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World Journal of Stem Cells, Editorial Office
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Re: MS ID (03837092) or MS NO: 57971

Date: Nov 4, 2020

Dear Dr. Ma:

Thank you very much for your constructive suggestions regarding our manuscript referenced above entitled “Stem cell transplantation and/or adenoviral GDNF promoted functional recovery in hemiparkinsonian rats” ” by Tsai et al. The attached manuscript (one with my changes blocked in gray) has been revised according to the suggestions made by the reviewers. Specifically,

1. We added “author contribution” in the end of main text.
2. We add project proposal in the end of Introduction
3. We incorporate 8 references as reviewer’s suggestion
4. We add ethical numbers of IRB and animal studies in Method
5. We replace Figures 1-5 with higher resolution images

Outline of our responses to each point raised by the referee is listed in the following pages. Once again, thank you very much and we look forward to hearing from you soon!

Best wishes,

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Reviewer 1: Comments and Suggestions for Authors

1) The hypothesis of this study must be added at the end of the “Introduction section”.

Answer: We have added the hypothesis of this study in Page 4 last paragraph of Introduction.

2) The ethical code must be added in the text of the manuscript.

Answer: We have added IRB number (VGHIRB 95-07-23A) for human MSC in Page? Lines? We also added Institutional animal care and use committee statement number (IACUC 98-061)

3&4) Whole part of “Methods section” must be referred with related references. The identification and characterization method of isolated mesenchymal stem cells must be mentioned in detail in the “Methods section”. You can use and refer the following papers which explained elaborately and completely the “flow cytometric analysis and multi-lineage differentiation method for characterization of mesenchymal stem cells”:

Immunophenotypic characterization, multi-lineage differentiation and aging of zebrafish heart and liver tissue-derived mesenchymal stem cells as a novel approach in stem cell-based therapy. *Tissue and Cell*. 2019 Apr 1;57: 15-21. Interleukin-6, -8, and TGF- β Secreted from Mesenchymal Stem Cells Show Functional Role in Reduction of Telomerase Activity of Leukemia Cell Via Wnt5a/ β -Catenin and P53 Pathways. *Advanced Pharmaceutical Bulletin*. 2020 Jun;10(2):307.

Answer: Thank you very much for your constructive suggestions. We have included the preparation and characterization for hMSC in Method sections with the newly added references, including the reviewer’s suggested ones.

5) The co-culture method was explained elaborately in reference appears bellow, you can use and refer it: Interleukin-6, -8, and TGF- β Secreted from Mesenchymal Stem Cells Show Functional Role in Reduction of Telomerase Activity of Leukemia Cell Via Wnt5a/ β -Catenin and P53 Pathways. *Advanced Pharmaceutical Bulletin*. 2020 Jun;10(2):307.

Answer: We have included this reference for coculture study in Method.

6) Since the discussion section is one of the most important parts of the paper, this section must be improved with more attention and explanation. In the discussion section, results must be compared with another results from previous studies. Also, you can discuss the signaling pathways related to neurodegenerative disease. In this regard, you can use the following paper which demonstrated the role of mesenchymal stem cell as a Candidate for further studies in cell-based therapy of Alzheimer’s

disease via signaling pathways: Mesenchymal Stem Cells Could Be Considered as a Candidate for Further Studies in Cell-Based Therapy of Alzheimer's Disease via Targeting the Signaling Pathways. ACS Chemical Neuroscience. 2020 Apr 20;11(10):1424-35. 7) The number of references are limited. Please extend them.

Answer: Thank you very much for your constructive suggestion. We compared our results with others in the Discussion. Furthermore, we added molecular mechanism of PD in the third paragraphs of Discussion section. In addition, we include more references in Discussion section.