

# The Evolutionary Arms Race Between Antibody-Mediated Immunity And SARS-Cov-2

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The ongoing COVID-19 pandemic has highlighted the need for accelerated research strategies that can keep up with the continued evolution of novel variants. Updated vaccination strategies and widespread breakthrough infections have led to a significant portion of the population developing hybrid immune responses that are better than vaccination or infection alone. Contemporary variants have demonstrated escalating levels of resistance to neutralization by antibodies raised against the original SARS-CoV-2. Here we quantify the hybrid neutralizing antibody responses against current and previous SARS-CoV-2 variants. Vaccination alone provides robust neutralization of wild type SARS-CoV-2 and the early variants, but is insufficient against newer variants (Delta and Omicron). Boosters improve the response to new variants, but the best neutralization is seen with hybrid immunity from breakthrough infection or infection prior to vaccination. As new variants diverge more from wild type SARS-CoV-2, existing vaccines based on the wild type spike protein sequence may not provide sufficient protection. A greater understanding of conserved neutralizing antibody epitopes will be necessary to deciding when this point might come, and further in deciding how to modify the vaccines to address future variants