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Mechanisms of SARS-CoV-2 Evolution Revealing Vaccine-Resistant Mutations in Europe and America

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Abstract

The importance of understanding SARS-CoV-2 evolution cannot be overlooked. Recent studies confirm that natural selection is the dominating mechanism of SARS-CoV-2 evolution, which favors mutations that strengthen viral infectivity. Here, we demonstrate that vaccine-breakthrough or antibody-resistant mutations provide a new mechanism of viral evolution. Specifically, vaccine-resistant mutation Y449S in the spike (S) protein receptor-binding domain, which occurred in co-mutations Y449S and N501Y, has reduced infectivity compared to that of the original SARS-CoV-2 but can disrupt existing antibodies that neutralize the virus. By tracking the evolutionary trajectories of vaccine-resistant mutations in more than 2.2 million SARS-CoV-2 genomes, we reveal that the occurrence and frequency of vaccine-resistant mutations correlate strongly with the vaccination rates in Europe and America. We anticipate that as a complementary transmission pathway, vaccine-breakthrough or antibody-resistant mutations, like those in Omicron, will become a dominating mechanism of SARS-CoV-2 evolution when most of the world's population is either vaccinated or infected. Our study sheds light on SARS-CoV-2 evolution and transmission and enables the design of the next-generation mutation-proof vaccines and antibody drugs.