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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"

Article citation: Hoffmann M, Kleine-Weber H, Schroeder S, Kruger N, Herrler T, Erichsen S, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor**.** Cell. 2020 Mar 4 [Epub ahead of print]. Available from: https://dx.doi.org/10.1016/j.cell.2020.02.052

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

Ontario Agency for Health Protection and Promotion (Public Health Ontario). Review of "SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor". Toronto, ON: Queen's Printer for Ontario; 2020.

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