SYNOPSIS

03/11/2020

Review of “SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor”


One-Minute Summary

- This paper examines how SARS-CoV-2, the virus that causes coronavirus disease 2019 (COVID-19), gains entry into cells and how this process can be blocked.
- Cell entry was assessed using a viral isolate and viral pseudotypes (artificial viruses) expressing the COVID-19 spike (S) protein. The S protein is used by coronaviruses to gain entry into cells.
- The ability of the viral pseudotypes (expressing S protein from SARS-CoV and COVID-19) to enter human and animal cell lines was demonstrated, showing that COVID-19 can enter similar cell lines as SARS-CoV.
- Amino acid analysis and cell culture experiments showed that, like SARS-CoV, COVID-19 S protein binds to human and bat angiotensin-converting enzyme 2 (ACE2) and uses a cellular protease TMPRSS2 for priming. Priming activates the S protein to facilitate viral fusion and entry into cells.
- The authors suggest that TMPRSS2 could be a potential therapeutic target for COVID-19 since entry into cells was reduced by camostat mesylate, a TMPRSS2 inhibitor.
- Sera from three convalescent SARS-CoV patients and rabbit sera raised against SARS-CoV S protein subunit, reduced COVID-19 S protein-mediated entry into cells, suggesting that the antibody response to SARS-CoV may offer some protection against COVID-19.

Additional Information

- This study used viral pseudotypes based on vesicular stomatitis virus (VSV) particles and a COVID-19 isolate Munich 929.
- COVID-19 S protein does not use the same entry receptor as MERS-CoV (human DPP4) or the seasonal coronavirus 229E (human APN).
- Cell culture experiments also showed that COVID-19 S protein can use the endosomal cysteine proteases cathepsin B and L (CatB/L) for priming in cells that do not express TMPRSS2.
- Cell culture experiments were performed using immortalized cell lines and primary human lung cells.
• The TMPRSS2 inhibitor camostat mesylate is approved for human use in Japan for another indication.

PHO Reviewer’s Comments
• None.

Citation
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