

Learning from our immunological history: What can SARS-CoV teach us about SARS-CoV-2?

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Abstract

Many strategies are being deployed to rapidly uncover targetable mechanisms of infection for SARS-CoV-2, and Hoffman *et al.* exploit our understanding and immunological experience with SARS-CoV in our global race to understand, mitigate, and eventually prevent COVID-19.

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The severe acute respiratory syndrome associated coronavirus (SARS-CoV) caused a worldwide epidemic nearly 20 years ago and was contained using public health strategies, without a successful vaccine or targeted therapy. At this time, there are already more than 240,000 confirmed worldwide cases of COVID-19, the disease caused by the related SARS associated coronavirus 2 (SARS-CoV-2). How can we use our historical experience with a related virus to better understand and combat our ongoing pandemic? Hoffman *et al.* assessed whether there are shared patterns of interaction for these viruses with host cells during infection, in order to identify possible strategies to block SARS-CoV-2: specifically, attachment of SARS-CoV to host cells via viral “spike” (S) protein, binding to a host cell membrane enzyme (e.g., angiotensin-converting enzyme 2 (ACE2)), and the priming of the S protein by the host cell proteases (e.g., serine protease TMPRSS2), which leads to the fusion of host and viral membranes and infection.

The general strategy, rather than using infectious virus, is the use of VSV pseudotypes containing S proteins from SARS-CoV (SARS-S) or SARS-CoV-2 (SARS-2-S). First, they showed that, in human cell lines, SARS-S and SARS-2-S facilitated entry into the same cell lines. This led to the question of whether SARS-CoV and SARS-CoV-2 use the same entry strategies. Using a SARS-CoV non-susceptible cell line (BHK-21) they found that

expressing the known SARS-CoV receptor ACE2 (but not the MERS-CoV receptor, DPP4, or other known viral host cell receptors) permitted SARS-2-S or SARS-S driven infection. They were also able to demonstrate in vivo that TMPRSS2 (the serine protease that primes SARS-S protein) can also prime SARS-2-S. Furthermore, blocking the action of this serine protease using camostat mesylate (a serine protease inhibitor) impaired infection of lung cells by SARS-CoV-2. As a final linkage, neutralizing antibodies from convalescent SARS patients impaired both SARS-S and SARS-2-S driven entry (though inhibited SARS-S more effectively), as did sera from rabbits inoculated with SARS-S. This work is limited somewhat by its general focus on SARS-S protein rather than infectious SARS-CoV-2. Nonetheless, it is important in that it uses a better characterized but related virus to identify shared targets for additional testing and validation, as well as providing a backup strategy while the field races to design a vaccine and identify therapeutic targets (ideally with approved agents).

HIGHLIGHTED ARTICLE

M. Hoffmann, H. Kleine-Weber, S. Schroeder, N. Krüger, T. Herrler, S. Erichsen, T. S. Schiergens, G. Herrler, N.-H. Wu, A. Nitsche, M. A. Müller, C. Drosten, S. Pöhlmann, SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. *Cell*, doi:10.1016/j.cell.2020.02.052 (2020).