



PEER-REVIEW REPORT

Name of journal: *World Journal of Stem Cells*

Manuscript NO: 67215

Title: Strategies to Improve Regenerative Potential of Mesenchymal Stem Cells

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03811591

Position: Peer Reviewer

Academic degree: BSc, PhD

Professional title: Research Associate

Reviewer's Country/Territory: Canada

Author's Country/Territory: Pakistan

Manuscript submission date: 2021-04-18

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-06-26 18:13

Reviewer performed review: 2021-07-04 02:37

Review time: 7 Days and 8 Hours

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 Grade E: Do not publish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 type="checkbox"/> Grade A: Priority publishing <input checked="" 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 type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



statements

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

SPECIFIC COMMENTS TO AUTHORS

This manuscript reviews the strategies to improve regenerative potential of mesenchymal stem cells (MSCs). The author first discusses the negative impact of advanced age, diseases, and long-term in vitro expansion on functionalities of MSCs. The author then reviews 4 strategies (hypoxia, heat shock, caloric restriction, and preconditioning with different growth factors and cytokines) that could be used to improve the compromised MSC function for maximizing the therapeutic effects of MSCs. Overall, the manuscript is well-written. However, there are several comments that the author needs to address.

1. This manuscript focuses on MSCs only. I would suggest the author to change the title to "Strategies to Improve Regenerative Potential of Mesenchymal Stem Cells".
2. The author should discuss the novelty of this review in the last paragraph of introduction.
3. There are a few typo errors. For example, hash (page 8) and stemeness (page 9).
4. Page 8: Please remove "is a potent signaling molecule whose".
5. The following word and symbols should be revised.
 - i. Page 12: Change "effect" to "affect".
 - ii. Page 12: Remove "-" from 32 °C and 41 °C.
 - iii. Pages 12-14: Change "C" to "°C".
 - iv. Page 13: Change "+" to "±".
6. Page 13: The author should add "compared to non-treated cells" after "applied".
7. Page 13: Please remove "In this study, the percentage viability as determined by the trypan blue exclusion assay as well as flow cytometry using 7-AAD/Annexin V was significantly higher at different passages".
8. Page 15: Please specify the chemotherapy induced model.
9. Page 18: Please discuss the challenges of preconditioning MSCs with different growth factors and cytokines for enhancing regenerative potential of MSCs.
10. Page 18-20: Please provide the glucose concentration used by each study.
11. Page 20: Please suggest a range of glucose concentration that could be used to improve regenerative potential of



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MSCs. 12. Page 20: Please discuss the challenges of enhancing regenerative potential of MSCs with a caloric restriction strategy. 13. Page 20: Please add “ROS” after “induced”. 14. The following relevant works should be cited and discussed. i. Biosafety and bioefficacy assessment of human mesenchymal stem cells: what do we know so far (2018) *Regenerative Medicine* 13(2): 219-232. ii. A revealing review of mesenchymal stem cells therapy, clinical perspectives and modification strategies (2019) *Stem Cell Investigation* 6: 34. iii. Understanding and leveraging cell metabolism to enhance mesenchymal stem cell transplantation survival in tissue engineering and regenerative medicine applications (2020) *Stem Cells* 38(1): 22-33.



RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Stem Cells*

Manuscript NO: 67215

Title: Strategies to Improve Regenerative Potential of Mesenchymal Stem Cells

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Peer-review model: Single blind

Reviewer's code: 03811591

Position: Peer Reviewer

Academic degree: BSc, PhD

Professional title: Research Associate

Reviewer's Country/Territory: Canada

Author's Country/Territory: Pakistan

Manuscript submission date: 2021-04-18

Reviewer chosen by: Jia-Ru Fan

Reviewer accepted review: 2021-11-11 20:36

Reviewer performed review: 2021-11-11 20:51

Review time: 1 Hour

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
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 quality of the manuscript has been greatly improved. I have no further comment.