Application of a SARS-CoV-2-specific serologic assay for translational research and surveillance

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Introduction

- Sensitive and specific SARS-CoV-2 antibody diagnostics are urgently needed to estimate the seroprevalence of SARS-CoV-2 infection in both the **general population and special risk groups**.
- Validated serologic assays are critical to:
  - **Understand immunity to SARS-CoV-2 infection over time**
  - Identify **correlates of protection**
  - Support **surveillance efforts**
- Although prior studies have described serology dynamics for patients with known COVID-19 disease [1], few have assessed the application of these novel assays for surveillance in a high-risk population or in people with mild illness.

Methods

Validation of an enzyme-linked immunosorbent assay (ELISA) using previously described protocols [2,3].
Assay: Indirect, antigen-coating ELISA to detect IgG antibodies binding to the receptor binding domain (RBD) of the SARS-CoV-2 spike protein (200mg recombinant SARS-CoV-2 RBD).

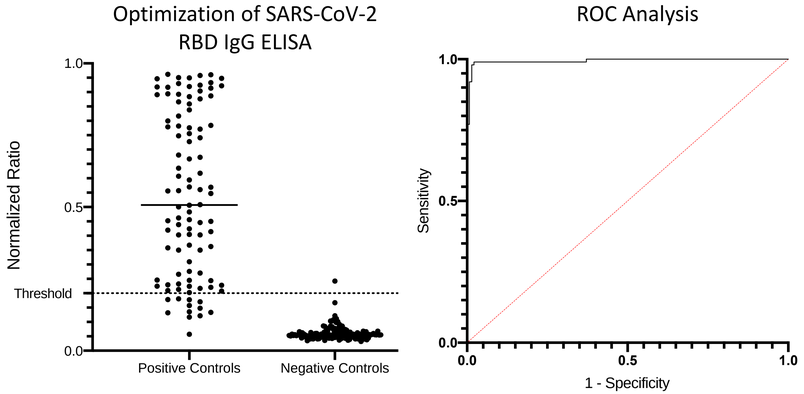
- Positive Controls: RT-PCR confirmed sera (N=100)
- Negative Controls: Pre-pandemic sera (N=140)
- Raw optical density (OD) normalized to absorbance of internal control (OD405 serum/ OD405 CR0322)
- ROC curve analysis performed (Prism GraphPad, v. 8.4.3)

Application of ELISA IgG in two distinct cohorts:

1) Healthcare personnel (HCP) enrolled in a longitudinal surveillance cohort (n=353)
2) Mildly symptomatic patients tested for SARS-CoV-2 in an ambulatory setting (n=37)

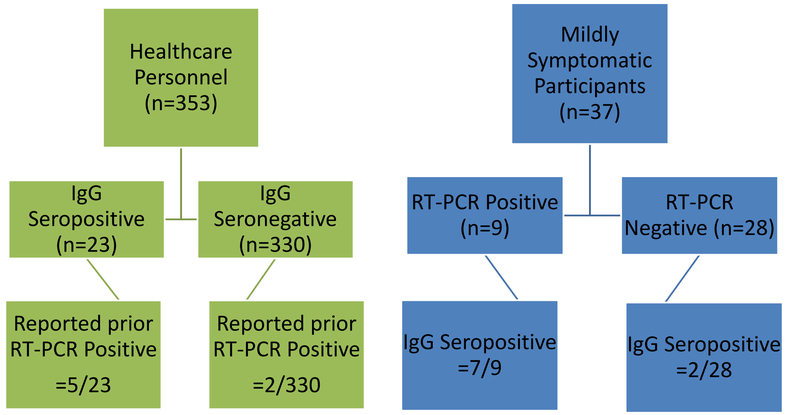
Results:

Validation:



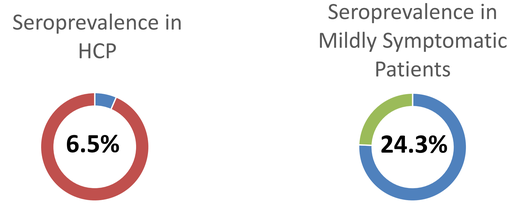
NR Threshold of 0.2
AUC from ROC = 0.9941
Sensitivity = 86%; Specificity = 99.3%

Application:



Summary and Conclusions

- ELISA SARS-CoV-2 RBD IgG assay was validated with high sensitivity and specificity at an OD normalized ratio of 0.2.
- Application in distinct cohorts showed:



- For the mildly symptomatic cohort, RT-PCR and IgG+ was concordant for 7/9 participants.
- This simple ELISA assay is an efficient method to track seroconversion and measure duration of antibody responses to SARS-CoV-2 for different populations.

Future Directions

- Correlation with neutralization activity to determine protective immunity of SARS-CoV-2 RBD IgG.
  - Will be especially useful to assess protection following natural infection or vaccination.
- Evaluation of Ig subtypes to better characterize immune responses.
- Correlation of serologies with saliva and dried blood spot antibody assessments, which would allow for additional testing modalities at a broader scale.

References: [1] Hou, Hongyan, Ting Wang, Bo Zhang, Ying Luo, Lie Mao, Feng Wang, Shiji Wu, and Ziyong Sun. "Detection of IgM and IgG Antibodies in Patients with Coronavirus Disease. 2019." *Clinical & Translational Immunology* 9, no. 5 (May 6, 2020). https://doi.org/10.1002/cti2.1136. [2] Amanat, Fatima, Daniel Stadlbauer, Shirin Strohmeier, Thi H. O. Nguyen, Veronika Chromikova, Meagan McMahon, Kaijun Jiang, et al. "A Serological Assay to Detect SARS-CoV-2 Seroconversion in Humans." *Nature Medicine*, May 12, 2020, 1–4. https://doi.org/10.1038/s41591-020-0913-5. [3] Suthar, Mehul S., Matthew G. Zimmerman, Robert C. Kauffman, Grace Mantus, Susanne L. Linderman, William H. Hudson, Abigail Vanderheiden, et al. "Rapid Generation of Neutralizing Antibody Responses in COVID-19 Patients." *Cell Reports Medicine* 1, no. 3 (June 2020): 100040. https://doi.org/10.1016/j.xcrm.2020.100040.

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