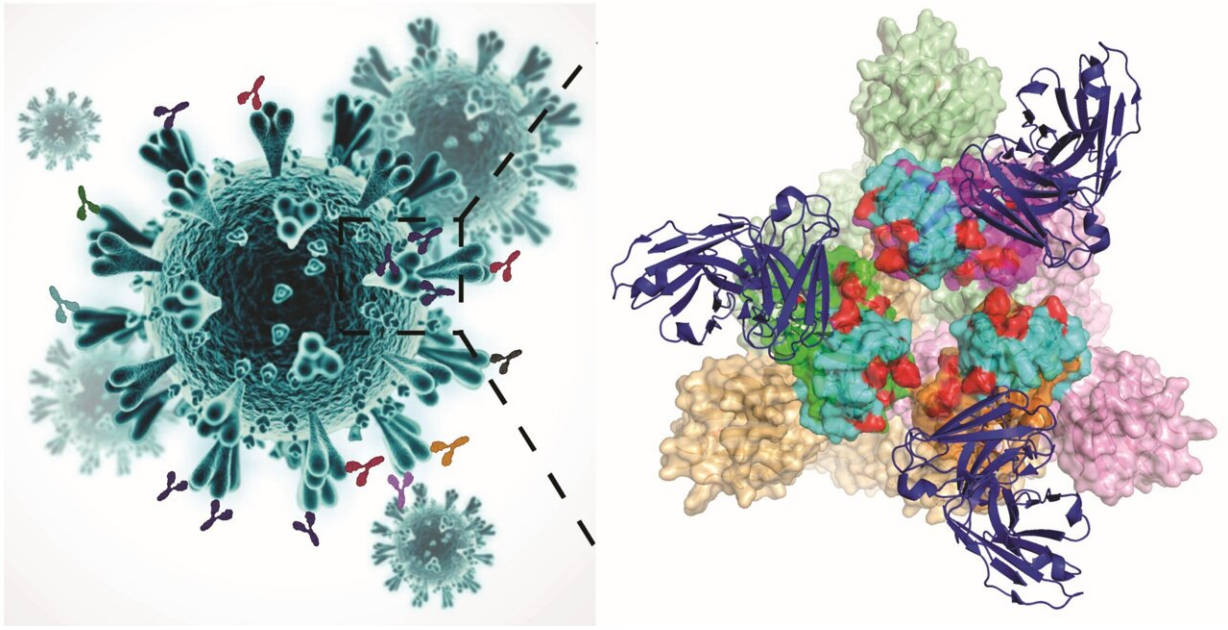
Mutations in SARS-CoV-2 spike protein receptor-binding domains may yield new vaccine-resistant variants

March 1 2022



Monoclonal antibody-mediated neutralization of SARS-CoV-2: The left panel illustrates the morphology of the SARS-CoV-2 virus and displaying the trimeric spike protein on its surface bound with antibodies. The right panel depicts the zoomed view of the trimeric spike protein (top view) in prefusion state bound with monoclonal antibodies. Each monomer of the spike protein shows the receptor binding domain (RBD) in green, orange and magenta, which contains a receptor binding motif in cyan on the top. Mutations emerged in the SARS-CoV-2 Omicron variants are shown in red. Here, the C309 (a parent of VIR-7831 or Sotrovimab) antibody is shown in blue, which is one of the antibodies in clinical use that is minimally impacted by the Omicron variant

mutations. Credit: Piyush Prakash, Anshumali Mittal, Vikash Verma, Arun Khatri (CC BY 4.0, https://creativecommons.org/licenses/by/4.0/)

The SARS-CoV-2 virus is continuously evolving and structural changes to the virus may impact the efficacy of antibody therapies and vaccines. A study published February 17 in *PLOS Pathogens* by Anshumali Mittal at the University of Pittsburgh and colleagues describes the structural and functional landscape of neutralizing antibodies against the SARS-CoV-2 spike protein and discuss the effects of mutations on the virus spike protein that may allow it to evade antibody responses.

All viruses mutate as they evolve, and most mutations have either negative or neutral effects on viral fitness. However, some mutations give viruses a selective advantage, making them more infectious, transmittable, and resistant to antibody responses and therapeutics. To better understand the relationship between immune responses to SARS-CoV-2 virus and how mutations may allow the virus to escape neutralization, researchers conducted a review of the literature, comprising approximately 139 studies. They synthesized research on emerging SARS-CoV-2 variants, described the structural basis of how antibodies may neutralize SARS-CoV-2, and mapped out the spike protein mutations or "escape variants" that resist antibody binding and neutralization.

The researchers summarized the structure-based classification of the spike protein receptor-binding domains (RBD) that target antibodies to better understand the molecular mechanisms of neutralization. They also further described the RBD escape mutations for several antibodies that resist vaccine-elicited and therapeutically relevant antibodies binding. Future studies are needed, however, to better understand how these mutations may affect illness severity and mortality.

According to the authors, "The potency of therapeutic antibodies and vaccines partly depends on how readily the virus can escape neutralization. The SARS-CoV-2 virus will continue to evolve resulting in the emergence of escape variants; therefore, worldwide genomic surveillance, better vaccination drive, development of broadly neutralizing antibodies, and new drugs are vital to combat COVID-19."

Mittal adds, "Structure-based escape maps combined with computational modeling are valuable tools to understand how mutations at each residue affect the binding of an antibody, and can be utilized to facilitate the rational design of escape-resistant antibody therapeutics, vaccines and other countermeasures."

More information: Anshumali Mittal et al, Structural and antigenic variations in the spike protein of emerging SARS-CoV-2 variants, *PLOS Pathogens* (2022). DOI: 10.1371/journal.ppat.1010260

Provided by Public Library of Science