SARS-CoV-2 Surrogate Virus Neutralization Test (sVNT)



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©2 SARS-CoV-2 Surrogate Virus Neutralization Test (sVNT)

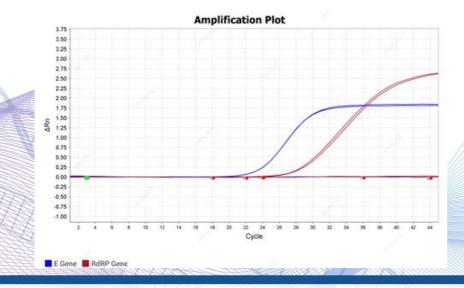
How can Nucleic Acid and Antibody- Based Tests Reduce Disease Period?

Nucleic Acid Test

- Highly sensitive test to detect the presence of the virus itself very early after infection.
- Dependent on sampling the appropriate tissue or fluids to avoid false negatives.
- Reduced disease period by revealing very early infected who can immediately self-quarantine.

Serological Test (Antibody-Based)

- Detects antibodies generated by infected people during their natural immune response.
- Antibody test result could be positive when the nucleic acid result is negative.
- Permits asymptomatic individuals to confirm past infection from which they recovered.
- Reduced disease period by tracking and isolating potentially infected to minimize spread.



Complimentary Tests To Confirm Infection

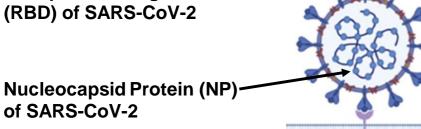




Currently available serological tests - ELISA-based



Receptor Binding Domain





Immune response antibodies (IgG and IgM) to NP from patient sample

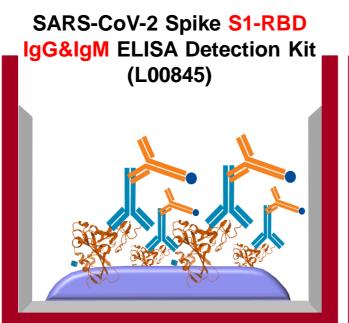


Immune response antibodies (IgG and IgM) to RBD from patient sample

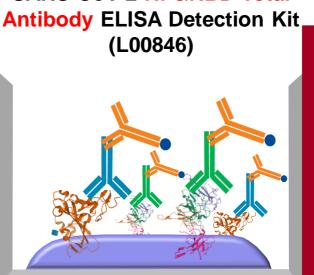


Mouse anti-human IgG or IgM detection antibodies

- ✓ Detects only anti-Spike S1-RBD protein antibodies.
- ✓ IgG and IgM can be detected together or in separate wells.
- Quantitative with standard curve or qualitative
- ✓ Useful for diagnostics, vaccine and drug development



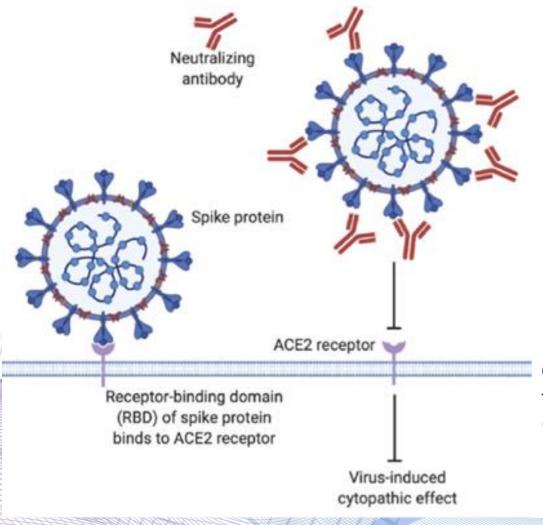
SARS-CoV-2 NP&RBD Total



- Detects anti-Spike S1-RBD and anti-nucleocapsid protein antibodies.
- IgG, IgM and IgA are detected together in each well.
- Qualitative assay.
- Useful for diagnostics, vaccine and drug development.



Neutralization Antibodies (NAbs)



- Block the virus from entering cells.
- Typically generated about 5 to 10 days postinfection and peak about 20 to 30 days.
- Can provide sustained immunity from four to six months (or longer).
- Typically produced from infection (natural immunity) or vaccination.

Chee Wah Tan et al. A SARS-CoV-2 surrogate virus neutralization test (sVNT) based on antibody-mediated blockage of ACE2-spike (RBD) protein-protein interaction; 23 April 2020, PREPRINT (Version 1) available at Research Square



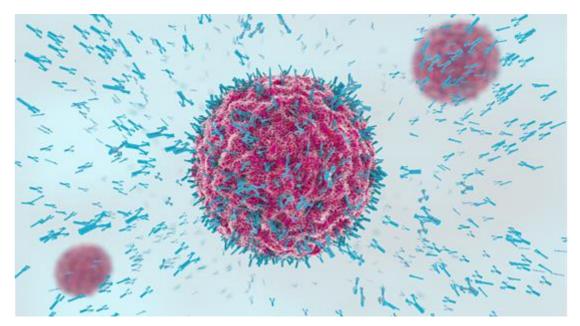
Does infection and recovery necessarily mean immunity?

Different Viruses with Varying Effects

- Varicella-zoster virus (which causes chicken pox), infection confers near-universal, long-lasting immunity.
- Clostridium tetani offers no protection (vaccination requires regular booster shots).
- HIV infection results in large antibody response that does nothing to prevent or clear the disease.

Evidence from SARS Pandemic 2004

- About 15% of 623 patients did not produce neutralizing antibodies (J Infect Dis. 2004 Sep 15;190(6):1119-26.).
- Antibodies persist on average about 2 years post infection (176 patients) (Emerg Infect Dis. 2007;13(10):1562–1564.).





Neutralizing antibody detection of COVID-19 post-infection

Evidence from Humans (medRxiv 2020.03.30.20047365)

- Neutralizing antibodies are detected about 10-15 days postinfection.
- Recognize spike protein S1, S2 and RBD regions.
- SARS-CoV2 NABs are ineffective against SARS-CoV.
- NAb titers varied greatly between young (less) and old (more) patients with 30% giving very low and 10 patients (out of 175) giving undetectable levels of neutralizing antibodies.

Evidence from rhesus macaques (bioRxiv 2020.03.13.990226)

- Rechallenging with the virus in recovered monkeys did not cause reinfection.
- Very small study with only 4 monkeys.



High variability in the production of neutralizing antibodies to COVID-19.

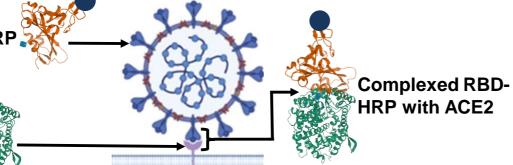
What does this mean?



SARS-CoV-2 Surrogate Virus Neutralization Test (sVNT) - L00847

Receptor Binding Domain of SARS-CoV-2 conjugated to HRP (RBD-HRP)

ACE2 Receptor Protein (ACE2) of Host Cells

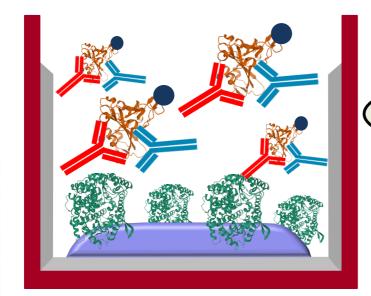




Neutralizing Antibodies from Patient Sample Blocking the Binding of RBD-HRP to ACE2

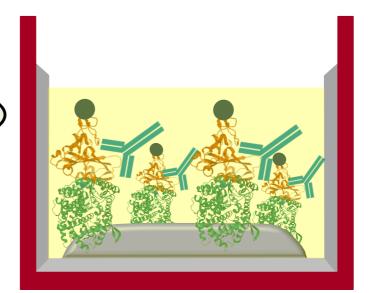


Non-Neutralizing Antibodies from Patient Sample that do NOT Block the Binding of RBD-HRP to ACE2



Species Independent!

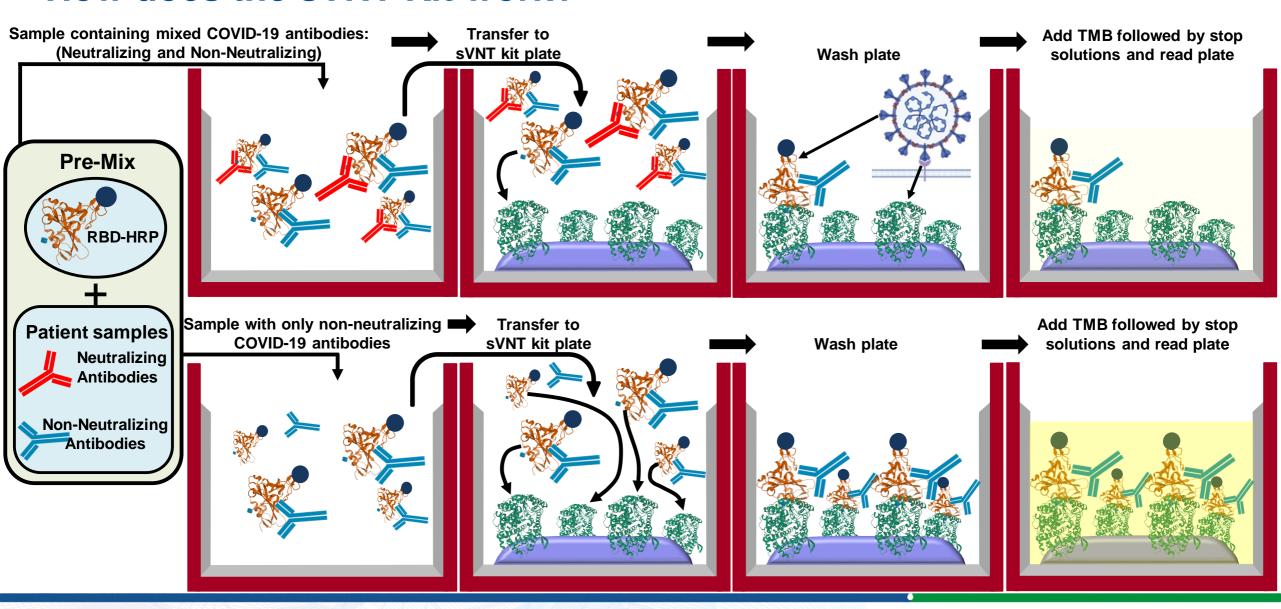
Dr. Lin-Fa Wang Lab



Chee Wah Tan et al. A SARS-CoV-2 surrogate virus neutralization test (sVNT) based on antibody-mediated blockage of ACE2-spike (RBD) protein-protein interaction; 23 April 2020, PREPRINT (Version 1) available at Research Square



How does the sVNT Kit work?





Key Advantages of sVNT vs Pre-Existing Neutralization Ab Tests

GenScript

GenScript

Product

Plasmid

Plasmid

Virus Neutralization Test (VNT)

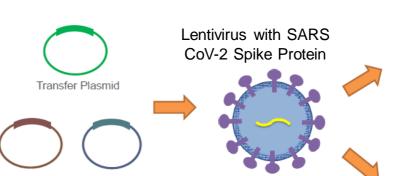
- Live cells and live SARS-CoV-2 virus (DANGEROUS) required.
- Specialized biosafety level 3 (BSL3) containment facility.
- Requires 2-4 days with complex equipment and reagents.

Pseudovirus-based Virus Neutralization Test (pVNT)

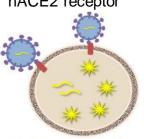
- Live cells and live pseudovirus (SAFER) required.
- Biosafety level 2 (BSL2) lab (much less restrictive).
- Requires 2-4 days with complex equipment and reagents.

SARS-CoV-2 surrogate virus neutralization test (sVNT)

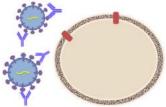
- No cells or live virus required (Basic ELISA Kit).
- Biosafety level 2 (BSL2) lab (much less restrictive).
- Requires 1-2 hours with basic equipment and reagents.
- Species independent (can be used with any organism infected and recovered from SARS-CoV-2 virus).



Host cells expressing hACE2 receptor



Pseudovirus simulates the entry of the SARS-CoV-2



Neutralizing antibodies preventing the pseudovirus from entering host cells

