

Responses to reviewers' comments.

Reviewer 1.

1. Could author review if there are some MSCs used in mechanism research of SARS-CoV-2.

Thank you for your comments. Mechanism research has been considered in the paper.

2. The Ethical Risk of MSCs used in the clinic need to be discussed.

In the same way, the ethical risk of SCs, including MSCs, has been discussed.

Reviewer 2.

1. The manuscript should be revised for linguistic errors.

Thank you for your comments. The manuscript has been revised, and a language editing certificate issued by AJE has been provided.

2. Wrong use of paragraphing is common in this manuscript. Authors may seek the help of a native speaker of English Language.

The paragraphing of the manuscript has been revised, and a language editing certificate issued by AJE has been provided.

3. Also, the presentation of the article should be more attentive. There are disconnections.

The manuscript has been restructured, and some paragraphs have been modified to connect them.

4. Classification of stem cells, especially according to their potency needs to be presented as a figure.

Thank you for your recommendation. A figure showing the classification of SCs according to their origin and potentiality has been included.

5. Clinical trials of exosomes and stem cells need to be presented in a table separately.

We appreciate your comment. Clinical trials of exosomes and stem cells have been presented in a table.

6. Please, double-check the reference list with in-text citations, sometimes not matched.

As the reviewer comments, some citations did not match; these have been checked and corrected.

7. Please tabulate the pros and cons of stem cells in ttt of COVID-19.

The pros and cons of SCs in COVID-19 have been tabulated.

8. For sure exosomes are considered to be safe candidates in comparison with stem cell therapy please discuss this situation.

We appreciate your comment. The safety of exosomes has been discussed.

### Reviewer 3.

The efforts need more inputs as specifically for the possible pathological effects during MSCs application. Also, authors are suggested to find more information about the research articles rather than summarising the information from some existent review articles such as Ref no.2 as mentioned below. Some references with the similar iteration of the documentation in the manuscript are:

1. <https://doi.org/10.1016/j.scr.2020.101859>
2. <https://doi.org/10.1186/s13287-020-01699-3>
3. <https://doi.org/10.1038/s41536-020-00105-z>
4. <https://doi.org/10.1038/s41586-020-2901-9>

Conclusively, the work needs more findings from the covid-19 research before being considered for publication.

Thank you for your comments. The suggested references have been considered in the manuscript. In the same way, more information about the research articles has been added.

- 1) The title “Different kinds of stem cells in the development of SARS-CoV-2 treatments” does not seems to be apt; authors can consider revising it to depict and encompass the entire content of the manuscript.

We appreciate your comment; nevertheless, the title has already been registered in the journal previous invitation.

- 2) In the section “ESCs AND COVID-19 INFECTION MODEL”, it would be better to put a table with a list of existing models of COVID-19, its advantages and disadvantages.

Existing models of COVID-19 have been tabulated in the manuscript.

3) In the section “PSCs AND ORGANOID MODELS FOR SARS-CoV-2”, it would be better to even mention the shortcomings of organoid models. Also, authors need to include more research articles in this section. A few examples:  
<https://doi.org/10.1101/2020.10.17.344002>  
<https://doi.org/10.1016/j.cell.2020.04.004>

We appreciate your comments. Shortcomings of organoid models have been considered in the manuscript, as well as the suggested references.

4) In the section “SCs AND EXOSOMES”, it would be better to mention the underlying mechanism for the functionality of exosomes as a potential vaccine candidate”. A paragraph emphasizing on the potential of SCs-exosomes as a delivery carrier can be added, citing a few references.

The mechanism of exosomes as a potential vaccine has been discussed in the manuscript. Similarly, a paragraph emphasizing the potential of SCs-exosomes as a delivery carrier has been added.

5) In the section “ARTIFICIALLY iPSCs IN COVID-19”, authors should elaborate briefly about the different machine learning models used in the investigation, and their shortcomings. The potential risk of comparing AI-based models and the real experimental models should be emphasized. Following papers may be cited to enrich this part: Authors can demarcate their opinion about prediction and classification-based models with potential application in COVID-19.  
<https://doi.org/10.1016/j.molmed.2020.04.007>  
<https://doi.org/10.2174/1381612826666200515131245> The sub-title “ARTIFICIALLY iPSCs IN COVID-19” does not depict the actual content; authors can consider revising it.

We appreciate your comments. Various machine learning models used in the investigation and its potential risk of comparing AI-based models as well as the real experimental models have been emphasized.

6) The conclusion has been written vaguely; authors can consider to revise it along with addition of FUTURE PERSPECTIVE.

Thank you for your comments. The conclusion has been rewritten considering perspectives.