Rapid Reviews COVID-19 •

Review 1: "SARS-CoV-2 spike downregulates tetherin to enhance viral spread"

Chin-Tien Wang

Published on: Aug 13, 2021

License: [Creative Commons Attribution 4.0 International License \(CC-BY 4.0\)](https://creativecommons.org/licenses/by/4.0/)

RR:C19 Evidence Scale rating by reviewer:

- **Reliable.** The main study claims are generally justified by its methods and data. The results and conclusions are likely to be similar to the hypothetical ideal study. There are some minor caveats or limitations, but they would/do not change the major claims of the study. The study provides sufficient strength of evidence on its own that its main claims should be considered actionable, with some room for future revision.

Review:

This article shows that SARS-CoV-2 spike (S) protein enhances viral spread through the downregulation of tetherin. Tetherin has been well documented as a host restriction factor capable of impeding the release of several types of enveloped viruses. Overall, the data presented supports the conclusion that the SARS-CoV-2 spike protein is able to promote viral spread by tetherin downregulation.

The authors demonstrated that the SARS-CoV-2 spike protein downregulates tetherin but did not explore how SARS-CoV-2 S mediates the downregulation of tetherin. They show that SARS-CoV-2 ORF7a does not downregulate tetherin but instead induces Golgi fragmentation. It has also been shown that SARS-CoV ORF7a does not downregulate tetherin, but binds to tetherin and interferes with tetherin glycosylation, leading to a loss of tetherin's antiviral function (reference 17). A number of studies have suggested that virus-encoded factors counteract tetherin-mediated restriction of virion release by downregulating tetherin through lysosomal and/or proteasomal degradation pathways. The authors are advised to mention these caveats.