

## Omicron has mutations detected in previous variants, which explains vaccine effectiveness, scientists say

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Omicron emerged as a variant of concern only in November 2021, but all the mutations it contains except one had been described before that.



Researchers at the Federal University of São Paulo (UNIFESP) in Brazil, supported by FAPESP, attribute this factor to the effectiveness of the existing vaccines against the variant, reflected in the relatively small number of severe cases and deaths despite Omicron's heightened transmissibility.

The hypothesis is raised in an article by the scientists published in the *Journal of Medical Virology (JMV)* as a Letter to the Editor in January 2022.

"In light of the data available so far, we believe the existing vaccines are indeed effective against all variants of the virus, all things considered. They may also be effective against any other variants that emerge in future," said Ricardo Durães-Carvalho, last author of the article. Durães-Carvalho is a researcher affiliated with the university's medical school (EPM-UNIFESP) and has a scholarship from FAPESP.

In October 2021, before the World Health Organization (WHO) recognized the emergence of Omicron, another study led by Durães-Carvalho described several <u>mutations</u> shared by a number of variants. A paper on the topic is published on the preprint platform *medRxiv* (not yet certified by peer review).

The group analyzed more than 200,000 genomes of SARS-CoV-2 and other human coronaviruses. They found identical mutations in different strains, which could serve as targets for future vaccines.

"Omicron corroborates our study. Out of 35 mutations in the variant's spike protein [used by SARS-CoV-2 to bind to a specific receptor when infecting human cells], only one was unknown. Twenty-five were in RBD [receptor-binding domain] 15 and RBM [receptor-binding motif] 10, regions of the virus that bind to human cells and are therefore potential targets for neutralizing antibodies," Durães-Carvalho said.



"That may explain why vaccination has so far been effective even though none of the vaccines on the market was designed specifically for Omicron. They don't prevent transmission, but they prevent severe cases and deaths, as can be seen by comparing this new wave with previous waves that occurred before there were vaccines or when a smaller proportion of the population had been fully immunized," said Robert Andreata-Santos, first author of the Letter to the Editor in JMV. Andreata-Santos is a postdoctoral fellow at EPM-UNIFESP with a scholarship from FAPESP.

The researchers stress that the article is based on the data currently available on Omicron and on the genomes of other variants sequenced so far. As the pandemic proceeds and more data is collected, it may be possible to confirm their hypotheses.

## **Shared mutations**

In the study posted to the preprint platform in October, Durães-Carvalho and different co-authors analyzed the dynamics of viral dissemination and evolution over time in Brazil, the United States and India, for the period between February and August 2021.

The analysis showed an increase in the number of mutation sites in the viral genome, above all in the spike protein, configuring what the researchers term convergent evolution, meaning that different variants undergo identical mutations that confer advantages such as evading the host's immune system or binding more efficiently to human cells.

"We show that the vast majority of the mutations resulted from this phenomenon," said Carla Torres Braconi, a professor at EPM-UNIFESP and co-principal investigator for the 2021 study.

Braconi is affiliated to a group of researchers who are working on



a project supported by FAPESP and led by Luiz Mário Ramos Janini, a professor at EPM-UNIFESP and the other co-author of the *JMV* article.

Nine directional spike mutation sites were detected prior to February 2021, followed by 14 between then and July. With the spread of the Delta <u>variant</u>, more spike protein mutations were observed, as well as signs of recombination, one of the factors that can lead to the emergence of novel variants.

Recombination is rearrangement of genetic material, especially by the joining of DNA segments from different strains. Signs of recombination involving Omicron were also observed.

In December, the researchers analyzed 146 Omicron whole-genome sequences from Australia, Austria, Belgium, Botswana, Canada, England, Germany, Hong Kong, Israel, Italy and South Africa. Evidence of recombination was found when sequences from beta, Delta and Omicron were aligned, suggesting that co-circulation of several variants may enhance recombination events.

"An increase in circulation of the virus increases the likelihood of infection of the same individual by different variants, leading to this exchange of genetic material among variants," said Danilo Rosa Nunes, first author of the 2021 article. Nunes is researching for a Ph.D. at EPM-UNIFESP.

The researchers now plan to investigate how blood serum and plasma from vaccinated patients respond to the different variants with the mutations they identified. "We want to use seroneutralization assays to find out whether these individuals are able to neutralize the different variants, including Omicron," Braconi said.

Another possible next step would be to use computational models to try



to predict what each mutation changes in the spike protein and its capacity to invade human cells.

By combining the results of these experiments, the researchers may elucidate the effects of these mutations shared by several variants, so that they can serve as targets for even more effective future vaccines.

As the researchers acknowledge, it is not yet possible to be sure that the vaccines currently available will work against future novel strains of SARS-CoV-2, so it remains essential to maintain social distancing, wear effective face coverings and complete the vaccination course in order to slow the viral evolution process and minimize the risk of novel mutations that favor immune evasion.

**More information:** Robert Andreata-Santos et al, From Alpha to Omicron SARS-CoV-2 variants: What their evolutionary signatures can tell us?, *Journal of Medical Virology* (2022). DOI: 10.1002/jmv.27555

Danilo Rosa Nunes et al, Deep phylogenetic-based clustering analysis uncovers new and shared mutations in SARS-CoV-2 variants as a result of directional and convergent evolution, *medRxiv* (2021). DOI: 10.1101/2021.10.14.21264474

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