

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Stem Cells

**Manuscript NO:** 56572

**Title:** Off-the-shelf mesenchymal stem cells from human umbilical cord tissue can significantly improve symptoms in COVID-19 patients: An analysis of evidential relations

**Reviewer's code:** 03478635

**Position:** Peer Reviewer

**Academic degree:** PhD

**Professional title:** Senior Research Fellow

**Reviewer's Country/Territory:** Japan

**Author's Country/Territory:** Viet Nam

**Manuscript submission date:** 2020-05-06

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2020-05-06 23:44

**Reviewer performed review:** 2020-05-08 04:46

**Review time:** 1 Day and 5 Hours

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|---------------------------|---|
| <b>Scientific quality</b> | <input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good<br><input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish            |
| <b>Language quality</b>   | <input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing<br><input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection |
| <b>Conclusion</b>         | <input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority)<br><input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection             |
| <b>Re-review</b>          | <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No   |
| <b>Peer-reviewer</b>      | Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous   |



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statements

Conflicts-of-Interest: [ ] Yes [Y] No

## **SPECIFIC COMMENTS TO AUTHORS**

This is very important to overcome COVID-19 in the world. The immuno-suppression effect of MSCs on COVID-19 inflammation would be one of the candidate treatments, although risk-benefit should be considered carefully. Please check and proofread your manuscript carefully, such as the description for granulocyte-colony stimulating factor (G-CSF).

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**Reviewer's code:** 01368755

**Position:** Peer Reviewer

**Academic degree:** MD, PhD

**Professional title:** Professor

**Reviewer's Country/Territory:** Taiwan

**Author's Country/Territory:** Viet Nam

**Manuscript submission date:** 2020-05-06

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2020-05-06 10:10

**Reviewer performed review:** 2020-05-09 02:02

**Review time:** 2 Days and 15 Hours

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|---------------------------|---|
| <b>Scientific quality</b> | <input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good<br><input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish            |
| <b>Language quality</b>   | <input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing<br><input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection |
| <b>Conclusion</b>         | <input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority)<br><input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection             |
| <b>Re-review</b>          | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No   |
| <b>Peer-reviewer</b>      | Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous   |

**statements**Conflicts-of-Interest: [ ☐ ] Yes [ ☒ ] No**SPECIFIC COMMENTS TO AUTHORS**

General comments: The authors commented on a clinical trial using mesenchymal stem cells (MSCs) to treat COVID-19 patients and discussed the mechanisms of MSCs in this treatment. Minor concerns: 1. The clinical characteristic COVID-19 is variable and the study numbers is small that don't have the power to reveal the efficacy and safety in report from Leng et al. (2020). Please discuss the possible side effects of MSCs treatment in COVID-19. 2. The references 65 and 66 were not completely listed. 65 Van Pham P, Vu NB, Phan NK. Umbilical cord-derived stem cells (modulatisttm) show strong immunomodulation capacity compared to adipose tissue-derived or bone marrow-derived mesenchymal stem cells. Biomed Res Ther 2016; 3: 687-696 [PMID, 66 Kim J-H, Jo CH, Kim H-R, Hwang Y-i. Comparison of immunological characteristics of mesenchymal stem cells from the periodontal ligament, umbilical cord, and adipose tissue. Stem cells international 2018; 2018: [PMID,

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**Name of journal:** World Journal of Stem Cells

**Manuscript NO:** 56572

**Title:** Off-the-shelf mesenchymal stem cells from human umbilical cord tissue can significantly improve symptoms in COVID-19 patients: An analysis of evidential relations

**Reviewer's code:** 03671529

**Position:** Editorial Board

**Academic degree:** MD, PhD

**Professional title:** Assistant Professor, Senior Lecturer

**Reviewer's Country/Territory:** Russia

**Author's Country/Territory:** Viet Nam

**Manuscript submission date:** 2020-05-06

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2020-05-06 14:11

**Reviewer performed review:** 2020-05-10 17:53

**Review time:** 4 Days and 3 Hours

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| <b>Scientific quality</b> | <input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good<br><input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish            |
| <b>Language quality</b>   | <input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing<br><input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection |
| <b>Conclusion</b>         | <input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority)<br><input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection             |
| <b>Re-review</b>          | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No   |
| <b>Peer-reviewer</b>      | Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous   |

**statements**Conflicts-of-Interest: [ ☐ ] Yes [ ☒ ] No**SPECIFIC COMMENTS TO AUTHORS**

In general, the review is well and logically written, there are a lot of fresh articles written in 2020. There is sufficient evidence of the safety and effectiveness of the use of umbilical cord MSCs in the treatment of COVID-19. This article, as well as the small preclinical study cited in it, can serve as the basis for larger studies. There are a couple of small notes: 1) It may be better to decipher the abbreviation ICU. 2) In the beginning, in one paragraph, the authors focus on chloroquine-as a promising drug, without specifying other substances. But the supporting article is only one and 2003. To draw such a conclusion, it would be more correct to survey contemporary studies. Although at the moment, more research is required.

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**Manuscript NO:** 56572

**Title:** Off-the-shelf mesenchymal stem cells from human umbilical cord tissue can significantly improve symptoms in COVID-19 patients: An analysis of evidential relations

**Reviewer's code:** 02540650

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Professor

**Reviewer's Country/Territory:** Egypt

**Author's Country/Territory:** Viet Nam

**Manuscript submission date:** 2020-05-06

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2020-05-12 11:12

**Reviewer performed review:** 2020-05-12 11:42

**Review time:** 1 Hour

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|---------------------------|--|
| <b>Scientific quality</b> | <input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good<br><input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish                                     |
| <b>Language quality</b>   | <input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/><br><input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection |
| <b>Conclusion</b>         | <input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority)<br><input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection                                      |
| <b>Re-review</b>          | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No  |
| <b>Peer-reviewer</b>      | Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous  |



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statements

Conflicts-of-Interest: [ ☐ ] Yes [ ☒ ] No

#### **SPECIFIC COMMENTS TO AUTHORS**

Interesting and innovative idea, some points are needed to be clear: -Why we use umbilical cord, other sources are more convenient?, please mention different sources suitable for this potential line of treatment with focusing on advantages and disadvantages of each source. -There is no any studies results are mentioned only suggested opinion for role of mesenchymal stem cells as an immunomodulatory choice of treatment - Inclusion criteria are cornerstone for possible use of this option of treatment please clarify. -Proper design and language editing is of intense priority



## RE-REVIEW REPORT OF REVISED MANUSCRIPT

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**Position:** Peer Reviewer

**Academic degree:** MD, PhD

**Professional title:** Professor

**Reviewer's Country/Territory:** Taiwan

**Author's Country/Territory:** Viet Nam

**Manuscript submission date:** 2020-05-06

**Reviewer chosen by:** Han Zhang

**Reviewer accepted review:** 2020-07-16 09:16

**Reviewer performed review:** 2020-07-16 09:32

**Review time:** 1 Hour

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|---------------------------------|---|
| <b>Scientific quality</b>       | <input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good<br><input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish            |
| <b>Language quality</b>         | <input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing<br><input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection |
| <b>Conclusion</b>               | <input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority)<br><input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection             |
| <b>Peer-reviewer statements</b> | Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous<br>Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No   |

#### **SPECIFIC COMMENTS TO AUTHORS**

The authors have addressed the concerns.

## RE-REVIEW REPORT OF REVISED MANUSCRIPT

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**Reviewer's Country/Territory:** Japan

**Author's Country/Territory:** Viet Nam

**Manuscript submission date:** 2020-05-06

**Reviewer chosen by:** Han Zhang

**Reviewer accepted review:** 2020-07-16 09:09

**Reviewer performed review:** 2020-07-16 09:49

**Review time:** 1 Hour

|                                 |   |
|---------------------------------|---|
| <b>Scientific quality</b>       | <input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good<br><input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish            |
| <b>Language quality</b>         | <input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing<br><input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection |
| <b>Conclusion</b>               | <input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority)<br><input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection             |
| <b>Peer-reviewer statements</b> | Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous<br>Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No   |

#### **SPECIFIC COMMENTS TO AUTHORS**

The manuscript has been improved.

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**Author's Country/Territory:** Viet Nam

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**Reviewer accepted review:** 2020-07-19 07:11

**Reviewer performed review:** 2020-07-19 07:32

**Review time:** 1 Hour

|                                 |   |
|---------------------------------|---|
| <b>Scientific quality</b>       | <input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good<br><input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish  |
| <b>Language quality</b>         | <input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/><br><input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection |
| <b>Conclusion</b>               | <input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority)<br><input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection   |
| <b>Peer-reviewer statements</b> | Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous<br>Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No   |

#### **SPECIFIC COMMENTS TO AUTHORS**

In this review major corrections are needed: 1. First of all many manuscripts tried mesenchymal stem cells for sever cases of covid-19 infection please correct your pioneer priority in this issue 2. Few data were mentioned about characteristics, method of action, optimum dose, best line of injection of MSC especially in covid-19 infected patients 3. Inclusion criteria of selected patients are not clear enough. 4. Recent clinical trials of use of MSCs in covid-19 treatment were not cited properly. 5. Great dealing of language is mandatory