

PEER-REVIEW REPORT

Name of journal: *World Journal of Stem Cells*

Manuscript NO: 88018

Title: ADSC-Exos outperform BMSC-Exos in alleviating hydrostatic pressure-induced injury to retinal ganglion cells by upregulating nerve growth factors

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02728252

Position: Editorial Board

Academic degree: PhD

Professional title: Professor

Reviewer's Country/Territory: Egypt

Author's Country/Territory: China

Manuscript submission date: 2023-09-06

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-09-09 12:10

Reviewer performed review: 2023-09-14 09:35

Review time: 4 Days and 21 Hours

Scientific quality	☐ Grade A: Excellent ☒ Grade B: Very good ☐ Grade C: Good ☐ Grade D: Fair ☐ Grade E: Do not publish
Novelty of this manuscript	☐ Grade A: Excellent ☒ Grade B: Good ☐ Grade C: Fair ☐ Grade D: No novelty
Creativity or innovation of this manuscript	☐ Grade A: Excellent ☒ Grade B: Good ☐ Grade C: Fair ☐ Grade D: No creativity or innovation

Scientific significance of the conclusion in this manuscript	☐ Grade A: Excellent ☒ Grade B: Good ☐ Grade C: Fair ☐ Grade D: No scientific significance
Language quality	☐ Grade A: Priority publishing ☐ Grade B: Minor language polishing ☒ Grade C: A great deal of language polishing ☐ Grade D: Rejection
Conclusion	☐ Accept (High priority) ☐ Accept (General priority) ☐ Minor revision ☒ Major revision ☐ Rejection
Re-review	☒ Yes ☐ No
Peer-reviewer statements	Peer-Review: ☒ Anonymous ☐ Onymous
	Conflicts-of-Interest: ☐ Yes ☒ No

SPECIFIC COMMENTS TO AUTHORS

1. This is a comparative study evaluating the effect bone marrow stem cell-derived exosomes and adipose stem cell-derived exosomes on retinal ganglion cell exposed to pressure injury (40, 80, and 120 mmHg), please consider these information in the title. 2. The title, aim and conclusion should be consistent, regarding hypothesis (null or alternative). 3. The method of obtaining BMSCs should be clearly described and referenced. 4. The concentration of exosomes were 20 $\mu\text{g/mL}$, depending on what? 5. Pancreatic enzyme, whish one was used, please specify. 6. Method of characterization of stem cells is not sufficient, positive and negative markers should be provided. 7. Exosome marker molecules CD9, CD63, and CD81, which one is positive and which one is negative. 8. Please report the significance of using TEM in the characterization of the stem cells (morphology/structure) and their derived exosomes (size). 9. The abbreviation NC referred to normal control or what? 10. Quantification and the purity of the exosomes should be considered in the methodology. 11. Figure 3 report the results of CREB and pCREB not β III-tubulin. 12. Figure 5 report the results of β III-tubulin not CREB and pCREB.

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Peer-review model: Single blind

Reviewer's code: 02446041

Position: Editor-in-Chief

Academic degree: MPhil, PhD

Professional title: Adjunct Professor, Research Scientist, Senior Research Fellow

Reviewer's Country/Territory: United States

Author's Country/Territory: China

Manuscript submission date: 2023-09-06

Reviewer chosen by: Yu-Lu Chen

Reviewer accepted review: 2023-10-09 19:01

Reviewer performed review: 2023-10-15 07:16

Review time: 5 Days and 12 Hours

Scientific quality	☐ Grade A: Excellent ☐ Grade B: Very good ☒ Grade C: Good ☐ Grade D: Fair ☐ Grade E: Do not publish
Novelty of this manuscript	☐ Grade A: Excellent ☒ Grade B: Good ☐ Grade C: Fair ☐ Grade D: No novelty
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Peer-reviewer statements	Peer-Review: ☐ Anonymous ☒ Onymous
	Conflicts-of-Interest: ☐ Yes ☒ No

SPECIFIC COMMENTS TO AUTHORS

Comment: The authors did not pay attention to definitions of scientific terminology. E.g., "After SD rats were anesthetized with 4% chloral hydrate (0.1 g/L) by intraperitoneal injection, rat bone marrow blood was collected for BMSC extraction, and inguinal adipose tissue was collected for ADSC extraction. The procedure of BMSC extraction was as follows: The collected rat bone marrow blood was placed in a 15 mL centrifuge tube," What did they use, "rat bone marrow blood" – either rat bone marrow or blood – did they mix both up? No QC for either. Another example was the retinal ganglion cell injury: Neither in vivo nor functional data was present but claimed its impact. Some essential elements were missing, such as the IACUC and reference structure. The entire manuscript was not written logically. Neither did the authors narrate why nor how, but they overstate their conclusion without data support. The following 20 specifics should be observed for clarity. Specific comments: 1) The current version of the title "Mesenchymal stem cell-derived exosomes from different sources significantly ameliorate the retinal ganglion cell injury induced by high-pressure" did not capture the content accurately or entirely. Thus, it misled the reader. 2) "The RGC

injury model was constructed by RGC damage under different pressures (40, 80, 120 mmHg).” How did these conditions differ from the in vivo pathological progression changes on RGCs? Any reference to the conditions? 3) The methodology was not written logically. 4) Lack of QC for BM-MSCs or ADSC-MSCs? 5) How did they isolate ADSC-MSCs? QC reports? Yields? 6) Rat RGC-5 cells: QC reports? 7) “The other tube of the tee tube was used to connect the pressure gauge and the culture bottle, so that the pressure reached the expected value (40 mmHg, 80 mmHg, 120 mmHg),” What was the device? For how long? QC reproducibility of the measurement and references? 8) “The RGC damage induced by different pressures (40, 80, 120 mmHg) was significantly reduced by ADSC-expos and BMSC-expos treatment. At the same time, the proliferative activity was increased, and the apoptosis was inhibited of RGCs.” Neither logical nor observable in the context of the logical flow. 9) How did they define “damaged RGCs?” 10) “These findings indicated that ADSC-expos and BMSC-expos could ameliorate optic nerve injury caused by pressure by inhibiting apoptosis and increasing the secretion of neurotrophic factors.” Which is not supported by its data. 11) Fig 1A, B, missing scale bars. Neither ADSCs nor BMSCs came with Quality control parameters support and yields. Fig 1C, size range? Fig D, negative controls? 12) Fig 2. That is not a sufficient description. How did they determine damages quantitatively in how many viewfields? Fig 2A missing scale bars embedded. 13) Fig 3. How did they quantify? 14) Fig 4: how did they ensure the time intervals were physiologically relevant? 15) Fig 5 missing scale bars embedded. How did they quantify? 16) Fig 6. How did this pattern relate to the above data sets? 17) Missing the names of the Journals and the authors: 28 Wang Y, Lv J. Human umbilical cord-mesenchymal stem cells survive and migrate within the vitreous cavity and ameliorate retinal damage in a novel rat model of chronic glaucoma. 2021; 2021: 8852517 [PMID: DOI: 10.1155/2021/8852517 [correct: Stem Cells Int . 2021 Oct 25:2021:8852517. doi: 10.1155/2021/8852517. eCollection 2021.] 29 Seyedrazizadeh



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SZ, Poosti S, Nazari A, Alikhani M, Shekari F, Pakdel F, Shahpasand K, Satarian L, Baharvand H. Extracellular vesicles derived from human es-mscs protect retinal ganglion cells and preserve retinal function in a rodent model of optic nerve injury. 2020; 11: 203 [PMID: DOI: 10.1186/s13287-020-01702-x [Journal?]] 18) Many grammar errors crawl around the pages. For example, "After digestion, add 7.5mL of DMEM containing FBS (low sugar 10%) to terminate the digestion, and filter through a strainer. Finally, the digested solution was collected and centrifuged at 1500 r/min for 5 min," – inconsistent in the tense usage. "FBS (low sugar 10%)" – FBS came with sugar? 19) The discussion was not tied to its data but drifted around without proper references. E.g., "There is evidence that ADSCs are most conducive to clinical utilization. Besides, adipose tissue is relatively abundant in the human body compared with other tissues. ADSCs can be isolated from adipose tissue. In addition, 500 times more stem cells were obtained from adipose tissue than from the same amount of bone marrow. Moreover, ADSCs are easier to obtain from the adipose tissue due to their subcutaneous location than BMSCs. Patients tend to choose less traumatic sites for collecting tissue." (who did what and how and why?) 20) The authors need to observe the format of manuscript structures.

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Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05246699

Position: Peer Reviewer

Academic degree: MSc, PhD

Professional title: Academic Research, Researcher

Reviewer's Country/Territory: Iran

Author's Country/Territory: China

Manuscript submission date: 2023-09-06

Reviewer chosen by: Yu-Lu Chen

Reviewer accepted review: 2023-10-08 06:25

Reviewer performed review: 2023-10-16 09:26

Review time: 8 Days and 3 Hours

Scientific quality	☐ Grade A: Excellent ☐ Grade B: Very good ☒ Grade C: Good ☐ Grade D: Fair ☐ Grade E: Do not publish
Novelty of this manuscript	☐ Grade A: Excellent ☐ Grade B: Good ☒ Grade C: Fair ☐ Grade D: No novelty
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Re-review	☒ Yes ☐ No
Peer-reviewer statements	Peer-Review: ☒ Anonymous ☐ Onymous
	Conflicts-of-Interest: ☐ Yes ☒ No

SPECIFIC COMMENTS TO AUTHORS

The manuscript entitled “Mesenchymal stem cell-derived exosomes from different sources significantly ameliorate the retinal ganglion cell injury induced by high-pressure” appears to be interesting. The paper presents novel and interesting data regarding investigate Mesenchymal stem cell-derived exosomes from different sources on the retinal ganglion cell injury induced by high-pressure, and provide a base for the retinal ganglion cell injury treatment. The structure of the manuscript appears adequate. The abstract is presented well with logically defined concept of the topic. Introduction part describes topic-related information and clearly discloses the object of the work. The research presented in the current manuscript would be on interest to many scientific groups with similar scientific interests, therefore, I recommend publishing this paper, but after revisions. 1. Title: the title is not appropriate. I suggesting making up it. 2. Some references missing. For example, “The mechanism of RGC apoptosis in glaucoma is rather complicated in which the molecular mechanism has not been fully studied.” and etc. The following reference may increase the reader’s comprehension: Sheykhhasan M, Amini R, Soleimani Asl S, Saidijam M, Hashemi SM, Najafi R. Neuroprotective effects of

coenzyme Q10-loaded exosomes obtained from adipose-derived stem cells in a rat model of Alzheimer's disease. *Biomed Pharmacother.* 2022 Aug;152:113224. doi: 10.1016/j.biopha.2022.113224. Epub 2022 Jun 6. PMID: 35679720. 3. The materials and Methods section requires more information: To confirm the success of mesenchymal stem cells derived from human adipose and bone marrow tissues isolation, in addition to the electron microscope method, it is necessary to confirm using trilineage differentiation potential by Alcian Blue, Alizarin Red staining and Oil Red O staining and flow cytometry. As a result, it is better to include the results of flow cytometry method and Alcian Blue, Alizarin Red staining and Oil Red O staining and flow cytometry in the result section of the present paper. Furthermore, to confirm the success of exosome isolation, in addition to the electron microscopy and western blotting methods, it is necessary to confirm using the size-based method, including DLS. As a result, it is better to include the results of DLS method in the result section of the present paper. 4. In order to make the paper more interesting to read, I suggested that the authors could add a graphical abstract to the manuscript.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Reviewer's code: 02446041

Position: Editor-in-Chief

Academic degree: MPhil, PhD

Professional title: Adjunct Professor, Research Scientist, Senior Research Fellow

Reviewer's Country/Territory: United States

Author's Country/Territory: China

Manuscript submission date: 2023-09-06

Reviewer chosen by: Jing-Jie Wang

Reviewer accepted review: 2023-11-20 07:10

Reviewer performed review: 2023-11-20 23:08

Review time: 15 Hours

Scientific quality	☐ Grade A: Excellent ☐ Grade B: Very good ☒ Grade C: Good ☐ Grade D: Fair ☐ Grade E: Do not publish
Language quality	☐ Grade A: Priority publishing ☒ Grade B: Minor language polishing ☐ Grade C: A great deal of language polishing ☐ Grade D: Rejection
Conclusion	☐ Accept (High priority) ☐ Accept (General priority) ☒ Minor revision ☐ Major revision ☐ Rejection
Peer-reviewer	Peer-Review: ☒ Anonymous ☐ Onymous



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statements

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

SPECIFIC COMMENTS TO AUTHORS

refer to the 4 pages of comments.

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Reviewer's code: 05246699

Position: Peer Reviewer

Academic degree: MSc, PhD

Professional title: Academic Research, Researcher

Reviewer's Country/Territory: Iran

Author's Country/Territory: China

Manuscript submission date: 2023-09-06

Reviewer chosen by: Jing-Jie Wang

Reviewer accepted review: 2023-11-20 07:14

Reviewer performed review: 2023-11-21 06:25

Review time: 23 Hours

Scientific quality	☐ Grade A: Excellent ☐ Grade B: Very good ☒ Grade C: Good ☐ Grade D: Fair ☐ Grade E: Do not publish
Language quality	☒ Grade A: Priority publishing ☐ Grade B: Minor language polishing ☐ Grade C: A great deal of language polishing ☐ Grade D: Rejection
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statements

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

SPECIFIC COMMENTS TO AUTHORS

The authors completely responded to the observations made previously. They also inserted useful and clarifying information. Thank you for editing the manuscript. Now, the manuscript is much better than the former.