

Editor-in-Chief, Li Ma,
World Journal of Stem Cells

February 17, 2023

Re: Manuscript NO.: 83200, Review entitled " *Cell transplantation therapies for spinal cord injury using bone marrow mesenchymal stem cells: advances and challenges* "

Dear Editor and Reviewers:

We are submitting our revised manuscript entitled "*Cell transplantation therapies for spinal cord injury using bone marrow mesenchymal stem cells: advances and challenges*" by Huang et al. to *World Journal of Stem Cells*. We thank you for your helpful comments and suggestions and have addressed them as outlined below and revised the manuscript accordingly. We uploaded revised manuscript that mark the new text added with RED highlight. We hope that the manuscript is ready to be published in *World Journal of Stem Cells*.

Reviewer #1: The manuscript by Huang et al. dedicated to the role of bone marrow derived mesenchymal stem cells (BMMSCs) in spinal cord regeneration, discussed the underlying mechanisms, prospects, and challenges of BMMSCs in spinal cord injury (SCI) therapy. The manuscript is interesting, and its data is actual and potentially can shed new light on the strategies for using MSCs in the field of regenerative medicine for SCIs. However, the manuscript needs some revision and I recommend extend some chapters. In summary, these above and subsequent major (marked as numbers) and minor (marked as letters) revisions are needed before it meets the publication criteria.

1. On what is the choice of discussing particular BMMSCs based? You claim that «...BMMSCs have low immunogenicity, easy isolation and few ethical concerns as well as reduced tumorigenesis risks». But at the same time, there is evidence (Mukhamedshina et al., 2019, doi: 10.3390/biom9120811) that MSCs obtained from adipose tissue are more accessible and have a better regenerative potential compared to

MSCs obtained from bone marrow and dental pulp. I'm not saying you're wrong, I just think it needs to be discussed in the last chapter.

Response:

We have added the reasons why BMMSCs were chosen for review. BMMSCs are the most widely studied cell type in the spinal cord injury field. According to the current research progress at home and abroad, BMMSCs-based treatment has an extraordinary prospect in the field of spinal cord injury. Our research group has also been engaged in the study of the therapeutic effect and mechanism of BMMSCs combined with other treatments on spinal cord injury for a long time. This is why we chose BMMSCs for our review. Thank you for your reminder.

2. Bibliography should be expanded. Some key publish are missed, such as: doi: 10.3390/biom9120811 doi: 10.4103/1673-5374.244778 doi: 10.3390/biology11121853 a) Missing page numbering b) Latin designations should be in italics, for example, in situ c) "Olig 2" should be without spacing – Olig2 d) FE@EVs in chapter "Axon growth" – I didn't understand what is it.

Response:

We have added the bibliography (ref 10, ref 11 and ref 19) as your suggestion; added page number; corrected 'in situ' in italics in page 7, deleted spacing of Olig 2 (Olig2) in page 8; FE@EVs is the abbreviation of F127-polycitrate-polyethyleneimine hydrogel (FE) with sustainable and long-term extracellular vesicle release. Thank you for your critique.

Reviewer #2: I commend the authors effort for an extensive literature search and thorough review on the topic.

Response:

Thank you very much.

Reviewer #3: Well written manuscript.

1. Add a note on neurogenic signaling mechanisms.

Response:

according to your suggestion, we added a detailed note on neurogenic signaling mechanisms (page 5). Thank you for your critique.

2. Highlight on small molecules involved in neurogenesis.

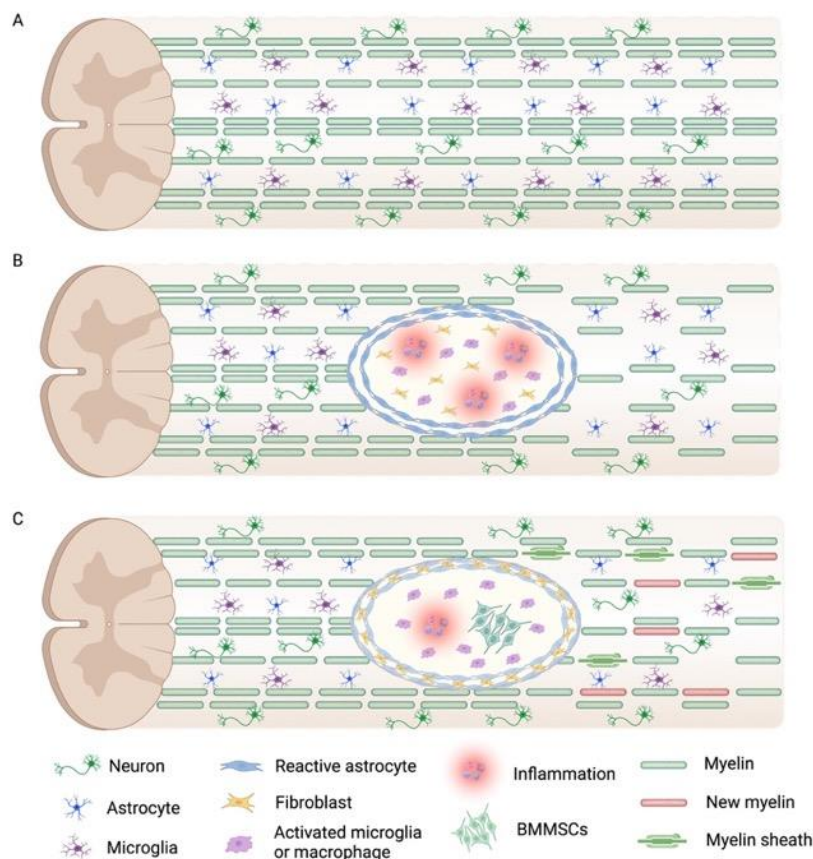
Response:

We have added some small molecules involved in neurogenesis including Gasdermin D (GSDMD), Nod1 inflammasome, cannabinoid receptor 1 (Cnr1), Rap1 (page 5). Thank you for your reminder.

3. Add immunomodulation image.

Response:

We have added immunomodulation image in the figure 1. Thank you for your critique.



4. Limit number of references to 120 with major references on the publications

within last 5 years from 2017 to 2022.

Response:

We have deleted some references published before 2017. We also have retained some of the earlier literature because it provides the original theory and is important to the field. Thank you for your reminder.

Your sincerely,

Quan Wei, M.D., Ph.D.

Professor, Vice-Chairman

Rehabilitation Medicine Center and Institute of Rehabilitation Medicine,

West China Hospital/West China School of Medicine,

Key Laboratory of Rehabilitation Medicine in Sichuan Province,

Sichuan University, Chengdu, China

Email: weiquan@scu.edu.cn