomic research and drug discovery. "On a larger scale, a universal digital highway system in Saudi Arabia would connect and integrate care and research, creating a learning health system that will speed up the development of new and improved drugs," says Chin.

Trust is paramount to the success of digital medicine, asserts Chin. As one designs and develops digital health and AI tools, it's important to remember that doctors have the trust of their patients.

"Therefore, by empowering the oncologists, we tap into this trust to bring digital solutions to their patients and improve care," says Chin. "Healthcare is, and always will be, human to its core. Technology should be an equalising force in healthcare, designed to augment the work of clinical experts in ways that strengthen trust in the eyes of their patients, and among their colleagues. We envision a future of digital medicine where care is without borders, optimised and personalised for every single person, no matter who or where they are."

Lynda Chin, co-founder and CEO of Apricity Health, and a leading cancer genomic scientist.

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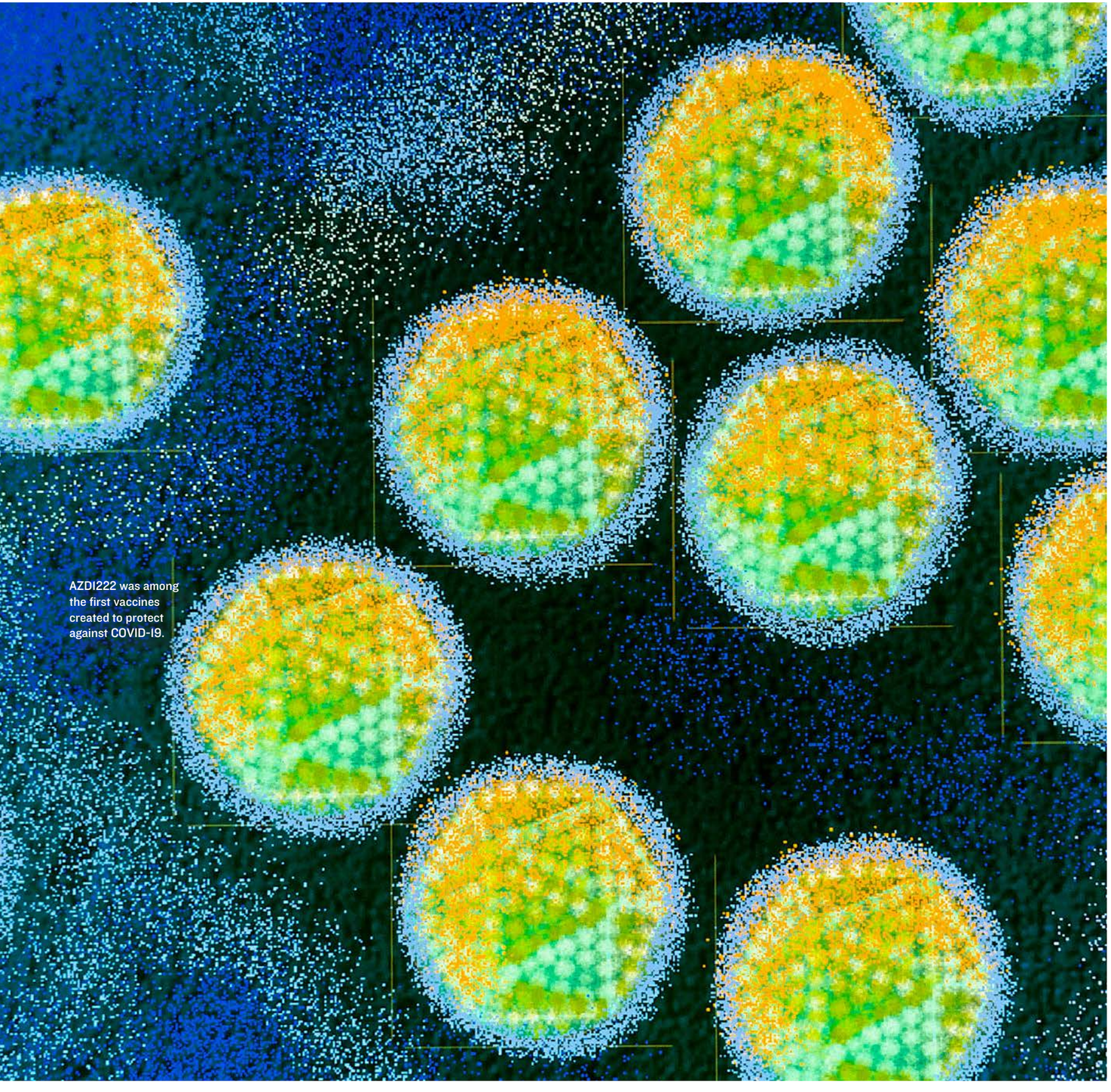


AZD1222 was among the first vaccines created to protect against COVID-19.

DESIGN CELLS/ ISTOCK / GETTY IMAGES PLUS

ChAdOx1: More than a coronavirus vaccine

At the core of a COVID-19 vaccine is a highly adaptable technology with the potential to protect against a range of viruses.

AZD1222, developed by the University of Oxford and licenced to AstraZeneca, was among the first vaccines created to protect against COVID-19. A non-replicating viral vector vaccine which was approved for emergency use in several countries, it was later put on hold because of links with the formation of dangerous blood clots. While the clinical trials and authorisation procedures have received significant press coverage, less has been said about the trailblazing technology that underpins AZD1222—a modified chimpanzee adenovirus called ChAdOx1.

Viral delivery

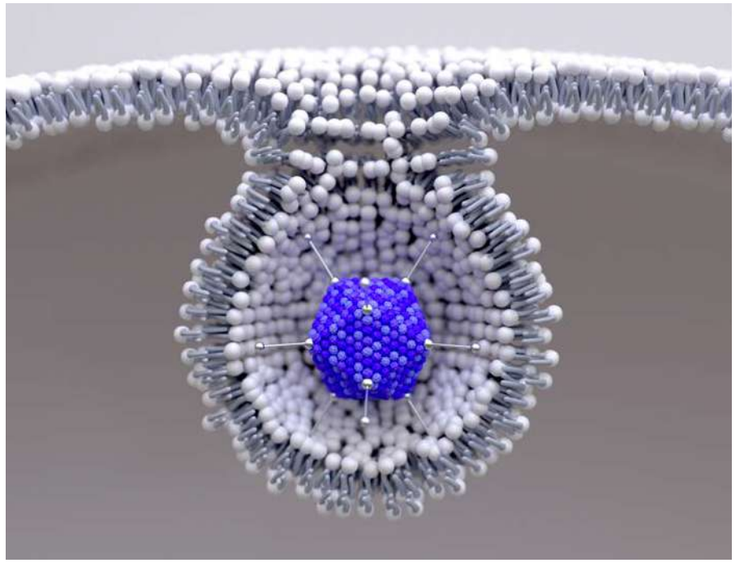
Viruses hijack infected cells and force them to produce copies of the virus itself. Scientists have long leveraged this ability to create non-replicating 'viral vector' vaccines, in which a virus is genetically engineered to reduce or eliminate pathogenicity but still prompt cells to produce the immunogenic proteins of another virus. This method exposes a host's immune system to specific proteins from a target virus but not the virus itself, enabling the host to safely build immunity. In the case of AZD1222, this protein is the spike protein of SARS-CoV-2, the virus that causes COVID-19.

In 2012, researchers at the University of Oxford created ChAdOx1, a virus vector vaccine based on a modified simian adenovirus. The researchers chose a simian adenovirus because "if you use a human adenovirus to immunise humans, you run into the problem of pre-existing immunity," says Sarah Gilbert, professor of vaccinology of the University of Oxford and co-founder of the spin-off Vaccitech, which patented the ChAdOx1 technology. Following successful collaborations with other institutions using other simian adenoviruses, Gilbert says "we wanted our own. We managed to acquire a chimpanzee virus that had been described in the literature, and then a student in the lab converted it to a vaccine vector"—and ChAdOx1 was born.

> "The host immune system learns to recognise and respond to the expressed protein.'

To create the platform, Gilbert's team modified the viral genome to remove its ability to replicate and to optimise its manufacture. They can then insert the gene encoding a desired viral protein. The end result is an injectable solution that infects cells around the injection site and causes very high expression of the target protein. In the case of AZD1222, "something like 80% of the protein expressed from the adenovirus is spike protein," says Gilbert.

The host immune system learns to recognise and respond to the expressed protein, but because the virus can't create new copies of itself, the short-lived infection doesn't proliferate around the body and cause disease. This makes the platform very safe to use, even in people with a compromised immune



The technology behind the COVID-19 vaccine has the potential to protect against a range of viruses.

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system, says Gilbert. "It's as if you have a coronavirus infection in your arm, but it's not coronavirus, it's the adenovirus and it can't replicate."

ChAdOx1 as platform rather than product

Gilbert describes the modified simian adenovirus as a "true platform technology" which can be modified to cause the expression of different viral proteins without any alterations to manufacturing or safety. Oxford researchers are using their platform to investigate vaccines for many diseases, such as tuberculosis, rabies, MERS, Dengue, and Zika virus.

Ahmed Salman, a senior vaccinologist and immunologist at the University of Oxford, adds that ChAdOx1-based vaccines are easy to produce and stable once made, saying that large quantities can be produced "at a really low cost in a short amount of time." The platform is also very effective at inducing a strong response from both B cells and T cells, whereas competing technologies often generate a skewed response.

At the virtual KAIMRC conference "COVID-19 Vaccines: Global Challenges & Prospects Forum," Gilbert described how her team managed to reach their first trials in humans just 103 days after receiving the genetic sequence of the spike protein.

Vaccine sceptics believe that such rapid development means that these therapeutics must be poorly understood or poorly tested. Salman argues that vaccine research is normally hampered by slow bureaucratic processes and time wasted waiting for grants, approvals, and publication—all while people are suffering from a disease. With COVID-19, he says, we have a "good example" that things can be more streamlined. "I work on malaria, which doesn't get [the same attention as COVID-19]. We'll be in clinical trials in a few weeks, but we started research more than seven years ago."

Furthermore, vaccines such as AZD1222 weren't created from scratch for COVID-19; rather, they build on decades of existing research. Scientists also did not have to face the pandemic blindly—it was anticipated. In 2016, Salman says, the University of Oxford started its "Pandemic X" project. Scientists prepared plans based on anticipating what diseases might cause a global pandemic, what therapeutics might help, and what infrastructure should be put to work to abate disaster. Salman adds that there have been many regional epidemics since 2000, such as swine flu, avian flu,

"Since 2000, regional epidemics such as swine flu, avian flu, SARS, MERS, Zika and Ebola have offered lessons in preparedness.'

SARS, MERS, Zika, and Ebola, which have offered lessons in preparedness. In this context, it's clear that the global research community needs to continue to prepare for what may come next.

Building for the future

For Gilbert and Salman, work hasn't stopped with the rollout of the Oxford/AstraZeneca vaccine. "We're really busy," says Gilbert, adding that the trials are ongoing. The researchers will follow up with trial participants six months and one year after their second dose to collect blood samples and generate long-term data. Gilbert and her team have extended their studies to include an HIV-positive cohort in the UK and South Africa. However, many of these trials have been halted because of fears that the vaccine can cause dangerous blood clots in rare cases.

The concerns appeared after the vaccine's rollout, when several countries reported that it appears to be linked with dangerous blood clots in very rare cases. Despite the rarity, this led some regulators to temporarily suspend use of the vaccine and later to authorise its use only by some groups, such as older people. Overall, the consensus among health officials is that the benefits still outweigh the risks, but research is being done to under the mechanism behind the clotting in the hope that this will make it possible to reduce the risks further, as well as helping guide the evaluation of other vaccines.

"We've got approval in 15 countries so far, but there are other regulators still making their assessments and sending through questions that we need to answer very quickly," says Gilbert. "And once there's any time to do anything else, I've got all the other vaccine projects that I should have been working on last year."

"Vaccines have never been as important as they have been in the past two years. A world without vaccines is not a world."

— Jamila Louahed, vice president and head, Global R&D, GSK

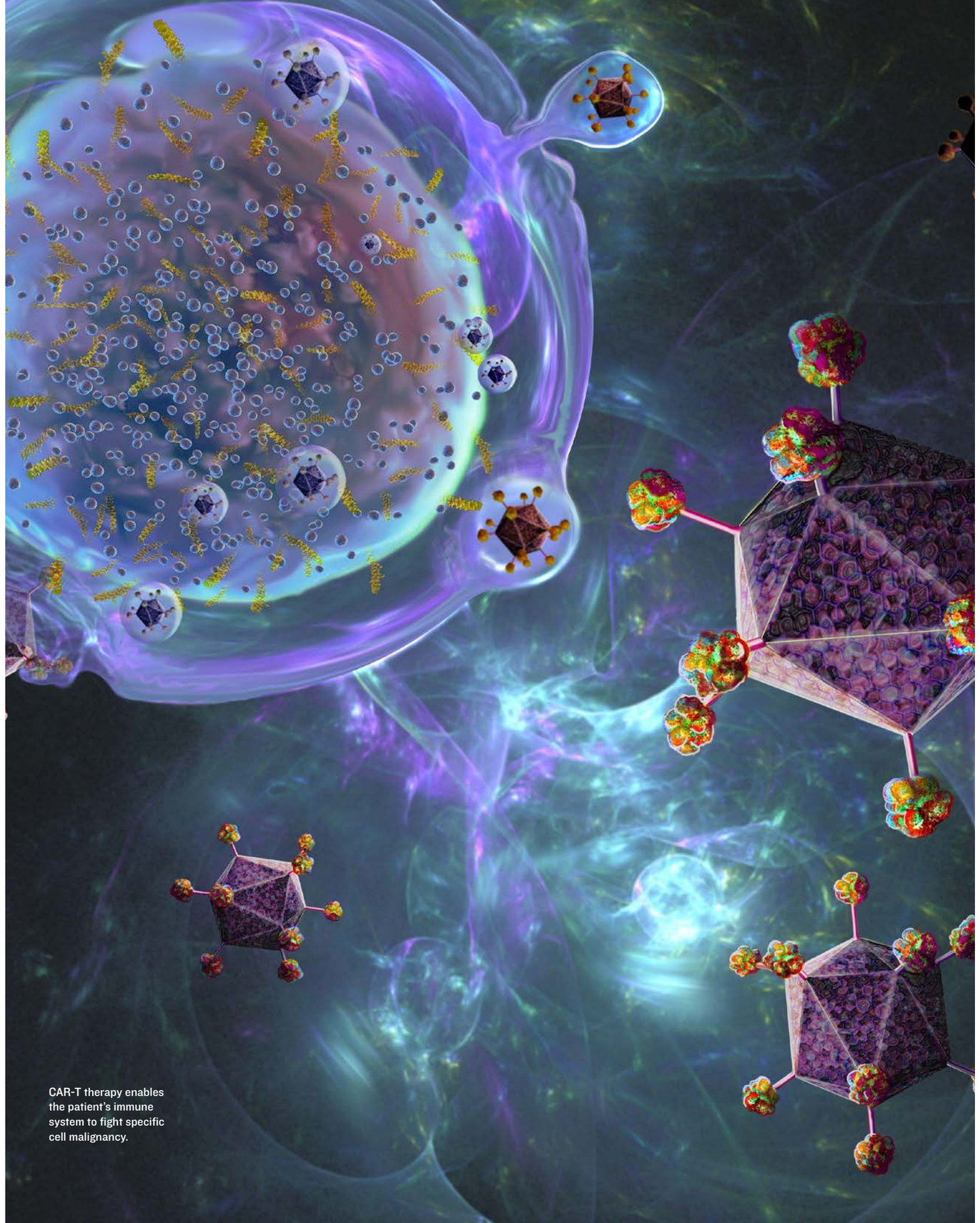
The growing role of cell and gene therapies

Extensive collaboration between various stakeholders in the field of cell and gene therapies should expand the reach of these advanced treatments for multiple diseases.

“We are in a dynamic environment in the cell and gene therapy space. The field is in the midst of groundbreaking innovations for the treatment of many diseases, and is benefitting more and more patients,” says Miriam Fuchs, a global therapeutic area lead in Regulatory Affairs at the Swiss-based global healthcare company Novartis. “Revolutions leading to new therapies, and evolutions to further improve these therapies, are moving at an amazing speed.”

Fuchs spent many years as an academic researcher in the field of cancer biology before joining the pharmaceutical industry. She has extensive experience in the field of haematology, and was involved in the development and registration of tisagenlecleucel, the first approved chimeric antigen receptor T-cell (CAR-T) therapy. The therapy is now available for the treatment of certain forms of B-cell malignancies including indications in paediatric and young adult B-cell acute lymphoblastic leukaemia and diffuse large B-cell lymphoma.

CAR-T therapy is an innovative, complex cell and gene therapy. Doctors collect T cells, a type of immune cell from a patient, which are reprogrammed using genetic modification to express a chimeric antigen receptor, directed against a cell surface protein on the target cancer cells to attack it. The modified cells are released in the body again. This precision, personalised therapy enables the patient’s immune system to fight their specific B-cell malignancy.



CAR-T therapy enables the patient’s immune system to fight specific cell malignancy.

SCIENCE PHOTO LIBRARY / ALAMY STOCK

“Cell and gene therapies are an amazing mix of science and innovation,” says Fuchs. “In the case of CAR-T therapy, every individual product has the potential to have a meaningful impact for its patient. This is very rewarding and extremely motivating for those of us working in this field.” At Novartis’s manufacturing sites for tisagenlecleucel, they maintain an illuminated ‘wall of hope’; for every patient batch they manufacture, they turn on one additional light as a symbol of their commitment to patients.

Fuchs shared some of Novartis’s key learnings from their journey in developing and commercializing tisagenlecleucel at the Riyadh summit. Their hope is to widen access to such therapies, alongside the continued efforts to refine and optimise each treatment.

“Our learnings may be valuable considerations for other developers in the advanced therapies field,” says Fuchs. “Most importantly, there needs to be a strong emphasis for all stakeholders —developers (academia, biotech, pharma), regulators, payers, physicians and patients—to work closely together to enable key innovations to reach those in need.”

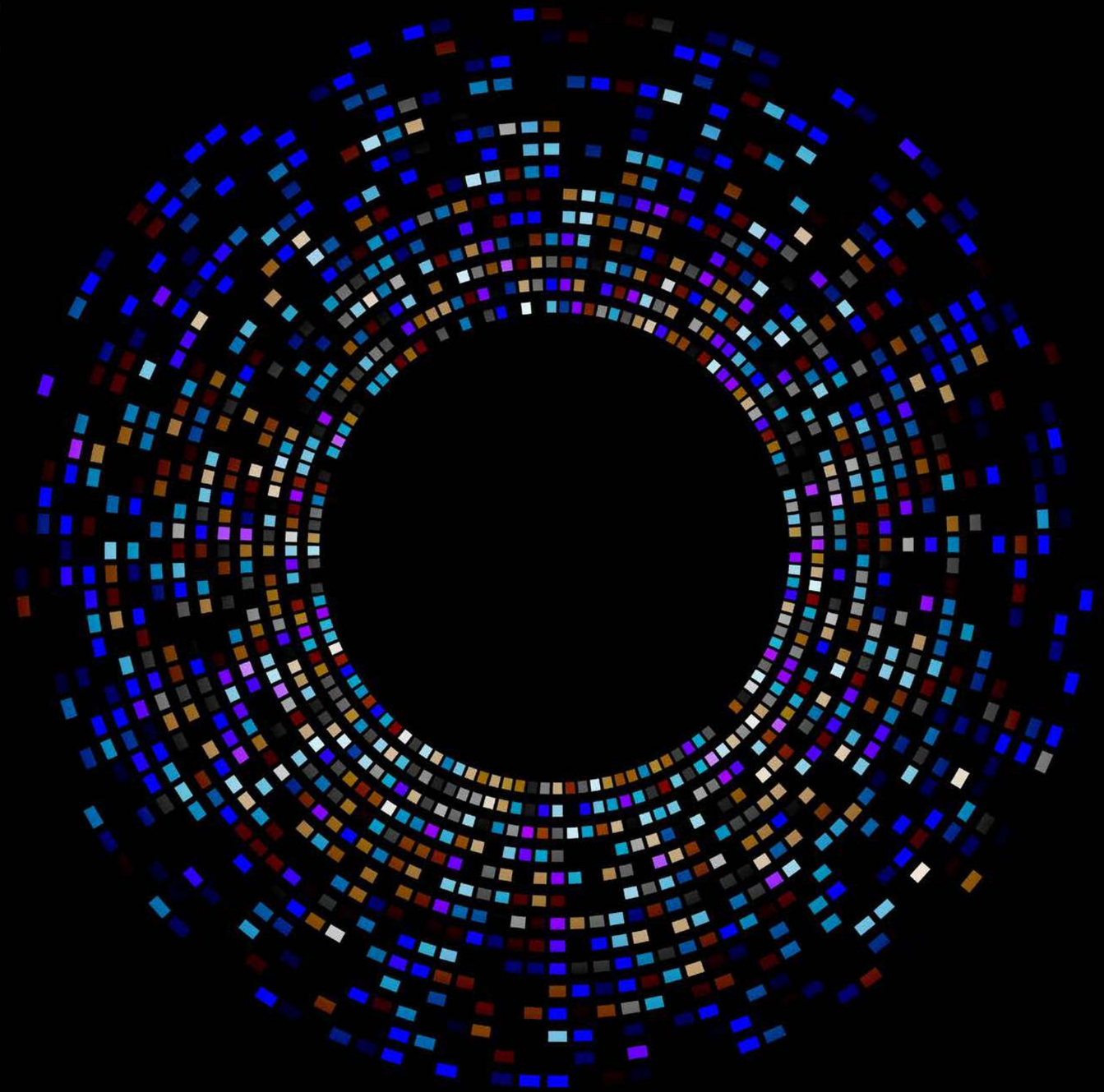
Public education about all forms of cell and gene therapy is required to build trust in novel therapeutics, which can sometimes seem like science fiction to the general public.

“We must drive education forward, ensuring that accurate information presented in lay terms is available to all patients and to the wider public,” says Fuchs. Describing the science behind new technologies and treatments clearly, and sharing success stories and case studies as well as the complexities of these innovations, will help the public better understand and accept these novel therapies. “As these therapies become reality for more and more people, awareness will be increased, helping to boost trust and enhance understanding of these therapies.”

Miriam Fuchs, global therapeutic area lead in Regulatory Affairs at Novartis.

Sequencing immune system genes for stem cell transplant success

Sequence data from immune system genes of nearly 29,000 Saudi stem cell donors will help match them to patients.



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KAIMRC researchers are assembling DNA fingerprints of immune genes in Saudi stem cell donors to help find a match.

An improvement in the Saudi Stem Cell Donor Registry (SSCDR) means that patients in need of stem cell transplants will have a lower risk of complications. The addition of sequence data from the immune genes of potential donors reduces the chance of a mismatch.

SSCDR, launched in 2011 by KAIMRC and the Ministry of National Guard Health Affairs, lists more than 75,000 registered potential donors who are willing to donate their blood-forming hematopoietic stem cells (HSCs) to patients around the world with life-threatening diseases such as leukaemia. Transplanted HSCs can reboot the production of healthy blood cells, but they need to be compatible with the patients' immune system.

"By sequencing such a large population, we found many new alleles that were not known before and were first reported in the Saudi population."

Human leukocyte antigen (HLA) genes play a key role in determining the success of HSCs transplantation. HLA genes produce cell surface proteins that bind to bacteria, viruses and cancer cells, and activate the immune system to attack them. The frequency and distribution of HLA alleles differ widely between different ethnicities and geographical areas.

"Matching HLA alleles between patient and donor in stem cell transplantation is an important factor for a successful outcome," says KAIMRC's Ali Hajeer, founder of the SSCDR, and lead author of the new study. A mismatch between donor and recipient HLA alleles can lead to organ rejection, graft failure and cause graft versus host disease, a major post-transplant complication in which donated cells recognise the host's cells as foreign and attack them.

The new study describes the frequencies of HLA types in nearly 29,000 Saudi stem cell donors. "By sequencing such a large population, we found many new alleles that were not known before and were first reported in the Saudi population, and we identified new associations between different genes of the HLA system that are not seen in other populations," Hajeer explains.

These data can be used to predict the chances of finding a compatible unrelated donor for patients who need a stem cell transplant but don't have an HLA-compatible relative. Although the chances of finding an HLA-matched relative are quite high in Saudi Arabia due to the high rate of consanguineous marriages, it is estimated that up to 40% of patients cannot find a matched HSCs donor within their family.

The results also provide a useful starting point for investigating associations between particular HLA alleles and autoimmune diseases such as type I diabetes, rheumatoid arthritis and celiac disease, among others. "We will continue sequencing HLA and other polymorphic genes in our donors creating a larger Saudi cohort to further understand the genetic basis of the immune response in Arabs," Hajeer says.

Jawdat, D., Uyar, F.A., Alaskar, A., Müller, C.R., Hajeer, A. HLA-A, -B, -C, -DRB1, -DQB1, and -DPB1 allele and haplotype frequencies of 28,927 Saudi stem cell donors typed by next-generation sequencing. *Front Immunol.* **11**, 544768 (2020).

Right to the heart of the matter

The future of treatment for cardiovascular diseases could lie in cell and gene therapies, with biotechnological advances paving the way for individualised therapies.

Philip Larsen, senior vice president and global head of research and early development at Bayer AG Pharmaceuticals.

Cardiovascular diseases remain one of the largest health challenges across the globe and the world's leading cause of death. But novel biotechnological advances, particularly in cell and gene therapies, offer great potential to provide optimal care for patients, and to aid in the early diagnoses and treatment of heart conditions.

"Considering the global change in demographics, a growing proportion of elderly patients will pose a challenge to health expenditure in the near future. To tackle this directly, the medical community will have to introduce more personalised approaches to heart disease management," says Philip Larsen, senior vice president and global head of research and early development at Bayer AG Pharmaceuticals. "Cell and gene therapies could become viable alternatives to heart transplantation and complex mechanical cardiac assist technologies."

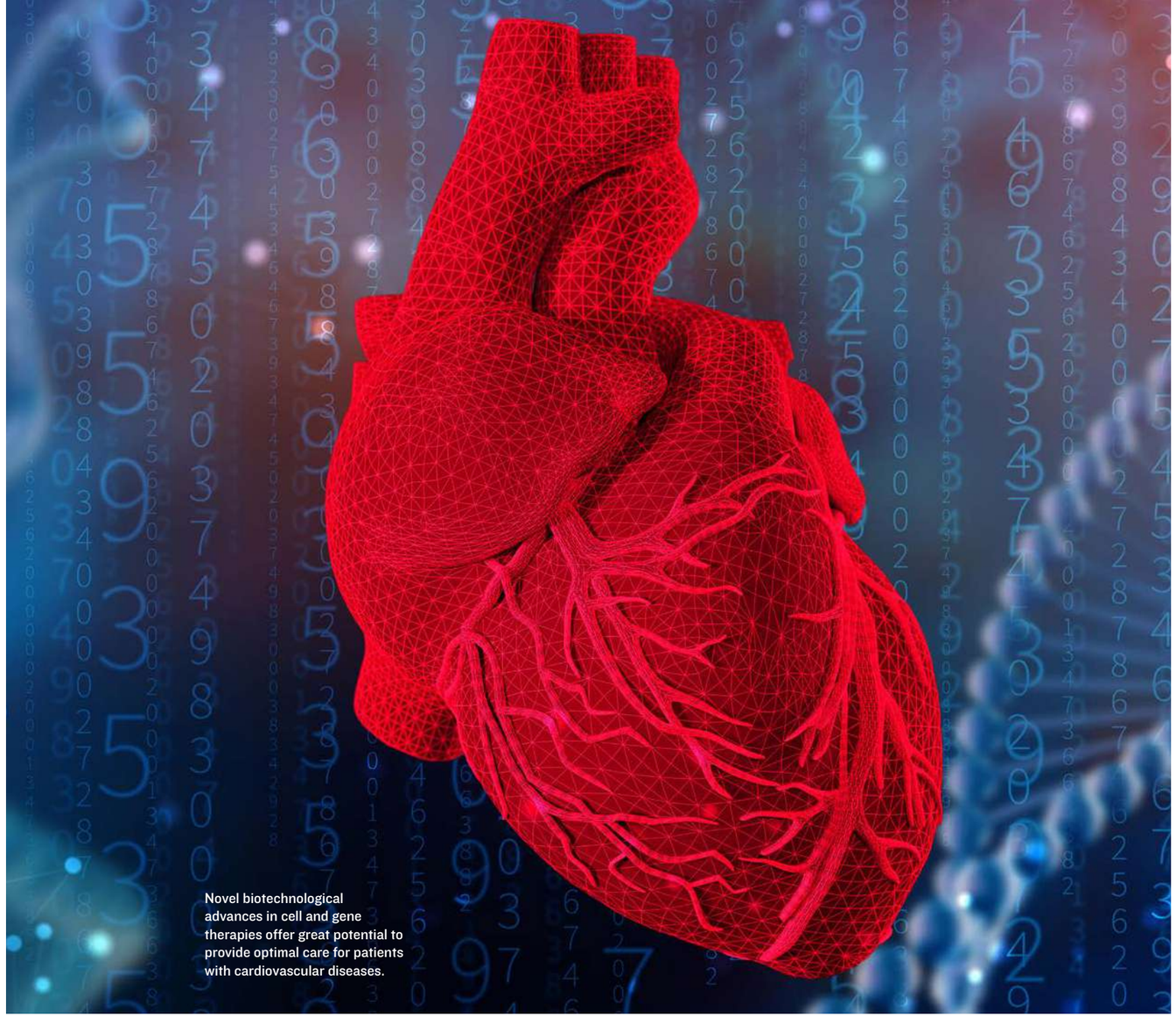
Cell and gene therapies target diseases at the molecular level, and are designed to repair or replace damaged or dysfunctional cells and genes before serious illness takes hold. This fledgling yet flourishing field holds great potential for the treatment and possible prevention of multiple diseases and hereditary conditions. Such therapies could open doors to personalised, targeted treatments, with drugs and therapies tailored specifically to an individual's needs.

"Cell and gene therapy for cardiovascular disease is still a young field of research and many uncertainties have to be managed satisfactorily before patients can directly benefit," explains Larsen. "Nevertheless, the field is facing some imminent breakthroughs. With this in mind, Bayer has recently acquired two companies with the aim of pursuing these potential treatment pathways for patients with cardiovascular disease needs."

The two companies are Asklepios Biopharmaceutical, a gene therapy company, and a cell therapy company called BlueRock Therapeutics. BlueRock is developing and investigating stem cell technology that can replace cells in the body that are lost or damaged due to diseases including cardiovascular and neurological disorders. Asklepios Biopharmaceutical is examining targets such as the gene mutations that make cardiovascular diseases more likely, and currently developing a gene therapy approach for congestive heart failure.

According to Larsen, both companies will initially be operating as independent entities in the Bayer family with their own R&D agendas, but with the aim of introducing novel products to Bayer's various pharmacotherapeutic franchises, including their cardiovascular offerings.

"The applied sciences of biotechnology bridge all aspects of disease – from providing deep insights into how diseases function, to informing practical therapeutic solutions," says Larsen. "This makes the field a very exciting place to be involved in at present."



Novel biotechnological advances in cell and gene therapies offer great potential to provide optimal care for patients with cardiovascular diseases.

ARTEM OLESHKO / ALAMY STOCK PHOTO

The COVID-19 pandemic has taught us to de-bureaucratise workflows, with resulting heightened agility and increased flexibility.

Larsen has noticed key changes in the biotechnology and pharmaceutical industries in light of the COVID-19 pandemic, not least a wider appreciation of the roles of biotechnology manufacturing and regulatory practices. With the whole world focused on the pandemic, this may accelerate the industry's implementation and dissemination of novel technologies such as mRNA-based products, notes Larsen.

"The pandemic has taught us to de-bureaucratise workflows, with resulting heightened agility and increased flexibility," he says. "At Bayer, we do not have an obvious right to innovate in the field of antivirals or vaccines. Rather, we have employed our expertise in cardiovascular medicine to join forces with academic centers to improve our understanding of the medical consequences of COVID-19 and so-called long-COVID syndrome."

Larsen is particularly excited to see how virtual and decentralised clinical trials are winning acceptance across the globe. "The pandemic has accelerated the implementation of such practices, which has broadened the reach of medical innovation to far more patients and medical centers, and will ultimately help boost the confident dissemination of novel therapies," he says.

Scientists in the US have shown how optimising vaccinations could help plug the gaps and boost the immune system's ability to neutralise viruses as they evolve.

DR_MICROBE/I STOCK / GETTY IMAGES PLUS

Optimising influenza vaccines to harness pre-existing immunity

Understanding how immune cells respond to natural infection compared with vaccination demonstrates how vaccines could broader immunity.

Researchers in the US have demonstrated why our immune response can struggle to fully neutralise mutated forms of the influenza virus. The study provides insight into how vaccines could be further honed to target specific viral components that our natural immunity might miss.

The question of how well our immune system can fight off repeated infections from viruses is critical, particularly as the world struggles to cope with a viral pandemic. When the immune system encounters a virus for the first time, it generates memory B cells that recognise protein segments that are part of the virus. Antibodies released by the memory B cells then bind to these epitopes and work to neutralise the virus. If the immune system encounters the virus again, the existing memory B cells are activated to release the same antibodies and quell infection.

"Unfortunately, our memory B cells don't always recognise epitopes that have mutated or drifted over time, leaving us susceptible to infection by different versions of the same virus," says Jenna Guthmiller at the University of Chicago, who was part of the research team, along with Haley Dugan and Patrick Wilson. "This is why influenza vaccines must change every year: to ensure they provide protection as viral epitopes evolve."

One outstanding question is whether different routes of initial exposure—natural infection versus vaccination—prompt a different level of recall by memory B cells and affect how protective the resulting immunity is. The researchers investigated this by comparing antibodies produced by memory B cells taken from people who had naturally been exposed to two influenza subtypes and from healthy people who had received an influenza vaccine.

"We found that the specificities of recalled memory B cells are drastically different depending on their original exposure route," says Dugan. Most antibodies derived from the infection-route B cells recognised conserved epitopes from past strains but would not neutralise current influenza viruses. Newer epitopes that had drifted were often missed by these antibodies. In contrast, antibodies derived from vaccinated individuals targeted both conserved epitopes from previous strains and epitopes which had changed through drift or mutation.

"While vaccination-induced antibodies were largely cross-reactive to past strains, they were still capable of neutralising the virus," notes Dugan. "This suggests the vaccinated response is better at recalling protective antibodies against both drifted and conserved epitopes."

"By developing vaccines focused on specific viral proteins that our immune systems might miss, we can optimise protective antibody responses," says Wilson.

Dugan, H.L., Guthmiller, J.J., Arevalo, P., Huang, M., Chen, Y-Q., Neu, K.E., Henry, C., Zheng, N-Y., Lan, L., Y-L., Tepora, M.E., Stovicek, O., Bitar, D., Palm, A-K.E., Stamper, C.T., Changrob, S., Utset, H.A., Coughlan, L., Krammer, F., Cobey, S., Wilson, P.C. Preexisting immunity shapes distinct antibody landscapes after influenza virus infection and vaccination in humans. *Science Translational Medicine* **12** eabd3601 (2020).

Saudi Arabia aims to develop a flourishing biotech ecosystem that can attract the world's best-in-class entrepreneurs.

SIMON KADULA / EYEEM / GETTY IMAGES

Tapping into talent to boost an emerging biotechnology ecosystem

How Saudi Arabia can leverage global best practices of biotech clusters to attract world-class entrepreneurs.

Enticing interest and investment from entrepreneurs, as well as nurturing new talent, is essential for a successful biotechnology industry. At the Riyadh Global Medical Biotechnology Summit 2021, Richard Smith talked about the biotech ecosystem in the Philadelphia region and events leading up to the emergence of cell and gene therapy within the region –now referred to as "Cellicon Valley." He discusses how Saudi Arabia can leverage best practices of biotech clusters around the world to develop a flourishing ecosystem that will attract the world's best-in-class entrepreneurs.

What inspired you to work in the field of biotechnology?

My route to biotechnology came after decades in the financial services industry, where I was fortunate to work with the top professionals who managed key levers of the global economy. Working in that environment was fun and had a major impact on my career. However, having moved into biotechnology, I now work with heroes whose work carries the possibility of enhancing the health and wellbeing of people across the globe. Working in such an industry is humbling and inspiring every day.

What roles can individual entrepreneurs play in developing and promoting biotechnology?

The individual entrepreneur is the lynchpin. Countries who are seeking to bolster and promote their fledgling biotech industry should nurture new entrepreneurs, as well as actively attract existing ones. Ultimately, it is the entrepreneurs who decide where to locate the research, development and manufacturing work that is needed to achieve a specific goal. An entrepreneur is looking for an advantage that accelerates their path to success. As Saudi Arabia is placing additional chips in the global biotech space, the country must create an attractive and resilient atmosphere for investment and business opportunities. Building a successful biotech ecosystem requires sustained collaboration and input from numerous multidisciplinary teams over time.

How do collaboration and multidisciplinary research fit into Rockland Immunochemicals?

As a small enterprise, Rockland embraces collaboration in every aspect of our business. As a leader in antibody engineering, we work with academic and industrial researchers on the most complex problems in the life sciences. For example, our products and services are used to measure and enhance the quality of the bioprocessing facilities that produce the latest drugs and vaccines. Diversity, in every sense of the word, is critical to our ability to understand, analyse and provide solutions that make a real and meaningful difference.

What advice would you give countries like Saudi Arabia, who have the opportunity to invest in biotechnology?

It is critical to understand the history of your journey in which lies the secrets to past successes. Leverage the strengths inherent within and across other disciplines and industries to develop a unique and dynamic value proposition, which in turn will help you attract and retain the essential elements of a strong and vibrant biotechnology ecosystem. Saudi Arabia, for example, has a tremendous cache of talented clinical physicians. The country can tap into this resource to produce a stream of highly qualified biotechnology entrepreneurs that build and define its biotech ecosystem.

Richard Smith, chief operating officer at Rockland Immunochemicals Inc.

Drugs formulated using nanocrystals help prevent preterm births in mice.

Nanotechnology prevents preterm birth in mice

Formulation helps overcome mucus barriers for targeted drug delivery.

A new nanomedicine strategy for delivering drugs to the female reproductive tract could help prevent women from going into labour prematurely.

Each year, around 1 in 10 babies worldwide are born before 37 weeks of gestation, resulting in more than 1 million deaths due to complications resulting from preterm birth. The steroid hormone progesterone is sometimes used to prevent early delivery in at-risk women, but current treatment formulations often have little effect because they fail to deliver the hormone to the appropriate tissues of the cervix and uterus.

A team from Johns Hopkins University in the USA designed a nanosuspension system that enables vaginally dosed drugs to overcome the mucus barrier of the female reproductive tract and reach uterine tissues, where they can forestall labour.

The system involves grinding drugs into miniature crystals about 200 to 300 nanometers in diameter—smaller than the size of a typical bacterium. A stabilizing agent is then added to keep the nanoparticles from getting stuck in the vagina's protective mucus, which normally traps foreign particles such as microbes—but also medicines—and prevents their entry into the body.

The researchers tested the system in mice experimentally induced to develop uterine inflammation, an unpredictable major condition that often leads to premature labour in humans and results in nearly 4 million global premature births annually. They focused on vaginal administration of two types of drugs: histone deacetylase (HDAC) inhibitors, which they showed can help to inhibit the contractility of the uterine wall in human cell experiments, and progesterone, which has known anti-inflammatory effects.

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Mice treated with mucus-penetrating nanosuspensions of HDAC inhibitors showed improved rates of full-term delivery.

The researchers found that mice treated with mucus-penetrating nanosuspensions of HDAC inhibitors, both with and without progesterone, showed improved rates of full-term delivery. Large litters of healthy, normal pups were born. By comparison, mice injected with the drugs in their body cavity—like untreated mice—went into labour prematurely, with no surviving offspring.

"Delivery matters," says Laura Ensign of Johns Hopkins, who led the research. "And we must sometimes think outside the box of pills and injections to develop effective treatments."

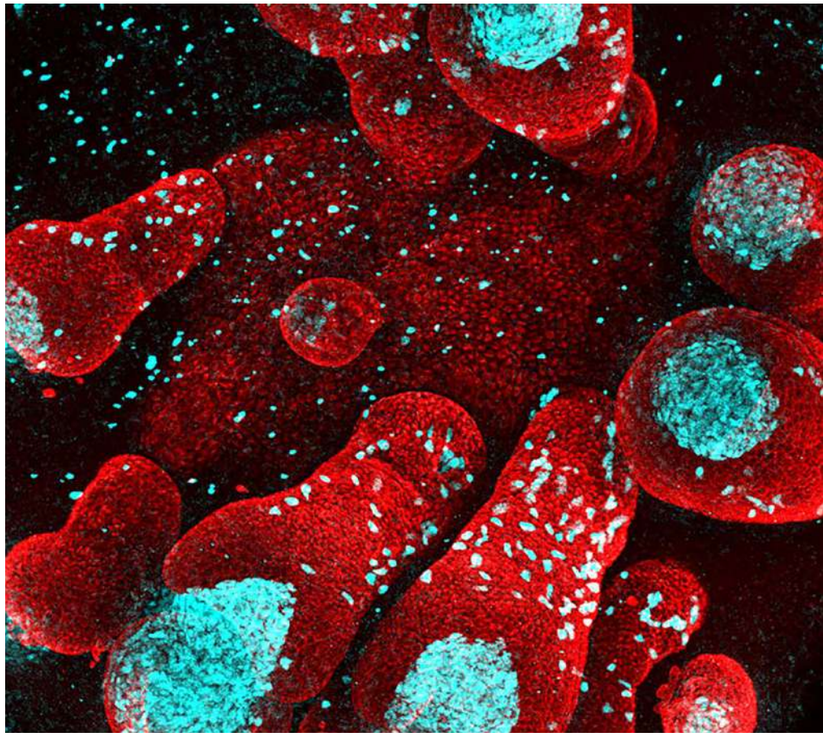
In other mouse studies, Ensign and her colleagues have used their nanosuspension system to enhance drug delivery in the gut, in the airways and at other mucosal surfaces. Kala Pharmaceuticals, a company cofounded by Ensign's close collaborator and mentor, Justin Hanes, has licensed the technology and developed two topical eye treatments for people, one for dry eye disease and one for post-operative ocular inflammation and pain.

"There are many diseases affecting mucosal surfaces that would benefit from more targeted local and sustained drug delivery," Ensign says. Fortunately, her technology now makes that possible.

Zierden, H.C. *et al.* Enhanced drug delivery to the reproductive tract using nanomedicine reveals therapeutic options for prevention of preterm birth. *Science Translational Medicine* **13**, eabc6245 (2021).

Hair-growing skin produced from human stem cells

Complete skin-in-a-dish tissue offers new options for wound healing, genetic skin conditions and baldness.



A stem cell-derived human skin organoid with sprouting hair follicles (red) with dermal papilla cells (cyan) after three months in culture.

DR. JIYOON LEE AND DR. KARL KOEHLER. BOSTON CHILDREN'S HOSPITAL/HARVARD MEDICAL SCHOOL

A new procedure enables researchers to generate skin from undifferentiated cells. As well as a tool for studying how skin develops, these skin organoids could be used as a source for grafts as well as for screen and testing drug treatments.

Skin is the body's largest organ. It is also multi-layered and multi-functional, acting as a protective barrier, helping to control body temperature and mediating sensation. Although outer-layer skin cells have been grown in laboratories for decades, scientists had previously not been able to recreate this organ, with its follicles and glands, in a dish.

Now, Karl Koehler at Boston Children's Hospital, United States, and his colleagues, have managed to generate skin organoids by directing the differentiation of human pluripotent stem cells in a 3D culture system.

Because the cells that form the main layers of skin (epidermis and dermis) are derived from different cell types in the early embryo, the authors first had to optimise the growth conditions. The sequential addition of growth factors triggered the differentiation of human pluripotent stem cells into non-neural ectoderm. This gave rise to epidermal cells, and cranial neural crest cells, which gave rise to cells of the dermis in the face.

After the cells grew for 70 days as spherical aggregates, the first hair follicles were observed on the surface along with some associated tissues such as sebaceous glands, nerves, muscles and fat. "We were truly astounded to see hair growing in our culture dish," says Koehler. "As we repeated the experiments we learned how the process closely mimics the sequence of human fetal skin development."

To further investigate the cellular composition of the skin organoids, the team performed single-cell RNA sequencing at various time points. They identified four main cell subtypes, but found them in slightly different proportions between organoids. Despite this variability, the gene expression signatures indicate that the organoids mimic facial skin. Tweaking the protocol could generate skin with the characteristics of other body parts and could shed new light on the mechanisms involved in skin growth.

To explore the therapeutic potential of these skin organoids, the authors transplanted them on to immunodeficient mice. Just over half of the grafts sprouted hair, highlighting the exciting possibility of using skin organoids for healing wounds or producing hair in bald scalps.

The authors also point out that skin organoids generated from patients with genetic skin disorders or skin cancers could be used to screen for drug efficacy and toxicity, accelerating the discovery of new treatments.

"The next steps will be to better understand how skin organoids might react with a patient's immune system," says Koehler. "The path to the clinic is going to be challenging, but these early results are quite promising."

Lee, J., Rabbani, C.C., Gao, H. *et al.* Hair-bearing human skin generated entirely from pluripotent stem cells. *Nature* **582**, 399–404 (2020).

Finding the sweet spot for clinical genomics

A review of genome sequencing strategies reveals cost-effective approaches for diagnosing hereditary disorders

Clinicians now have the capacity to comb through entire genomes in search of mutations underlying hereditary disorders, but a narrower approach may be a more efficient diagnostic strategy, according to new research.

Some children exhibit complex combinations of birth defects and symptoms that are difficult to diagnose. Whole-genome sequencing (WGS) allows clinicians to home in on the causative mutations by scanning through the complete nucleotide sequences of genes and the regulatory sequences that control them. But this is relatively expensive, and a strategy known as whole-exome sequencing (WES) offers a simpler alternative.

In WES, only the sequences of protein-coding genes are analyzed. This cuts the cost of sequencing and analysis in half, making it a good first step. "Most hospitals in Saudi Arabia go with WES first, and if that proves negative, they proceed with WGS," explains KAIMRC's Majid Alfadhel, who led a team to investigate whether this is the best strategy, or if starting with the broader dragnet of WGS might offer a more cost-effective road to a diagnosis.

To address this, they reviewed four years of WES and WGS data from King Abdulaziz Medical City in Riyadh. This center has produced a plethora of genetic diagnostics data, and Alfadhel and colleagues have already published 17 studies based on these data in 2020. Some of these were from 'solo' patients who were sequenced individually, but in most cases the clinicians performed 'trio' sequencing, which includes the patient's parents to more easily distinguish between harmless and potentially harmful mutations. A subset of the cases were 'trio plus' analyses, which also includes siblings.

Modern DNA sequencing instruments can deliver comprehensive information about genetic mutations, but clinicians are still learning how to use this technology to make diagnoses in the most efficient manner.

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Though each additional family member adds cost and delay to the analysis, the extra data should increase the 'hit rate' for identifying disease-related mutations, particularly with WGS. "But surprisingly, there was no difference in the hit rate between WES and WGS-solo, WGS-trio, or WGS-trio plus," says Alfadhel. Indeed, every single hit found with WGS could also be detected in the WES data, suggesting that more thorough reanalysis might be better than additional sequencing.

This work indicates that broader genome coverage generally does not deliver extra clinical value—in fact, it yields numerous enigmatic mutations that are impossible to interpret with current genetics knowledge. As a consequence, Alfadhel says that Saudi Arabia's clinical genetics teams "will do more WES- or WGS-solo than trio or trio-plus to conserve the budgets of our hospitals."

Alfares, A., Alsubaie, L., Aloraini, T., Alaskar, A., Althagafi, A. *et al.* What is the right sequencing approach? Solo VS extended family analysis in consanguineous populations. *BMC Med. Genomics* **13**, 103 (2020).

"The hard-earned wisdom of 2020 and 2021 has shown that to succeed in the future, leaders in healthcare will have to focus on three things: digital growth and the virtualisation of care, leverage data analytics and AI to strengthen clinical decision, and manage capacity with enterprise-wide surveillance."

—Elie Chaillot, vice president and chief executive officer, GE Healthcare, EMEA

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