「《Nature》Vaccines may be less effective against British and South African variant viruses」

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Each passing week brings more questions about the SARS-CoV-2 variants. One of the biggest questions has been whether the emerging variants will respond differently to neutralizing antibodies made by people who have been infected. This point is important to understand, as it may alter the ability of our current arsenal of therapeutics and vaccines to combat the infection.

Now, new research from Columbia University College suggests that two of the variants, the B.1.351 and B.1.1.7 SARS-CoV-2 variants (first detected in South Africa and the U.K., respectively), show increased resistance to antibody neutralization in laboratory experiments. The findings suggest that current monoclonal antibody therapies and vaccines may be less effective against some variants of the virus and that the new variants raise the specter that reinfections could be more likely.

The study was published in Nature on March 8, 2021. This study assessed the ability of neutralizing virus with 18 monoclonal antibodies, 20 plasma from patients who recovered from COVID-19 and 22 sera from people who have been vaccinated. David Ho, the study's lead author 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 B.1.1.7 variant was resistant to neutralization by monoclonal antibodies that target the N-terminal domain of the spike protein and was relatively resistant to some antibodies that target the receptor-binding domain. In addition to resistance to neutralization by antibodies to the N-terminal domain, the B.1.351 variant was found to be resistant to a group of monoclonal antibodies that is currently used in therapies that target the receptor-binding motif of the spike protein, which was primarily attributed to the E484K mutation. The neutralizing activity of plasma from patients who had recovered from COVID-19 and sera from people who had been vaccinated was reduced by approximately 9- and 10–12-fold, respectively, against this variant. The study's predictions are now being borne out with the first reported results of the Novavax vaccine, says 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.

The study measured 18 different monoclonal antibodies, including 12 antibodies targeting the viral receptor-binding domain (RBD), and 6 antibodies targeting the N-terminal domain (NTD) is the target

antibody. Among the 12 RBD monoclonal antibodies, for the British variant virus, most antibodies were still potent, although the neutralizing activity of two antibodies in development was modestly impaired. However, for the South African variant virus, the neutralizing ability of 5 antibodies has almost completely disappeared, including LY-CoV555 (Lilly's approved antibody for use in the United States). Casirivimab, of Regeneron double antibody cocktail therapy REGN-COV, which is also authorized by the United States, has almost lost its ability to neutralize the South African variant as well. However, the other antibody, imdevimab, still maintains its ability. The cocktail therapy of two complete antibodies is also effective. Moreover, six NTD monoclonal antibodies all revealed poor effects on the British and South African variant viruses.

This study implies that current monoclonal antibody therapy should be adjusted. This study did not include the recent Brazilian B.1.1.28 variant virus, but based on Brazil and South Africa variant viruses have similar spike protein mutations, the researchers believe that the results of the Brazilian variant virus may be similar to the South African variant virus. Decisions of the use of these treatments will depend heavily on the local prevalence of the South Africa and Brazil variants, highlighting the importance of viral genomic surveillance and proactive development of next-generation antibody therapeutics.

Reference:

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