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## Vaccines being redesigned to tackle new variants

Barely three months after the front-runner Pfizer-BioNTech Covid-19 vaccine was rolled out in a mass vaccination campaign in Britain, some vaccine developers are already redesigning their vaccines to tackle new variants.

Last week, United States biotechnology firm Moderna announced that it had dosed the first participant in a trial evaluating a booster vaccine it designed to target a new variant of the virus first identified in South Africa.

Pfizer-BioNTech has also said it will be evaluating a booster shot and is preparing to tweak its vaccine to address new variants that might escape the current version of its mRNA-based vaccine.

The B.1.1.518 variant, which has become dominant in South Africa, is one of three "variants of concern", as the World Health Organisation (WHO) calls them, that the scientific community is watching out for. The other two are the B.1.1.7 (British) and P.1 (Brazilian) variants.

There is early data to show that the B.1.1.7 variant, which has spread widely beyond Britain's shores, has a possible increased risk of hospitalisation, severity and mortality, according to the WHO.

But scientists are especially concerned about the more infectious variants that involve mutations in the spike protein of the coronavirus that could help them evade antibodies. This is the case with the South African and Brazilian variants.

Preliminary studies in Manaus, Brazil, where the P.1 variant was first identified, showed that it can evade 25 per cent to 61 per cent of the protective immunity provided by the previous infection, thereby making people susceptible to reinfection, said the WHO.

It said there is a need to conduct these studies outside of Manaus as there has been a sharp increase in hospitalisations during the second wave that has resulted in the collapse of health systems there. It is thus difficult to determine the cause of high mortality, which could be due either to the variant P.1 or collapsed health systems, or both.

The Amazonian city was hard hit in the first wave last year, with blood test results showing about 75 per cent of the population may have been infected at some point.



A burial site for Covid-19 victims at the Nossa Senhora Aparecida cemetery in the Brazilian city of Manaus, where the P.1 variant was first identified. World Health Organisation director-general Tedros Adhanom Ghebreyesus said "the longer the virus circulates, the higher the chances that variants will emerge that make vaccines less effective". PHOTO: AGENCE FRANCE-PRESSE

But from late last year, despite apparent herd immunity, the city saw another spike in infections.

### VACCINES STILL WORK

The Covid-19 vaccines in use are to protect people from severe disease, hospitalisations and deaths.

Experts say there is, thus far, no evidence that any of the variants can evade the immune response of current vaccines.

Associate Professor Hsu Li Yang, vice-dean of global health and programme leader of infectious diseases at the National University of Singapore's Saw Swee Hock School of Public Health, said the infectious variants are still recognised by immune systems primed by the current vaccines, but the antibodies produced are less effective at neutralising the variant viruses in laboratory studies. "Whether this translates into an actual drop in protective efficacy in real life is not known for sure yet."

In Britain, where the B.1.1.7 variant is dominant, the mass vaccination campaign has resulted in a significant decline in new Covid-19 cases, and in particular, cases of people falling severely ill, he said.

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### NOT THE SAME THING

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PROFESSOR OOI ENGEONG from Duke-NUS Medical School, on the impact of variants on vaccine effectiveness.

man host, so it has to adapt... What we're seeing is its adaptation to life in humans. That doesn't mean that as the virus adapts, we should be worried that the current vaccines won't work. These are two different things."

Professor Ooi, who is from the programme in emerging infectious diseases at Duke-NUS Medical School, said the impact of variants on vaccine effectiveness is "likely minimal".

"Laboratory-based studies on Sars-CoV-2 variants have shown that more vaccine-generated antibodies are needed to neutralise these variants," he said.

"However, RNA and recombinant adenovirus vaccines generate both antibodies and T cells, espe-

cially the killer T cells. A recent study has found that these viral variants have negligible impact on T cell reactivity," he pointed out.

These T cells are immune cells that can target and destroy virus-infected cells. They are part of the broad immune response generated by the vaccines.

For now, vaccine developers are watching out for the possibility of future mutations that may require them to alter their vaccines. Some, like Moderna, are planning ahead because it is fairly easy for them to update their mRNA vaccine.

Unlike traditional vaccines that may use an inactivated or killed virus to stimulate an immune response, mRNA vaccines deliver a tiny bit of the genetic code of the

spike protein into the cells to instruct them to produce these proteins, which will then trigger immunity.

All viruses change over time. Each time the Covid-19 virus replicates, copying errors or small changes are introduced into its genetic code.

Changes or mutations in the virus should not make vaccines completely ineffective, said the WHO in a recent article on new variants.

In the event that any of the current vaccines prove to be less effective against one or more variants, it will be possible to change the composition of the vaccines to protect against these variants, it added.

The WHO had thus called for countries to increase genome sequencing efforts in order to know how the virus is changing and how to respond. More variants detected recently were the result of countries increasingly sequencing the virus.

"Eventually, if the virus continues to spread unchecked, variants will evolve that may not only evade the vaccine, but may also reinfect those who were previously already infected by Sars-CoV-2," said Prof Hsu.

"We will be able to develop new vaccines far more quickly to these

future variants – a situation analogous to the annual influenza vaccine – but this is obviously not the preferred situation."

Hence, it is important that the global vaccine roll-out should continue as rapidly as possible, along with other community measures that slow or stop the spread of Covid-19, he stressed.

WHO director-general Tedros Adhanom Ghebreyesus said in a speech last Friday: "The emergence of new viral variants, the limited supply of vaccines, the lag in uptake of new diagnostics and oxygen, and the lack of funding to support the distribution of these life-saving tools are a major challenge for the global control of the pandemic."

"The longer the virus circulates, the higher the chances that variants will emerge that make vaccines less effective."

But they do not make public health measures such as physical distancing less effective, he noted.

Indeed, Prof Hsu said the situation with new variants in other parts of the world is virtually beyond any country's control.

"But it does help to be mindful and to continue practising the measures that have been effective in Singapore in stopping the spread of the virus so far."

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