

## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Stem Cells*

**Manuscript NO:** 80420

**Title:** Barriers to mesenchymal stromal cells for low back pain

**Provenance and peer review:** Unsolicited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 00462474

**Position:** Editorial Board

**Academic degree:** PhD

**Professional title:** Full Professor

**Reviewer's Country/Territory:** Italy

**Author's Country/Territory:** China

**Manuscript submission date:** 2022-09-29

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2022-10-04 10:59

**Reviewer performed review:** 2022-10-04 11:07

**Review time:** 1 Hour

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<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
<b>Conclusion</b>	<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
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous

statements

Conflicts-of-Interest: [ ☐ ] Yes [ ☒ ] No

## SPECIFIC COMMENTS TO AUTHORS

The authors have to provide a detailed and proper definition for human mesenchymal stem cells (MSCs). They define these cells as stem cells, but the proper definition is stromal cells. The authors should also better explain that the isolation of MSCs, according to current criteria, produces heterogeneous, non-clonal cultures of stromal cells containing stem cells with different multipotential properties, committed progenitors and differentiated cells (PMID: 34398443). There are several issues related to MSC transplants that authors should address. For example, in recent years, some investigators carried out meta-analysis studies to identify the potential variables affecting cellular therapies based on MSCs. Donor variance, ex vivo expansion and senescence, immunogenicity and cryopreservation are among the main factors that can compromise the effectiveness of MSC transplants. Immunoregulatory properties of MSCs may have a significant inter-donor variability. Interferon-gamma-induced IDO (Indoleamine 2,3-Dioxygenase) upregulation may be used as a marker of immunosuppression activity. The authors should consider this issue. See for example, Galipeau addressed the importance of senescence in failure of stem cell-based trials (Cytotherapy. 2013 Jan;15(1):2-8. doi: 10.1016/j.jcyt.2012.10.002. The mesenchymal stromal cells dilemma--does a negative phase III trial of random donor mesenchymal stromal cells in steroid-resistant graft-versus-host disease represent a death knell or a bump in the road?)

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**Peer-review model:** Single blind

**Reviewer's code:** 06394523

**Position:** Peer Reviewer

**Academic degree:** PhD

**Professional title:** Associate Professor

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** China

**Manuscript submission date:** 2022-09-29

**Reviewer chosen by:** Dong-Mei Wang

**Reviewer accepted review:** 2022-10-11 03:57

**Reviewer performed review:** 2022-10-11 05:09

**Review time:** 1 Hour

<b>Scientific quality</b>	<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
<b>Language quality</b>	<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
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous

**statements**Conflicts-of-Interest: [ ☐ ] Yes [ ☒ ] No**SPECIFIC COMMENTS TO AUTHORS**

The manuscript discussed the possibility and potential mechanisms of MSCs therapy in intervertebral disc degeneration (IDD). Several issues should be addressed: 1. The authors should add a figure to illustrate the mechanisms of MSCs for alleviate IDD. 2.

The authors have mentioned extracellular vesicles (EVs) and microvesicles (MVs), what's the different roles involving the MSCs biological activities.

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**Peer-review model:** Single blind

**Reviewer's code:** 03478635

**Position:** Editorial Board

**Academic degree:** PhD

**Professional title:** Senior Research Fellow

**Reviewer's Country/Territory:** Japan

**Author's Country/Territory:** China

**Manuscript submission date:** 2022-09-29

**Reviewer chosen by:** Dong-Mei Wang

**Reviewer accepted review:** 2022-10-13 01:38

**Reviewer performed review:** 2022-10-21 01:20

**Review time:** 7 Days and 23 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<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
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<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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statements

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

#### **SPECIFIC COMMENTS TO AUTHORS**

This study demonstrates the effect of mesenchymal stem cells on low back pain.