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EDITORIAL COMMENTARY

Lack of Severe Acute Respiratory Syndrome Coronavirus 2 Neutralization by Antibodies to Seasonal Coronaviruses: Making Sense of the Coronavirus Disease 2019 Pandemic

Mikyung Lee

Division of Infectious Disease, Department of Medicine, Icahn School of Medicine at Mt. Sinai, New York, New York, USA

When the novel coronavirus, now known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first reported in December 2019 [1], no one could have predicted the rapidity or magnitude of its spread into a full blown global pandemic. Respiratory infections caused by the 4 seasonal human coronaviruses, HCoV-HKU1, HCoV2-NL63, HCoV-229E, and HCoV-OC43, are mild and categorized as the "common cold." The 2 human coronaviruses associated with severe pneumonia, severe acute respiratory syndrome (SARS, caused by SARS-CoV-1) and Middle East respiratory syndrome (MERS, caused by MERS-CoV), resulted in significant outbreaks, but neither came close to the scale of the current pandemic of the 2019 coronavirus, now referred to as coronavirus disease 2019 (COVID-19). The study of a familial cluster of pneumonia from this novel coronavirus in January 2020 [2] revealed features similar to the 2003 SARS outbreak, with evidence of significant person-to-person transmission. The first case in the United States was reported on 20 January 2020 in Washington State [3], and New York City emerged as an epicenter of COVID-19 by April 2020 [4]. As of December 2020, global COVID-19 cases had exceeded 76 million, with more than 17 million cases and more than 300 000 COVID-19 deaths in the United States [5].

In their study, Poston et al noted the wide range of clinical presentations of COVID-19, from being asymptomatic or having mild infection to having severe pneumonia with respiratory or death, and sought to determine if prior infection with a seasonal human coronavirus provides a degree of protective immunity against severe infection from SARS-CoV-2. They used 37 prepandemic serum samples from symptomatic patients confirmed to have seasonal human coronaviruses by polymerase chain reaction (PCR) and 10 positive control COVID-19 serum samples from patients confirmed to have mild, symptomatic SARS-CoV-2 infection by PCR. These serum samples were diluted and mixed with seasonal HCoV-OC43, HCoV-229E, and HCoV-NL63 virus strains and recombinant vesicular stomatitis virus encoding SARS-CoV-2 spike and green fluorescent protein (rVSV/SARS-CoV2/GFP). Of note, strains of the fourth seasonal coronavirus, HCoV-HKU1, were not available for this study. The use of flow cytometry–based neutralization assays provided a concrete measure of the neutralizing activity of the different coronavirus antibodies against each virus strain.

Although the sample size was small and a recombinant virus encoding SARS-CoV-2 spike and green fluorescent protein was used rather than actual SARS-CoV-2 virus, this study's use of flow cytometry to measure infected cells rather than cross-reactivity of neutralizing antibodies strongly suggests that immunity to seasonal coronaviruses does not protect individuals from SARS-CoV-2. This evidence helps explain the rapid spread of the novel coronavirus during a time when the "common cold" due to the endemic human coronaviruses was frequent. Furthermore, the results of this study encourage us to pursue vaccines and therapeutics that specifically target SARS-CoV-2.

Heterologous immunity has been looked at in both animal models and in humans. Poston et al acknowledge that the seasonal endemic human coronaviruses share overlapping T-cell epitopes with SARS-CoV-2 but share only 24%–29% amino acid identity with the SARS-CoV-2 spike (S) protein, suggesting that the S protein plays an important role in COVID-19. Their results also suggest that heterologous immunity will not be as effective in the development of treatments for COVID-19.

The S protein has emerged as the main target of both vaccines and therapeutics for COVID-19 infection. The BNT162b2 that was recently granted emergency use authorization (EUA) by the US Food and Drug Administration (FDA) is a modified RNA virus that targets the SARS-CoV-2 S protein with promising results of 95% efficacy [6]. The FDA also recently granted EUA for bamlanivimab, a monoclonal antibody that binds to the S protein of

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Correspondence: M. Lee, Division of Infectious Disease, Department of Medicine, Icahn School of Medicine at Mount Sinai, One Gustave L. Levy Pl, Box 1090, New York, NY 10029 (mikyung.lee@mssm.edu).

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SARS-CoV-2, and for the combination of casirivimab and imdevimab, both recombinant monoclonal antibodies that bind to different epitopes of the S protein receptor-binding domain. Although these vaccines and monoclonal antibodies were already in development, the work by Poston et al helps us understand why focusing our research efforts on targets specific to SARS-CoV-2 has been more effective than the much broader approach to management taken earlier in the pandemic.

Note

Potential conflicts of interest. The author: No reported conflicts of interest. The author has submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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