What is SARS-CoV-2 serological testing and why do we need it?

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ICAP
‘SARS-CoV-2 serological testing: What is it and what does it mean?’
Webinar
May 13th, 2020
What is serology?

• When we get infected with viruses or other pathogens, our B-cells make antibodies to the invading microbe to ‘neutralize it’
• There antibodies can be found in the blood serum, hence the name
Why is serology useful?

• Finding donors for convalescent plasma therapy

• Sero-surveys to determine true infection rates

• Tool to understand dynamics of antibody responses to SARS-CoV-2

• Establish correlates of protection
  • Is somebody protected by the antibody response?
  • Does the antibody response need to reach a certain level to be protective?
The spike protein is the main target of neutralizing antibodies for many coronaviruses.

PBD # 6VXX
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How does this work? – Negative serum:
How does this work? – Positive serum:
Types of tests

Assay with binary result (e.g. lateral flow assay)

- Response
- No response

Result: Can be linked to protection?
Yes or no: A positive result can potentially be loosely associated with protection
Can be used to predict protected period?: No
Scalability: High
Ease of use: Easy to use, even as point of care test

Quantitative assay (e.g. ELISA)

- Titers:
  - Titer 1:12,150: Yes
  - Titer 1:36,450: Yes
  - Titer 1:50: No
  - Titer 1:450: No
  - Titer 1:4050: Yes
  - Negative: No
  - Titer 1:1350: Yes

Protected?: Yes

Quantitative titer: A quantitative titer can be firmly linked to protection
Scalability: Moderate
Ease of use: Can only performed in specialized laboratories
Sensitivity and specificity

• Sensitivity: How many real positives are detected
  • For serology that is often influenced by when sample is taken

• Specificity: How many false positives are detected

• Both should be in the high 90% range
• Only use tests with known performances and at least an FDA EUA
• Different tests are useful for different things
Human serum reactivity in RBD and spike ELISA

Amanat et al., Nat. Med., in press
Spike ELISA endpoint titers correlate well with virus neutralization

Correlation

Spearman $r=0.9279$

$P<0.0001$

Amanat et al., Nat. Med., in press
Mount Sinai Plasma Donors

• >22,000 donors screened by ELISA
  • Mostly mild cases
  • PCR confirmed donors
  • Donors with suspected COVID19 (but without PCR confirmation)

• >250 patients treated with convalescent plasma

• ELISA and PCR results from the ~1350 donors can be found at: https://www.medrxiv.org/content/10.1101/2020.04.30.20085613v1
Proportion of antibody positive donors

PCR-confirmed donors
- Antibody positive (n=568, 99.5%)
- Antibody negative (n=3, 0.5%)

COVID-19-suspected donors
- Antibody positive (n=269, 38.2%)
- Antibody negative (n=436, 61.8%)

Wajnberg et al., under review
Proportion of antibody positive donors

**A**

ELISA titer post symptom onset upon initial donor screen

**B**

Increase in titers of PCR confirmed/Ab low individuals between 1st and 2nd screen

Wajnberg et al., under review
What does this all mean?

• Usually, antibodies are a good thing
• Antibodies protect from (re)infection for most viruses
• Neutralizing antibodies are usually associated with protection from viruses
• We know that antibodies protect from human CoV infections

• We need to now proof that antibodies against SARS-CoV-2 protect from infection
• What titer is protective?
• Important for vaccine development
Acknowledgements

Viviana Simon
Maria Bermudez-Gonzalez
Denise Jurczyszak

Adolfo Garcia-Sastre
Lisa Miorin
Teresa Aydillo

Tom Moran

Ania Wajnberg
(Mount Sinai Hospital)

Katherine Kedzierska (U Melbourne)
Jussi Hepojoki (U Helsinki)
Olli Vapalahti (U Helsinki)

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