COVID-19 Immunity Assessment Test

Simple, Accurate & Reliable

DxTerity

SARS-CoV-2 (COVID-19) Neutralizing Antibody Clinical Data Sheet

1. Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection.

Khoury D.S., Cromer D., Reynaldi A., et al. Nat Med (2021). https://www.nature.com/articles/s41591-021-01377-8

Abstract

Predictive models of immune protection from COVID-19 are urgently needed to identify correlates of protection to assist in the future deployment of vaccines. To address this, we analyzed the relationship between in vitro neutralization levels and the observed protection from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection using data from seven current vaccines and from convalescent cohorts. We estimated the neutralization level for 50% protection against detectable SARS-CoV-2 infection to be 20.2% of the mean convalescent level (95% confidence interval (CI)=14.4– 28.4%). The estimated neutralization level required for 50% protection from severe infection was significantly lower (3% of the mean convalescent level; 95% CI=0.7–13%, P=0.0004). Modeling of the decay of the neutralization titer over the first 250d after immunization predicts that a significant loss in protection from SARS-CoV- 2 infection will occur, although protection from severe disease should be largely retained. Neutralization titers against some SARS-CoV-2 variants of concern are reduced compared with the vaccine strain, and our model predicts the relationship between neutralization and efficacy against viral variants. Here, we show that neutralization level is highly predictive of immune protection, and provide an evidence-based model of SARS-CoV-2 immune protection that will assist in developing vaccine strategies to control the future trajectory of the pandemic.

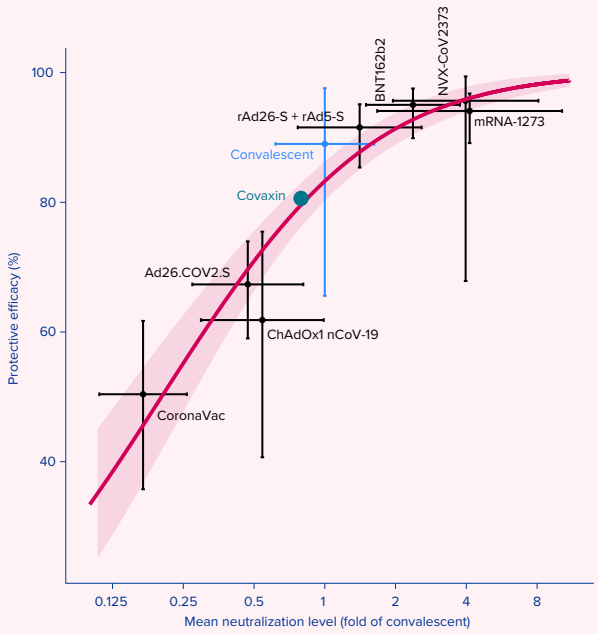
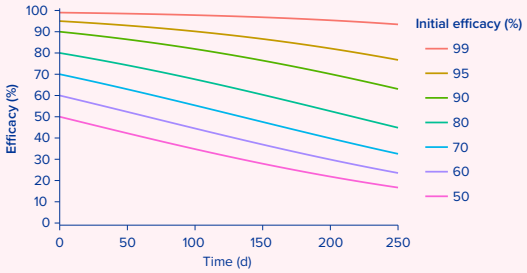
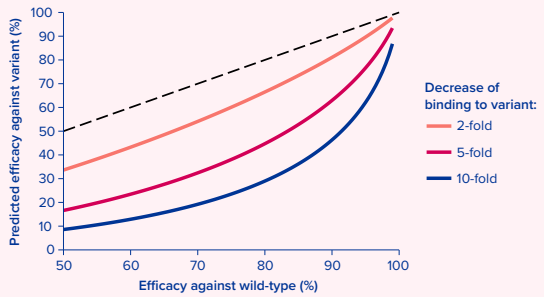


Figure 1: Understanding the relationship between neutralization and protection. a, Relationship between neutralization level and protection from SARS-CoV-2 infection. The reported mean neutralization level from phase 1 and 2 trials and the protective efficacy from phase 3 trials for seven vaccines, as well as the protection observed in a seropositive convalescent cohort, are shown (details of data sources are given in Supplementary Tables 1 and 2). The 95% CIs are indicated as vertical and as horizontal whiskers. The red solid line indicates the best fit of the logistic model and the red shading indicates the 95% predictive interval of the model. The mean neutralization level and protective efficacy of the Covaxin vaccine are indicated as a green circle (data from this study were available only after modeling was complete and did not contribute to fitting).

Figure 2: The effects of waning neutralization titer on protection.



a, Prediction of the effects of declining neutralization titer. Assuming that the observed relationship between neutralization level and protection is consistent over time, we estimate the decline in efficacy for vaccines with different levels of initial efficacy. The model assumes a half-life of the neutralization titer of 108d over the first 250d (as observed in a convalescent cohort5).



c, Estimation of the impact of viral antigenic variation on vaccine efficacy. In vitro studies have shown that neutralization titers against some SARS-CoV-2 variants are reduced compared with titers against wild-type virus. If the relationship between neutralization and protection remains constant, we can predict the difference in protective efficacy against wild-type and variant viruses from the difference in neutralization level. The dashed line indicates equal protection against wild-type and variant strains. Details of the data and modeling are provided in the Methods.

SARS-CoV-2 (COVID-19) Neutralizing Antibody Clinical Data Sheet

2. A SARS-CoV-2 Surrogate Virus Neutralization Test Based on Antibody-Mediated Blockage of ACE2–Spike Protein–Protein Interaction. Tan C.W. et al. A SARS-CoV-2 Surrogate Virus Neutralization Test Based On Antibody-Mediated Blockage of ACE-2-Spike Protein-Protein Interaction. Nat. Biotechnol. 23 July, 2020.

Abstract

A robust serological test to detect neutralizing antibodies to SARS-CoV-2 is urgently needed to determine not only the infection rate, herd immunity and predicted humoral protection, but also vaccine efficacy during clinical trials and after large-scale vaccination. The current gold standard is the conventional virus neutralization test requiring live pathogen and a biosafety level 3 laboratory. Here, we report a SARS-CoV-2 surrogate virus neutralization test that detects total immunodominant neutralizing antibodies targeting the viral spike (S) protein receptor-binding domain in an isotype- and species-independent manner. Our simple and rapid test is based on antibody-mediated blockage of the interaction between the angiotensin-converting enzyme 2 (ACE2) receptor protein and the receptor-binding domain. The test, which has been validated with two cohorts of patients with COVID-19 in two different countries, achieves 99.93% specificity and 95–100% sensitivity, and differentiates antibody responses to several human coronaviruses. The surrogate virus neutralization test does not require biosafety level 3 containment, making it broadly accessible to the wider community for both research and clinical applications.

Summary

In summary, we have addressed the challenge of COVID-19 serology with an approach that enables the detection of NAbs in an easy, safe and rapid manner with enhanced specificity and sensitivity. Although the sVNT assay may never be able to completely replace cVNT, our data indicate that the performance of sVNT is well correlated with that of both cVNT and pVNT. Its application can cover many aspects of COVID-19 investigation from contact tracing, seroprevalence surveying and reservoir/intermediate animal tracking to the assessment of herd immunity and longevity of protective immunity. It can also be used to assess vaccine efficacy during preclinical and clinical trials of different vaccine candidates and to monitor neutralizing titers in vaccinees after mass vaccination in human populations.

Additional References

3. Mann P, Curtis N. Factors that influence the immune response to vaccination. Clin Microbiol Rev. April 2019 Volume 32 Issue 2. 1-50. https://doi.org/10.1128/CMR.00084-18.
4. Achiron A et al, Humoral immune response to COVID_19 mRNA vaccine in patients with multiple sclerosis treated with high-efficacy disease-modifying therapies, Ther Adv Neurol Disord 14:1-8 2021, https://journals.sagepub.com/doi/10.1177/17562864211012835.
5. Deepak D et al, Glucocortoids and B Cell Depleting Agents Substantially Impair Immunogenicity of mRNA Vaccines to SARS-CoV-2, medRxiv preprint doi: https://doi.org/10.1101/2021.04.05.21254656; version posted April 7, 2021.
6. Rice A, Verma M, Shin A, et al. A Next Generation Bivalent Human Ad5 COVID-19 Vaccine Delivering Both Spike and Nucleocapsid Antigens Elicits Th1 Dominant CD4+, CD8+ T-cell and Neutralizing Antibody Responses. bioRxiv. Published online July 30, 2020:2020.07.29.227595. doi:10.1101/2020.07.29.227595.
7. Jeewandara C, Jayathilaka D, Gomes L, et al. SARS-CoV-2 neutralizing antibodies in patients with varying severity of acute COVID-19 illness. Scientific Reports. 2021;11(1):2062. doi:10.1038/s41598-021-81629-2.
8. Toelzer C, Gupta K, Yadav SKN, et al. Free fatty acid binding pocket in the locked structure of SARS-CoV-2 spike protein. Science. 2020;370(6517):725-730. doi:10.1126/science.abd3255.
9. DxTerity White Paper – SARS-CoV-2 Neutralizing Antibody Levels Provide Estimate of COVID-19 Protection Following Vaccination or Infection. 2021.
10. Addetia A, Crawford KHD, Dingens A, et al. Neutralizing Antibodies Correlate with Protection from SARS-CoV-2 in Humans during a Fishery Vessel Outbreak with a High Attack Rate. Journal of Clinical Microbiology. 2020;58(11). doi:10.1128/JCM.02107-20.
11. Tan SS, Saw S, Chew KL, et al. Head-to-head evaluation on diagnostic accuracies of six SARS-CoV-2 serological assays. Pathology. 2020;52(7):770-777. doi:10.1016/j.pathol.2020.09.007.
12. von Rhein C, Scholz T, Henss L, et al. Comparison of potency assays to assess SARS-CoV-2 neutralizing antibody capacity in COVID-19 convalescent plasma. Journal of Virological Methods. 2021;288:114031. doi:10.1016/j.jviromet.2020.114031.
13. J.M. Dan et al, Immunological memory to SARS-CoV-2 assessed for up to 8 months after infection. Science 371, Issue 6529,eabf4063 DOI:10.1126/science.abf4063
14. Rouphael NG, Durability of Responses After SARS-CoV-2 mRNA-1273 Vaccination. N. Engl J. Med. January 7, 2021; Vol. 384 Issue 1.
15. Saadat S et al, Binding and Neutralization Antibody Titers After a Single Vaccine Dose in Health Care Workers Previously Infected With SARS-CoV-2. JAMA April 13, 2021; Vol. 325, Number 14.
16. Ebinger JE et al, Antibody Response to the BNT162b2 mRNA Vaccine in Individuals Previously Infected with SARS-CoV-2. Nat. Medicine, June 2021; Vol. 27, 981-984.
17. Krammer F et al, Antibody Responses in Seropositive Persons After a Single Dose of SARS-CoV-2 mRNA Vaccine. N Engl J Med; April 8, 2021; Vol. 384 Issue 14.