CORONAVIRUS

Recurrent deletions in the SARS-CoV-2 spike glycoprotein drive antibody escape

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Zoonotic pandemics, such as that caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), can follow the spillover of animal viruses into highly susceptible human populations. The descendants of these viruses have adapted to the human host and evolved to evade immune pressure. Coronaviruses acquire substitutions more slowly than other RNA viruses. In the spike glycoprotein, we found that recurrent deletions overcome this slow substitution rate. Deletion variants arise in diverse genetic and geographic backgrounds, transmit efficiently, and are present in novel lineages, including those of current global concern. They frequently occupy recurrent deletion regions (RDRs), which map to defined antibody epitopes. Deletions in RDRs confer resistance to neutralizing antibodies. By altering stretches of amino acids, deletions appear to accelerate SARS-CoV-2 antigenic evolution and may, more generally, drive adaptive evolution.

Effect of natural mutations of SARS-CoV-2 on spike structure, conformation, and antigenicity

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SARS-CoV-2 variants with multiple spike mutations enable increased transmission and antibody resistance. Here, we combine cryo-EM, binding and computational analyses to study variant spikes, including one that was involved in transmission between minks and humans, and others that originated and spread in human populations. All variants showed increased ACE2 receptor binding and increased propensity for RBD up states. While adaptation to mink resulted in spike destabilization, the B.1.1.7 (UK) spike balanced stabilizing and destabilizing mutations. A local destabilizing effect of the RBD E484K mutation was implicated in resistance of the B.1.1.28/P.1 (Brazil) and B.1.351 (South Africa) variants to neutralizing antibodies. Our studies revealed allosteric effects of mutations and mechanistic differences that drive either inter-species transmission or escape from antibody neutralization.