

20 October 2022

Respected Sir/Madam

Reference#: 79117

Title: Circulating Angiotensin Converting Enzyme 2 and COVID-19

I am hereby giving points response to your comments;

Reviewer #1

Comment #1: 1. The aim of this review is to investigate how the presence of SARS-CoV-2 and cACE2 is related and potential therapeutic strategies targeting the ACE/ACE-2 axis. However, the effect of systemic administration of hrsACE2 on clinical outcomes of COVID-19 has not been explained. It is recommended to cite relevant literature and expand relevant discussions in this paper.

Author answer: I already added a relevant discussion as your suggestion (highlighted texts).

Comment #2: Significant digits. The general rule is that no more non-zero digits should be given than are justified by the uncertainty of the value. See "Too many digits: the presentation of numerical data" <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4483789/> If the uncertainty is greater than about 7%, only two non-zero digits are justified. P values should be given to two decimal places unless the first two are 00 or the number lies between 0.045 and 0.054. P values should be adjusted.

Author answer: I already adjusted P value digits as your suggestion.

Reviewer #2

Comment #1: The manuscript devotes a large number of paragraphs to the current findings, it would have been better if it had been simpler.

Author answer: I've already included a paragraph to clarify the potential pathways of hrsACE2 on clinical outcomes in COVID-19 patients. However, before investigating cACE2 in COVID-19 patients, the link of cACE2 with healthy individuals and other disorders needed to be clarified.

Reviewer #3

Comment #1: Thank you very much for submitting this article But unfortunately this manuscript is not well organized at all and does not follow a clear flow. There are no standards for writing mini-review articles. The scattering of unnecessary content is too much. The main focus should be on ACE2 from the point of view of the covid disease. While most of the focus is on ACE2. And even the material presented about ACE2 from the point of view of the covid disease is very irregular and confused and there is no coherence in the presentation of the material. So that the presented content is more like the original articles.

Author answer: Thank you for the comment. The title of this minireview is "Circulating Angiotensin Converting Enzyme 2 and COVID-19" so we should describe the evidences of cACE2 in other diseases to understand the relationship of cACE2 and clinical outcome. After that we reviewed the association of cACE2 and disease severity of COVID-19 patients. Furthermore, we explored the new treatment options such as hrsACE2 to decrease morbidity and mortality.

Language polishing requirement:

Comment #1: Authors are requested to send their revised manuscript to a professional English language editing company or a native English-speaking expert to polish the manuscript further.

When the authors submit the subsequent polished manuscript to us, they must provide a new language certificate along with the manuscript.

Author answer: I already submitted the manuscript to be edited by **TM editing** and already received the English Language Certificate.

Best regards,

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