Study of 'breakthrough' cases suggests COVID testing may be here to stay

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Teresa Rozza of Rockefeller's Clinical Genomics Lab runs COVID saliva tests for the whole university community. Credit: Matthew Septimus

In rare cases, people who have been fully vaccinated against COVID and are immune to the virus can nevertheless develop the disease. New

findings from The Rockefeller University now suggest that these so-called breakthrough cases may be driven by rapid evolution of the virus, and that ongoing testing of immunized individuals will be important to help mitigate future outbreaks.

The research, published this week in the *New England Journal of Medicine*, reports results from ongoing monitoring within the Rockefeller University community where two fully vaccinated individuals tested positive for the coronavirus. Both had received two doses of either the Moderna or the Pfizer vaccine, with the second dose occurring more than two weeks before the positive test. One person was initially asymptomatic and then developed typical COVID-19 symptoms; the other developed symptoms prior to testing. Both individuals recovered at home, an outcome consistent with evidence suggesting vaccination is effective in preventing severe disease.

Genome sequencing revealed multiple mutations in both viral samples, including the E484K variant in one individual, first identified in South Africa and Brazil, and the S477N variant in the other individual, which has been spreading in New York since November.

"These patients got vaccinated, had great immune responses, and nonetheless broke through with a clinical infection," says Robert B. Darnell, The Robert and Harriet Heilbrunn Professor, who led the research with immunologist Michel C. Nussenzweig, virologist Paul Bieniasz, and geneticist Richard P. Lifton. The researchers were able to discern a quantifiable amount of virus in saliva samples from routine testing ongoing at Rockefeller, and sequence the viral RNA using a new coronavirus testing method developed in Darnell's lab by postdoctoral associate Ezgi Hacisuleyman with help from senior research associate Nathalie Blachere. Since January, the university has required all employees working on-site to be tested weekly using this saliva-based PCR assay.

The observations suggest what is likely a small but ongoing risk among vaccinated individuals, and the possibility that they may continue to spread the virus.

"The idea that we could be entirely done with testing in the post-vaccine world is probably not a good one right now; for example, even fully vaccinated people who develop respiratory symptoms should consider getting tested for COVID-19," says Darnell. "Conversely, exposure to individuals with known infection, even if fully vaccinated, should be taken seriously and again individuals should consider getting tested."

"Given the scope of the pandemic, there's a huge amount of virus in the world right now, meaning a huge opportunity for mutations to develop and spread," he adds. "That is going to be a challenge for the developers of vaccines over the next months and years."

More information: Ezgi Hacisuleyman et al. Vaccine Breakthrough Infections with SARS-CoV-2 Variants, *New England Journal of Medicine* (2021). DOI: 10.1056/NEJMoa2105000

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