

Manuscript ID: 77709

Title: Strategies to Improve the Effect of Mesenchymal Stem Cell Therapy on
Inflammatory Bowel Disease

Dear reviewer:

We deeply appreciate your constructive comments on our manuscript. According with your advice, we amended the relevant part in manuscript.

Here below is our description on revision according to your comments.

Reviewer #1 Comments

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: This paper is well written focused to stem cell therapy for inflammatory bowel disease. With only one minor concern, it is considered that more studies on the conditioned medium or exosome derived from MSC should be added.

Answer: Thank you for the comment. We agree with the reviewer and as suggested have added the supplement to the studies of exosomes on page 9. In addition, we added the studies of conditioned medium from MSC in the part of modification of the culture medium.

Reviewer # 2 Comments

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: This is compressive review. I suggest you, to explain MSCs and all source of this cells in separate paragraph.

Answer: Thank you for the comment. When we introduce mesenchymal stem cells and their derivatives, we introduce mesenchymal stem cells and other sources of mesenchymal stem cells in a separate paragraph, such as bone marrow, fat, umbilical cord, dental pulp, etc., and also summarize the advantages, disadvantages and applications of these different sources of cells.

Reviewer # 3 Comments

Scientific Quality: Grade A (Excellent)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: This manuscript is very interesting, showing Effect of Mesenchymal Stem Cell Therapy Improve Inflammatory Bowel Disease. The manuscript has no defect.

Answer: Thank you for the comment. We appreciate it.

Reviewer # 4 Comments

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: I would like to congratulate the authors for this manuscript. It is interesting and can bring new perspective. I have some comments: Please check for grammatical errors and mistyped words. Page 18 line 11: should be basic fibroblast growth factor (b-FGF), provide the long form before abbreviation. Page 18 line 19, 20, 24: deadapted or deconditioned hUCMSCs (De-hUCMSCs) please use accordingly. Page 20 line 1: a more obvious... Page 20 line 19: BMMSCs chemotaxis, to... Please replace Discussion and Summary into Conclusion, and provide your own conclusion (no citation) as this is the conclusion of your review. Please check the abbreviations provided in the abbreviations section for any mistakes.

Answer: Thank you for the comment. We checked the word and grammatical errors in the review and corrected the application of abbreviations such as basic fibroblast growth factor (b-FGF), deadapted or conditioned hUCMSCs (De-hUCMSCs) in the part of modification of the culture medium. At the end of review, we replaced the discussion and summary with conclusions, summarized some methods and strategies to enhance the effect of mesenchymal stem cells in the treatment of colitis, and also expressed our expectations for its follow-up development.

Reviewer # 5 Comments

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: The manuscript entitled "Strategies to Improve the Effect of Mesenchymal Stem Cell (MSC) Therapy on Inflammatory Bowel Disease (IBD)" and authored by Shi et al discussed some potential mechanisms of MSCs in the treatment of IBD, summarized the experimental results, then provided new insights to enhance the therapeutic effects of MSCs

in future applications. The following studies where different biomolecules serve as potent anti-inflammatory agents in different model systems should be considered for integration in this manuscript: PMID: 33338743, PMID: 32837538, PMID: 21258076, <https://doi.org/10.3844/ajptsp.2006.21.25>, PMID: 32460808, PMID: 33782460, PMID: 34202689, PMID: 33255507, <https://doi.org/10.1186/s41936-020-00177-9>, PMID: 34639131, PMID: 26034352, PMID: 32837538, <https://doi.org/10.1039/D1NA00475A>, PMID: 34662244. One major setback is the fact that it is not clear what time range of publication did this review article cover, what keywords did the search for literature include, what were the inclusion criteria, how many studies did the search find and how many were primary research vs review articles, of those how many were selected for evaluation in this study, and finally what criteria were used for selecting the articles that were reviewed (was it the subject of the study, its novelty or both). Other comments 1. English editing is required. 2. Some of the following studies/patents may prove useful and would enrich the discussion: US Patent 20210015835, US patent 20200276133, US patent 20200276133, PMID: 29959408.

Answer: Thank you for the comment. By consulting the relevant materials and literatures provided by you, we finally cited 33255507 and 33338743 to enrich the anti-inflammatory content we introduced in this article. In addition, we supplemented the search strategy on page 4. We conducted a comprehensive literature search on the following databases: Pubmed, Google Scholar, SpiScholar, free text words and database-specific index terms were combined with Boolean operators (“AND” and “OR”) to improve the sensitivity of our search. We searched some keywords, the identified studies were not constrained by publication language, or publication status. Most of the publications are published in the last five years, but there are also some classical studies cited.

Revision reviewer 5 Comments

The revised manuscript is much improved and ready to move forward.

Answer: Thanks for your comments.

Science Editor

The manuscript has been peer-reviewed, and it's ready for the first decision.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade C (Good)

Answer: Thank you for the comment.

Company Editor-in-Chief

I have reviewed the Peer-Review Report, the full text of the manuscript, the relevant ethics documents, and the English Language Certificate, all of which

have met the basic publishing requirements of the World Journal of Stem Cells, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. However, the quality of the English language of the manuscript does not meet the requirements of the journal. Before final acceptance, the author(s) must provide the English Language Certificate issued by a professional English language editing company. Please visit the following website for the professional English language editing companies we recommend: <https://www.wjgnet.com/bpg/gerinfo/240>. Before final acceptance, uniform presentation should be used for figures showing the same or similar contents; for example, "Figure 1 Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...". Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file. Please authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

Answer: Authors would like to thank Editor-in-Chief for conditional acceptance of the manuscript. As the English language editing service includes unlimited free re-editing, our manuscript has been re-edited by AJE (American Journal Experts), carefully re-edited to remove any English language errors. We have provided point-by-point response to the concerns raised by all learned reviewers. We have provided a standard three-line tables, all the figures are original and as per the suggestion, we have added "Copyright ©The Author(s) 2022" in the ppt.

Thank you and best regards!

Yours sincerely,

Mengyue Shi