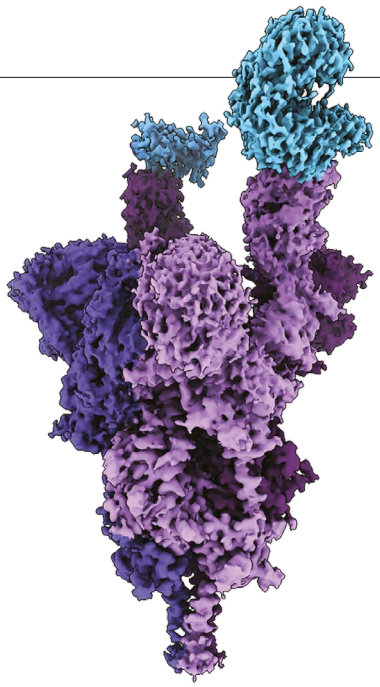
a lot more of the vaccine. Jason McLellan, a structural biologist at the University of Texas at Austin whose work was foundational to the development of several COVID-19 vaccines, says he is not surprised that South African researchers seem to have copied Moderna's vaccine, but he adds that scaling up production of that original shot required a lot of extra innovation by manufacturers.

For the next phase of the project, several companies in the global south will learn from Afrigen and attempt to create batches of vaccine themselves, in preparation for testing the shots in rodents. The WHO expects a Moderna mimic to be ready for phase I trials in people by the end of November.

What will happen next year remains uncertain. Charles Gore, director of the Medicines Patent Pool in Geneva, Switzerland — an organization working with the hub that is devoted to expanding drug and vaccine access around the world — says that the initiative has no intention of infringing Moderna's patents. Laboratory research is generally not subject to patent rules, Gore explains.

And he hopes that once the vaccine is ready for use, Moderna might then license its patents — or that by then, there might be alternatives that companies could produce without fear of a lawsuit. Scientists at several universities are currently developing next-generation mRNA vaccines that might be cheaper to make or not require the ultracold storage needed for Moderna and Pfizer–BioNTech's vaccines.

Although the pace of this effort will not meet the urgent need for vaccines across Africa, many researchers from the continent are enthusiastic. A reliance on vaccines from wealthy countries and companies has proved dangerous during the pandemic — only about 10% of people in Africa have been fully vaccinated — and this initiative aims to help nations to protect themselves. "Global health's dysfunction derives from power imbalances," explains Olusoji Adeyi, president of the organization Resilient Health Systems in Washington DC. "Addressing that will come from countries in the global south developing their own capabilities and taking responsibility for their own health."



SRIRAM SUBRAMANIAM/UNIV. BRITISH COLUMBIA

Researchers have found that despite myriad mutations, Omicron's spike protein binds tightly to the ACE2 receptor (blue) on cells.

OMICRON'S STRUCTURE COULD HELP EXPLAIN ITS GLOBAL TAKEOVER

Studies hint at why the SARS-CoV-2 variant spreads fast, yet seems to cause milder disease than earlier versions.

By Diana Kwon

After it was first detected in South Africa last November, Omicron spread around the globe faster than any previous variant of the coronavirus SARS-CoV-2, readily infecting even those who had been vaccinated or had had COVID-19 before. To learn how it was able to do this, scientists have turned to techniques such as cryo-electron microscopy, to visualize Omicron's molecular structure at near-atomic resolution.

By comparing Omicron's structure with that of the original version of SARS-CoV-2 and its other variants, they have begun to shed light[1] on which features of the highly mutated virus have enabled it to evade the body's immune defences, while also maintaining its ability to attack a person's cells. And they've begun to unpick why Omicron seems to cause milder disease than previous variants.

"Omicron is very different structurally than all the other variants we have known so far," says Priyamvada Acharya, a structural biologist at the Duke Human Vaccine Institute in Durham, North Carolina.

Omicron has dozens of mutations not seen in the original SARS-CoV-2 strain that researchers first detected in Wuhan, China. More than 30 of those mutations are in the spike protein on the coronavirus's surface, which helps the virus to latch on to and infect host cells. No previous SARS-CoV-2 variant seems to have accumulated so many genetic changes.

Fifteen of Omicron's spike mutations are found in the protein's receptor binding domain (RBD), a region that binds to a receptor called ACE2 on a person's cells to gain entry. A research team including David Veesler, a structural biologist at the University of Washington in Seattle, has shown[2] that these changes, along with 11 mutations in a region of the spike called the N-terminal domain, have completely remodelled the areas of the protein that are recognized by 'neutralizing' antibodies. These antibodies are generated after a person receives a vaccine against SARS-CoV-2 or is infected; they later recognize the pathogen and prevent it from entering cells. The remodelling severely hinders the ability of most neutralizing antibodies to recognize the virus.

With such a big shift in shape, there's a huge question over how Omicron can still bind strongly to ACE2. "Normally, when you have so many mutations all over, you expect that you will also have compromised the ability to bind the receptor," says Sriram Subramaniam, a structural biologist at the University of British Columbia in Vancouver, Canada.

A net effect

Subramaniam and his colleagues answered the question by demonstrating that although some of the mutations in Omicron's RBD hinder its ability to bind to ACE2, others strengthen it[3]. For example, the K417N mutation disrupts a key salt bridge — a bond between oppositely charged bits of protein — that helps to link the spike protein to ACE2. A combination of other mutations, however, helps to form new salt bridges and hydrogen bonds that strengthen the link to ACE2. The net effect is that Omicron binds to ACE2 more strongly than does the original version of SARS-CoV-2, and as strongly as does the Delta variant.

Veesler and his colleagues have also found[2] enhanced interactions between Omicron's RBD and ACE2. Omicron has adopted a "very elegant molecular solution, where the mutations are mediating immune evasion while enhancing receptor binding", Veesler says.

Martin Hällberg, a structural biologist at the Karolinska Institute in Stockholm, applauds the work by these groups, but points out that it's an open question how some neutralizing antibodies can still detect Omicron. If researchers can understand the structural

basis for that recognition, he adds, that knowledge might help to counter variants that emerge in future.

Some structural studies have also provided possible explanations for another of Omicron's properties: that it seems to have more difficulty infecting the lungs than the nose and throat. This could be a reason it might cause milder disease than other variants.

Many studies focus on two possible mechanisms by which SARS-CoV-2 and its variants might enter a person's cells after binding to ACE2. The first involves a host-cell enzyme called TMPRSS2, which helps the virus to fuse with the cells and inject its genetic material directly into them. The other, slower pathway involves the virus entering host cells through bubbles known as endosomes before releasing its contents.

Several groups have found evidence that Omicron prefers the slower route[4]. For example, Veesler and his colleagues found[5] that cleavage of the spike protein, required for the TMPRSS2 pathway, was less efficient for Omicron than for Delta. The researchers also noted that there are higher levels of TMPRSS2 in the lungs than in the upper airways — possibly explaining Omicron's preference for infecting the nose and throat.

But not everyone agrees that Omicron prefers this entry route. Bing Chen, a structural biologist at Harvard Medical School in Boston, Massachusetts, suggests mechanism slightly different from either of the other two. He says that Omicron's mildness is related to ACE2.

To bind to ACE2, the virus's RBD needs to flip from a 'down' to an 'up' position. In a preprint[6], Chen and his colleagues have reported evidence that Omicron's RBD has difficulty moving into the 'up' conformation because of a structural change induced by one of its many mutations. As a result, Omicron requires higher levels of ACE2 to fuse with host cells than do other variants. "This could explain why Omicron doesn't really infect the lung cells, because lung cells generally have much lower ACE2 levels compared to the cells in the upper respiratory tract," Chen says. But further investigation is needed, he adds.

Researchers are hoping to use structural knowledge about Omicron to help develop more effective treatments and vaccines against it — and against future variants of concern. "Omicron really redefines what we thought variants look like," Veesler says.

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BELINDA JIAO/SOPA IMAGES/LIGHTROCKET VIA GETTY

Prolonged Brexit negotiations mean some UK researchers can't access EU grant funding.

BREXIT ONE YEAR ON: PATIENCE 'WEARING THIN' AMONG UK SCIENTISTS

Researchers brace for tense weeks ahead as Europe turns up the heat on research negotiations.

By Holly Else

It has been just over a year since UK scientists celebrated a long-awaited trade deal between their government and the European Commission that defines their relationship after Brexit. After years of uncertainty, researchers welcomed the pact, which had wide-ranging effects on science, including on data regulation, nuclear and space research and clinical trials.

It also promised to pave the way for a formal partnership between the United Kingdom and the commission that would allow British researchers to bid for funding from the commission's flagship €95-billion (US$107-billion) research programme, Horizon Europe, which started doling out money last month.

But the two sides have yet to ratify the final agreement because of a row over a customs border between Great Britain and the island of Ireland. As a result, the UK government has deployed its safety-net funding guarantee to underwrite successful bids by UK scientists for Horizon Europe funding in the programme's early stages.

"We're starting to become very concerned about the situation," says Jo Burton, a policy manager at the Russell Group, a consortium of top UK research universities, with headquarters in Cambridge.

Research-policy scholars say that the commission is holding science "hostage" to achieve its wider political aims, and urge for progress in talks before patience in the United Kingdom wears out and the government abandons plans to associate with Horizon Europe.

Deal delayed

UK research was thrown into turmoil in the wake of the country's vote to leave the European Union in 2016. The uncertainty left many UK-based scientists unsure whether workers and research funding would continue to flow freely between the two entities. Much of the confusion around immigration has been resolved: EU researchers working in the United Kingdom have opted to either leave the country or apply for permission to stay. The UK government has also established new visa routes for scientists.

The eleventh-hour trade deal struck between Britain and the EU in January 2021 paved the way for Britain to 'associate' with Horizon Europe as a non-member state. It came as a huge relief to scientists, who finally had clarity that they would, in principle, be able to apply for funding from the