Study of coronavirus variants predicts virus evolving to escape current vaccines

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A new study of the U.K. and South Africa variants of SARS-CoV-2 predicts that current vaccines and certain monoclonal antibodies may be less effective at neutralizing these variants and that the new variants raise

the specter that reinfections could be more likely.

The study was published in *Nature* on March 8, 2021. A preprint of the study was first posted to BioRxiv on January 26, 2021.

The study's predictions are now being borne out with the first reported results of the Novavax vaccine, says the study's lead author David Ho, MD. The company reported on Jan. 28 that the vaccine was nearly 90% effective in the company's U.K. trial, but only 49.4% effective in its South Africa trial, where most cases of COVID-19 are caused by the B.1.351 variant.

"Our study and the new clinical trial data show that the virus is traveling in a direction that is causing it to escape from our current vaccines and therapies that are directed against the viral spike," says Ho, the director of the Aaron Diamond AIDS Research Center and the Clyde'56 and Helen Wu Professor of Medicine at Columbia University Vagelos College of Physicians and Surgeons.

"If the rampant spread of the virus continues and more critical mutations accumulate, then we may be condemned to chasing after the evolving SARS-CoV-2 continually, as we have long done for influenza virus," Ho says. "Such considerations require that we stop virus transmission as quickly as is feasible, by redoubling our mitigation measures and by expediting vaccine rollout."

After vaccination, the immune system responds and makes antibodies that can neutralize the virus.

Ho and his team found that antibodies in blood samples taken from people inoculated with the Moderna or Pfizer vaccine were less effective at neutralizing the two variants, B.1.1.7, which emerged last September in England, and B.1.351, which emerged from South Africa in late 2020.

Against the U.K. variant, neutralization dropped by roughly 2-fold, but against the South Africa variant, neutralization dropped by 6.5- to 8.5-fold.

"The approximately 2-fold loss of neutralizing activity against the U.K. variant is unlikely to have an adverse impact due to the large 'cushion' of residual neutralizing antibody activity," Ho says, "and we see that reflected in the Novavax results where the vaccine was 85.6% effective against the U.K. variant."

Data from Ho's study about the loss in neutralizing activity against the South Africa variant are more worrisome.

"The drop in neutralizing activity against the South Africa variant is appreciable, and we're now seeing, based on the Novavax results, that this is causing a reduction in protective efficacy," Ho says.

The new study did not examine the more recent variant found in Brazil (B.1.1.28) but given the similar spike mutations between the Brazil and South Africa variants, Ho says the Brazil variant should behave similarly to the South Africa variant.

"We have to stop the virus from replicating and that means rolling out vaccine faster and sticking to our mitigation measures like masking and physical distancing. Stopping the spread of the virus will stop the development of further mutations," Ho says.

The study also found that certain monoclonal antibodies used now to treat COVID patients may not work against the South Africa variant. And based on results with plasma from COVID patients who were infected earlier in the pandemic, the B.1.351 variant from South Africa has the potential to cause reinfection.

New study contains comprehensive analysis of variants

The new study conducted an extensive analysis of mutations in the two SARS-CoV-2 variants compared to other recent studies, which have reported similar findings.

The new study examined all mutations in the spike protein of the two variants. (Vaccines and monoclonal antibody treatments work by recognizing the SARS-CoV-2 spike protein.)

The researchers created SARS-CoV-2 pseudoviruses (viruses that produce the coronavirus spike protein but cannot cause infection) with the eight mutations found in the U.K. variant and the nine mutations found in the South African variant.

They then measured the sensitivity of these pseudoviruses to monoclonal antibodies developed to treat COVID patients, convalescent serum from patients who were infected earlier in the pandemic, and serum from patients who have been vaccinated with the Moderna or Pfizer vaccine.

Implications for monoclonal antibody treatments

The study measured the neutralizing activity of 18 different monoclonal antibodies—including the antibodies in two products authorized for use in the United States.

Against the U.K. variant, most antibodies were still potent, although the neutralizing activity of two antibodies in development was modestly impaired.

Against the South Africa variant, however, the neutralizing activity of

four antibodies was completely or markedly abolished. Those antibodies include bamlanivimab (LY-CoV555, approved for use in the United States) that was completely inactive against the South Africa variant, and casirivimab, one of the two antibodies in an approved antibody cocktail (REGN-COV) that was 58-fold less effective at neutralizing the South Africa variant compared to the original virus. The second antibody in the cocktail, imdevimab, retained its neutralizing ability, as did the complete cocktail.

"Decisions of the use of these treatments will depend heavily on the local prevalence of the South Africa and Brazil variants," Ho says, "highlighting the importance of viral genomic surveillance and proactive development of next-generation antibody therapeutics."

Reinfection implications

Serum from most patients who had recovered from COVID earlier in the pandemic had 11-fold less neutralizing activity against the South Africa variant and 4-fold less neutralizing activity against the U.K. variant.

"The concern here is that reinfection might be more likely if one is confronted with these variants, particularly the South Africa one," Ho says.

More information: Pengfei Wang et al. Antibody Resistance of SARS-CoV-2 Variants B.1.351 and B.1.1.7, *Nature* (2021). DOI: 10.1038/s41586-021-03398-2

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