



### PEER-REVIEW REPORT

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

**Manuscript NO:** 54910

**Title:** Exosomes derived from stem cells as an emerging strategy for intervertebral disc degeneration

**Reviewer's code:** 03197771

**Position:** Editorial Board

**Academic degree:** PhD

**Professional title:** Full Professor

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

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

**Manuscript submission date:** 2020-02-27

**Reviewer chosen by:** Xiao-Quan Yu

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**Review time:** 1 Day and 4 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" 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 Grade E: Do not publish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 type="checkbox"/> Grade B: Minor language polishing <input checked="" 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 type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



**Baishideng  
Publishing  
Group**

7041 Koll Center Parkway, Suite  
160, Pleasanton, CA 94566, USA  
**Telephone:** +1-925-399-1568  
**E-mail:** [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
**https://**[www.wjgnet.com](http://www.wjgnet.com)

## **SPECIFIC COMMENTS TO AUTHORS**

The review by Hu et al., starts by presenting intervertebral disc (IVD) degeneration as a common health issue that may be alleviated by exosome-based therapy. The remaining follows by introducing basic features of exosomes and their cargo to follow with evidence of their therapeutic potential on different scenarios. The title should be adjusted to present exosomes as therapeutic entities rather than tools. Although the value of the information gathered is appreciated, it seems that the authors fail to clearly communicate the level of evidence available for the information provided. For example, it is not properly indicated whether the cited results come from animal experimentation or from human clinical trials. In either case, the number of individuals studied (N of the study) may also help readers understand if the data comes from pilot preliminary results or more statistically robust assays. Perhaps this information could be added to Table 2. A critical review of the markers assayed by each study mentioned, in order to claim exosome rather than extracellular vesicle function would improve the quality of the review. A drawing summarizing the potential mechanisms used by exosomes to improve IVD would be greatly appreciated by the readers. The first page including title and author information seems missing. In addition, the document could benefit from some editing as advised below: Table 2 should be cited in the body of the text. The following statement: “..lipids, proteins, and nucleic acids are the three main substances that determine the specificity of exosomes” might not be correct if considering specificity comes from the surface and glycans reside on the outer leaflet of the vesicles. Please rephrase the sentence: “...because of the complex and harsh in vivo environment of the IVD, there have been different results in preclinical studies” . As no direct evidence to support the claim is provided. Please try to avoid terms that can be confused with statistical calculations as in the following: “Among them, the role of exosomes is



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7041 Koll Center Parkway, Suite  
160, Pleasanton, CA 94566, USA  
**Telephone:** +1-925-399-1568  
**E-mail:** [bpoffice@wjgnet.com](mailto:bpoffice@wjgnet.com)  
**https://**[www.wjgnet.com](http://www.wjgnet.com)

particularly significant..". How is the gradual attraction referred "...and has gradually attracted the interest of a growing number of researchers." documented? Cites should be provided at the end of the statements and not when the group is mentioned. As for example, cite 29, should appear after "...the noninjection groups" on line 212 and not on line 205, after "Cheng et al". Please review the whole document to consistently adhere to this rule. Please clarify what the authors refer as "effective cells" (line 236). Line 18 and line 83, the word "will" in the sentence "This paper will mainly review .." should be removed as the review has been completed Line 30, "drop" by reduction Line 85, please review the sentence: will give a cautious outlook on their future applications in this field. Lines 88 and 89: please review the sentence "...the other two types of vesicles" as there may be more than 3 types of vesicles. It would be more appropriate to mention that the other two main types of extracellular vesicles described are...to contemplate that classifications are subjectively imposed by selective criteria. Line 114 and 115: please avoid term repetition in: "The function of exosomes mainly depends on the contents they contain" and Line 119: "Lipids in exosomes are mainly located in the membrane of exosomes... and other types of lipids" and other sentences. Please review the whole manuscript. Line 135: replace long by longer in the sentence: "Mature miRNAs are produced from long primary transcripts" Line 140: replace degrees by degree in the sentence: "...based on the degrees of complementarity[65]" Line 198: review the meaning of reversed in the following sentence: "while the degradation-related genes MMP-1 and MMP-3 were reversed" Line 200: "Therefore, MSC-derived exosomes have the ability.." perhaps should be rephrased with more appropriate terms like "seems to indicate" "it suggests" rather than using a rotund affirmation with a questionable level of evidence. Line 204: please add the term "their" in the sentence: "proliferation of NPCs but also inhibit apoptosis" Text editing by a native English scientist is highly recommended.



### PEER-REVIEW REPORT

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**Title:** Exosomes derived from stem cells as an emerging strategy for intervertebral disc degeneration

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<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 checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" 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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7041 Koll Center Parkway, Suite  
160, Pleasanton, CA 94566, USA  
**Telephone:** +1-925-399-1568  
**E-mail:** [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
**https://**[www.wjgnet.com](http://www.wjgnet.com)

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

This is a very interesting review about stem-cell derived exosomes. Conclusion may be revised to include the detailed description about the further research needed. Proofreading is needed.



## RE-REVIEW REPORT OF REVISED MANUSCRIPT

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

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**Title:** Exosomes derived from stem cells as an emerging strategy for intervertebral disc degeneration

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**Academic degree:** PhD

**Professional title:** Full Professor

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

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

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**Reviewer performed review:** 2020-06-22 16:31

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<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 type="checkbox"/> Grade B: Minor language polishing <input checked="" 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>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



**Baishideng  
Publishing  
Group**

7041 Koll Center Parkway, Suite  
160, Pleasanton, CA 94566, USA  
**Telephone:** +1-925-399-1568  
**E-mail:** [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
**https://**[www.wjgnet.com](https://www.wjgnet.com)

The answers to the points raised in the previous review seem satisfactory, with the exception of Comment 7. The sentence provided should be replaced by the following: "However, because of the complex and harsh in vivo environment of the IVD, there are obstacles to be overcome by IVD degeneration stem cell therapy approaches". The manuscript still needs English native review. For example in the last sentence of the abstract both verbs appear in plural, and they should be third person of the singular. Namely, "reviews" and "highlights" instead of "review" and "highlight" for the subject "This paper" Although Minor revision is selected as conclusion, the paper could be accepted after language quality check.