

PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 57934

Title: Mesenchymal stem cells secretome: The cornerstone of cell-free Regenerative Medicine.

Reviewer's code: 02492656

Position: Peer Reviewer

Academic degree: BSc, MSc, PhD

Professional title: Emeritus Professor

Reviewer's Country/Territory: United States

Author's Country/Territory: Spain

Manuscript submission date: 2020-06-29

Reviewer chosen by: Ya-Juan Ma

Reviewer accepted review: 2020-09-03 20:04

Reviewer performed review: 2020-09-19 17:17

Review time: 15 Days and 21 Hours

| | |
|---------------------------------|---|
| Scientific quality | [<input checked="" type="radio"/>] Grade A: Excellent [<input type="radio"/>] Grade B: Very good [<input type="radio"/>] Grade C: Good [<input type="radio"/>] Grade D: Fair [<input type="radio"/>] Grade E: Do not publish |
| Language quality | [<input checked="" type="radio"/>] Grade A: Priority publishing [<input type="radio"/>] Grade B: Minor language polishing [<input type="radio"/>] Grade C: A great deal of language polishing [<input type="radio"/>] Grade D: Rejection |
| Conclusion | [<input type="radio"/>] Accept (High priority) [<input checked="" type="radio"/>] Accept (General priority) [<input type="radio"/>] Minor revision [<input type="radio"/>] Major revision [<input type="radio"/>] Rejection |
| Re-review | [<input checked="" type="radio"/>] Yes [<input type="radio"/>] No |
| Peer-reviewer statements | Peer-Review: [<input checked="" type="radio"/>] Anonymous [<input type="radio"/>] Onymous Conflicts-of-Interest: [<input type="radio"/>] Yes [<input checked="" type="radio"/>] No |

SPECIFIC COMMENTS TO AUTHORS

This is an excellent and extensive review of a highly significant topic. There is no question that MSCs will be a focus of multiple therapeutic approaches far into the future. Just a couple of minor points- 1) In the section entitled "Role of EVs in Cell-to-cell communication", there is reference to "Toll-Like" receptors, but toll is misspelled (tool). 2) In the first paragraph of the Discussion, it is stated "...approval as a drug is proving tough...", while this is true, a more professional way of saying this would be "... is proving to be elusive..." 3) While the literature review is extensive with an excellent choice of references, there is another paper that could be considered because it fits perfectly into the sense of this paper, supports the conclusions that the secretome is key and includes an additional cytokine released by MSCs that did not receive much (if any) consideration in this review: Salazar, K. D., S. M. Lankford, and A. R. Brody. Mesenchymal stem cells produce Wnt isoforms and TGFb1 that mediate proliferation and pro-collagen expression by lung fibroblasts. *Am J Physiol, Lung Cell Mol Physiol*, 297: 1002-1011, 2009.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Professional title: Emeritus Professor

Reviewer's Country/Territory: United States

Author's Country/Territory: Spain

Manuscript submission date: 2020-06-29

Reviewer chosen by: Jia-Ru Fan

Reviewer accepted review: 2020-10-08 14:47

Reviewer performed review: 2020-10-08 14:52

Review time: 1 Hour

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

SPECIFIC COMMENTS TO AUTHORS



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The authors have revised the paper in accordance with the reviewer's suggestions.