

Immunity to SARS-CoV-2 induced either through natural infection or vaccination has been shown to afford a degree of protection against reinfection and/or reduce the risk of clinically significant outcomes.

However, the duration of protective immunity is presently unclear, primary immune responses are inevitably waning, and there is ongoing transmission of increasingly concerning viral variants that may escape control by both vaccine-induced and convalescent immune responses.

A defined correlate of protection will permit both confidence in opening economies and facilitate rapid improvements in vaccines and immunotherapies.

Although antiviral T and B cell memory certainly contribute some degree of protection, strong evidence of a protective role for neutralizing serum antibodies exists. We therefore focus on the in vitro virus neutralization titers.

Normalization of responses against a convalescent serum standard has been suggested to provide greater comparability between the results from different assays.

Understanding the relationship between measured immunity and clinical protection from SARS-CoV-2 infection is urgently needed to plan the next steps in the COVID-19 vaccine program. Placebo-controlled vaccine studies are unlikely to be possible in the development of next-generation vaccines, and therefore correlates of immunity will become increasingly important in planning booster doses of vaccine and prioritizing next-generation vaccine development.

Neutralization titer will be an important predictor of vaccine efficacy in the future as new vaccines emerge. This test also predicts that immune protection from infection may wane with time as neutralization levels decline, and that booster immunization may be required within after a period of time.

Our work identifies neutralizing antibodies as an immune correlate of protection and provides a quantitative prediction of the link between neutralizing antibody levels and clinical protection.

This approach utilizes the wide range of immunogenicity and protective efficacy across different vaccines to estimate the 30% protective titer.

data from vaccination and convalescent testing will provide a tool for predicting the uncertain future of SARS-CoV-2 immunity.