

PEER-REVIEW REPORT

Name of journal: *World Journal of Biological Chemistry*

Manuscript NO: 73021

Title: Mesenchymal stromal cell delivery as a potential therapeutic strategy against COVID-19: Promising evidence from in vitro results

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06200781

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: Greece

Manuscript submission date: 2021-11-06

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-11-10 01:03

Reviewer performed review: 2021-11-19 13:52

Review time: 9 Days and 12 Hours

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 Grade E: Do not publish |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



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| Peer-reviewer statements | Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No |
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SPECIFIC COMMENTS TO AUTHORS

Mallis P et al present in their current manuscript the mesenchymal stromal cell delivery as a potential therapeutic strategy against COVID-19. The presented study lacks the novelty, pioneering and in-depth molecular investigation levels. At the same time, I think the author lacks the rigor and objectivity of scientific researchers. This article is not for consideration of publication in the World Journal of Stem Cells.

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Title: Mesenchymal stromal cell delivery as a potential therapeutic strategy against COVID-19: Promising evidence from in vitro results

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05630825

Position: Peer Reviewer

Academic degree: PhD

Professional title: Lecturer

Reviewer's Country/Territory: Romania

Author's Country/Territory: Greece

Manuscript submission date: 2021-11-06

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-12-14 04:53

Reviewer performed review: 2021-12-17 12:46

Review time: 3 Days and 7 Hours

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

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| Peer-reviewer statements | Peer-Review: [<input type="checkbox"/>] Anonymous [<input checked="" type="checkbox"/>] Onymous Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No |
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SPECIFIC COMMENTS TO AUTHORS

- The title seems, for me, a little confusing. The contrast between Advances ... and ... Preliminary creates a strange combination, although there are many articles on this topic that can be found by searching on literature databases. The subject is exciting and comprises valuable data regarding COVID-19. Accurate data provided regarding COVID-19 incidence for a specific time are irrelevant in the article's subject development, giving the pandemic evolution and many other factors. Few general remarks are sufficient, and more detailed data can be obtained from dedicated platforms. In the abstract is stated that morbidity is less than 6%. However, in the above paragraph, mortality is indicated at the same level. Therefore, it is necessary to be clarified this aspect. The explanatory link between the characterization of MSCs and their use as a cell therapy for COVID-19 need a more detailed argumentation given the intense attention they receive from many researchers in their articles, as stated above: over 80 clinical trials for COVID-19 and as also sustained by the authors: "interplay between MSCs and hyper-stimulated immune cells in COVID-19 patients has not been satisfactorily explained." "Cytokine storm" is a dominant paradigm in explaining the pathogenesis of SARS-CoV-2 infection. However, it remains unclear to me if MSCs can calm this turbulent immunological imbalance that can deteriorate the internal homeostasis of the patient's body. On this fundament, how are acting these cells, what they are doing and what are their functional limits in reducing or calming the earlier mentioned "Cytokine storm"? It was great to read, understand, and evaluate this high-level, scientifically challenging article with a high-performance experimental design.

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Title: Mesenchymal stromal cell delivery as a potential therapeutic strategy against COVID-19: Promising evidence from in vitro results

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05432496

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: N/A, Research Fellow

Reviewer's Country/Territory: Brazil

Author's Country/Territory: Greece

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Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-12-14 14:43

Reviewer performed review: 2021-12-18 17:27

Review time: 4 Days and 2 Hours

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

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|-------------------------------------|---|
| Peer-reviewer statements | Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No |
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SPECIFIC COMMENTS TO AUTHORS

The manuscript Mallis P et al. entitled "Advances in Mesenchymal Stromal Cell delivery as a potential therapeutic strategy against COVID-19: Preliminary evidence from in vitro results" is well-written, with proper methods and interesting results. Although the authors highlighted that this is a preliminary finding, and the potential for the anti-inflammatory effects, and prevention the overactivation of the immune responses by Mesenchymal Stromal Cell in COVID-19, the authors should explore more the possible implications of this findings to the treatments of SARS-CoV-2-infected individuals. The authors should discuss more the importance of this treatment, delivery routes of treatment, or the treatment should be performed in vitro and cells transferred to the sick person, etc.