

## PEER-REVIEW REPORT

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

**Manuscript NO:** 57725

**Title:** The multifunctional role of microRNA in mesenchymal stem cell-derived exosomes in the treatment of diseases

**Reviewer's code:** 02839880

**Position:** Editorial Board

**Academic degree:** PhD

**Professional title:** Full Professor

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

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

**Manuscript submission date:** 2020-06-21

**Reviewer chosen by:** Le Zhang

**Reviewer accepted review:** 2020-07-16 20:45

**Reviewer performed review:** 2020-07-20 12:27

**Review time:** 3 Days and 15 Hours

<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 Grade E: Do not publish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 statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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

This is an interesting review that focused on the role of miRNA in MSC derived exosomes and the methods commonly used to study miRNA in exosomes. The clinical applications of miRNAs from MSC derived exosomes are also discussed. In general, the manuscript is well written; please revise the English language and check throughout the text for spelling errors. Tables and figures are detailed and helpful for the reader. I would suggest to include a brief discussion on the importance of regulatory mechanisms that could represent a promising target to develop RNA-based therapeutics against tumors (i.e. Barbagallo C et al, Mol Ther Nucleic Acids 2018).

## PEER-REVIEW REPORT

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**Title:** The multifunctional role of microRNA in mesenchymal stem cell-derived exosomes in the treatment of diseases

**Reviewer's code:** 00503560

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**Academic degree:** MD, PhD

**Professional title:** Professor

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

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

**Manuscript submission date:** 2020-06-21

**Reviewer chosen by:** Le Zhang

**Reviewer accepted review:** 2020-07-21 23:32

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<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 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 statements</b>	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**

In this review, the authors described mainly the association of microRNA in Mesenchymal stem cell (MSC) derived exosomes with diseases. Firstly, the authors provided general information about exosomes and miRNA, then focused on the function of miRNA in MSC derived exosome. Subsequently, the authors touched upon the prospects for its therapeutic potential for some diseases. Overall, this review is well-written and I believe this paper would be suitable for publication after several improvements.

**Major comments** The authors explained that miRNAs in MSC derived exosomes can affect several biophysical functions, such as regulation of inflammation, injury repair, and tumor. However, the description of its potential target diseases is insufficient. MSC transplantation has already been put into practical use in some diseases such as graft-versus-host disease after bone marrow transplantation. In addition, several MSC transplantation therapies for liver cirrhosis are recently under clinical trials (Tsuchiya et al. *Inflamm Regen.* 2019, 39: 18 doi: 10.1186/s41232-019-0107-z). MSC derived exosomes recently attracted much attention on their roles in a novel therapeutic strategy for a lot of diseases because it is expected to exhibit potentially a similar effect to MSC transplantation. In fact, in animal disease models, several researches using animal disease models reportedly showed the effect of the miRNAs in MSC derived exosomes (Donald et al. *Stem Cells.* 2017, 35: 851-858). Therefore, authors should mention a possibility of clinical applications for miRNAs in MSC derived exosomes and their targeted diseases more specifically, and summarize the combinations of the miRNAs and the candidate diseases, then create a schema or a summary table.

**Minor comments** 1. In this review, the term “mesenchymal stem cell derived exosomes” were not unified. The authors use only one abbreviation. 2. Several abbreviations were noted without the long forms. 3. In “Biogenesis of exosomes”



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section, RAF-1 must be a typo. It should be RAL-1. 4. In “Identification of exosomes” section, the long form of AF4 would be also a typo. 5. Several reference numbers were missing.

## RE-REVIEW REPORT OF REVISED MANUSCRIPT

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

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

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**Reviewer chosen by:** Jia-Ping Yan

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<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 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
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Peer-reviewer statements</b>	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 replied satisfactorily to all my comments