Assessing How SARS-CoV-2 Mutations Might Affect Rapid Tests

Researchers found that today's COVID rapid antigen tests can identify all current variants of concern and interest.

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Since the start of the pandemic, diagnostic testing has played a crucial role in controlling the spread of SARS-CoV-2, the virus that causes COVID-19. Rapid antigen tests, taken at home or in a clinical setting, can provide results in 15 minutes or less. The sooner a person is diagnosed, the sooner they can seek medical care and isolate from others. But when new viral variants appear, the variants may escape detection by these tests.

Most rapid antigen tests are designed to detect the SARS-CoV-2 nucleocapsid protein, or N protein. This protein is abundant in viral particles and infected people. Rapid test kits generally contain two different diagnostic antibodies that bind to different parts of the N protein. When the antibodies bind to the N protein in a sample, the test kit displays a colored line or another signal to indicate infection.

The N protein is made of 419 amino acid building blocks. Any of these could be replaced through mutation by a different amino acid. A research team led by Drs. Filipp Frank and Eric Ortlund at Emory University set out to learn how such single amino acid substitutions could affect the performance of rapid antigen tests. They used a technique called deep mutational scanning to simultaneously evaluate how each mutation to the virus' N protein affected binding to diagnostic antibodies. Their results appeared in Cell on September 15, 2022.

The researchers generated an exhaustive library of nearly 8,000 mutations to the N protein. The variations represent more than 99.5% of all possible mutations. They then assessed each variant's interactions with 17 different diagnostic antibodies that are used in 11 commercially available rapid antigen tests, including common at-home kits.

The team assessed which mutations to the N protein affected antibody recognition. From this information, they created an "escape mutation profile" for each diagnostic antibody. This profile identifies the specific mutations to the N protein that could affect the antibody's ability to bind its target. The analysis showed that the antibodies used in today's rapid tests could recognize and bind to all past and present SARS-CoV-2 variants of concern and interest.

While several diagnostic antibodies recognized the same region of the N protein, the researchers found that each antibody had a unique escape mutation profile. As the SARS-CoV-2 virus continues to mutate and create new variants, this data can be used to flag test-kit antibodies that may need to be re-assessed.

“Accurate and efficient identification of infected individuals remains a critically important strategy for COVID-19 mitigation, and our study provides information about future SARS-CoV-2 mutations that may interfere with detection,” Ortlund says. “The results outlined here can allow us to quickly adapt to the virus as new variants continue to emerge, representing an immediate clinical and public health impact.”

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