D4P Discussion Guide

Dr. Odaelys Walwyn Pollard presents on the development of a test for COVID-19 immunity

D4P Video: https://bit.ly/2yUjjWO

A serological assay to detect SARS-CoV-2 seroconversion in humans · Fatima Amanat, Thi H.O. Nguyen, Veronika Chromikova, Shirin Strohmeier, Daniel Stadlbauer, Andres Javier, Kaijun Jiang, Guha Asthagiri Arunkumar, Jose Polanco, Maria Bermudez-Gonzalez, Daniel Caplivski, Allen Cheng, Katherine Kedzierska, Olli Vapalahti, Jussi M. Hepojoki, Viviana Simon, and Florian Krammer · medRxiv · March 2020 · PDF · preprint doi: https://doi.org/10.1101/2020.03.17.20037713

In this paper, which was submitted to medRxiv in March 2020, the researchers have developed a potential diagnostic tool for COVID-19. More specifically, they are testing if their tool can be used to learn about how people's immune systems responded to SARS-CoV-2 infection by examining data points with regard to antibodies.

questions for learners	discussion points for educator
1. *Which part of the SARS-CoV-2 virus serves as the model for the creation of the synthetic antigen, and why?*	SARS-CoV-2 has many copies of it's spike protein on its surface. This spike protein contains a receptor binding domain (RBD) that is specific for the ACE2 receptor on human cells. When the SARS-CoV-2 spike protein makes contact with the ACE2 receptor, it initiates endocytosis of the viral particle, allowing for internalization of the virion so the replication of viral building blocks can take place. The researchers of this paper understood that the RBD of coronavirus spike proteins is a target for neutralizing antibodies produced by our immune system. They surmised that if they generated a synthetic version of *only* the spike protein, it could serve as the antigen for their diagnostic test. This is beneficial because it allows for scientists to create the necessary elements for the test *without* needing to work with the whole virus, which also means reduced risk for the people working in the laboratory.
2. *Comparing tests types and their applications* a. *How does the antibody test differ from the genetic test?* b. *What kind of molecules does each test detect?*	The antibody test lets a patient know if they had an immune response to SARS-CoV-2. This diagnostic tool is based on protein biochemistry to detect the presence or absence of antibodies that can recognize the spike protein of SARS-CoV-2. It uses a blood or serum sample as an input. This is because antibodies circulate in our blood stream. If a patient tests positive for the antibody test, it means that they ***had*** COVID-19 in the past, and have since recovered. If used widely, this test can provide insights into immunity levels within a population, and could serve as data to create

c. *What does each result mean for the patient?*	relevant policies, such as how to craft reopening plans. The antibody test differs from the genetic test, which tells a patient if they are *currently* infected with SARS-CoV-2. The genetic test is based on the RNA genome of SARS-CoV-2. It utilizes RT-PCR technology to reverse transcribe viral RNA into DNA, which is then amplified and detected/measured. The genetic test tells a patient if they are *currently* infected with SARS-CoV-2. This test does not measure immunity.
3. *Will "the test" in this paper be able to detect whether or not people were asymptomatic carriers of COVID19? Do they carry antibodies as well?*	To be asymptomatic for COVID19, a person would need to be infected with the live virus and not have any symptoms. The live virus would best be detected by the RT-PCR test, which detects the presence or absence of genetic material from the virus. Asymptomatic carriers who recovered from COVID19 would have antibodies from that infection. Their lack of symptoms could be due to genetic variation(s) that impact the immune response. Thus, the human immunity test (by ELISA) mentioned in this paper will give useful information about whether someone was an asymptomatic carrier.
4. *Why is it important for us to have an antibody test for SARS-CoV-2?*	The antibody test would allow us to understand how many people in the population were infected with SARS-CoV-2, and have recovered from COVID-19. These data would give us a window into *how* the immune system is responding to infection, as well as the rate of infection within a population (including a more precise understanding of the rate of fatality). This test can also identify patients who have had a particularly strong antibody response, which is helpful for developing antibody therapies. Lastly, with wide testing, we can get a sense of what percentage of the population is already immune to COVID-19, providing data-driven insights that are useful for reopening strategies.
5. *Are there different strains of COVID-19? If so, would this have any effect on the antibodies tests being developed?*	While we have seen mutations in the SARS-CoV-2 virus over the duration of this pandemic (allowing scientists to track things like the global spread patterns), this virus mutates extremely slowly. This is largely due to this virus having an error-checking protein encoded in its genome (which would be like your homework coming with its own spell & grammar checker!). While in theory mutations could affect antibody binding, there is not yet evidence of this from the observed mutations.

6. *What do the concepts "specificity" and "sensitivity" mean in this context? Why are these concepts important for the creation of an antibody test?*	"Specificity" means that the antibody test will *only* show positive results for SARS-CoV-2, and not other coronaviruses. By ensuring that this antibody test is specific, it allows for the reduction of false positives (i.e. instances when other coronavirus infections are mistaken for SARS-CoV-2 infection). "*Sensitivity*" describes the ability for the antibody test to detect the presence of antibodies early in infection. A person can start producing antibodies as soon as ~3 days post infection, so sensitivity would allow for early detection, when only small amounts of antibodies are being produced. This would reduce the amount of false negatives (i.e. instances where someone was recently infected but are mistaken to be negative for SARS-CoV-2 infection and antibody production)