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JOURNAL EDITORIAL BOARD'S REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 86992

Title: How to enhance the ability of mesenchymal stem cells to alleviate intervertebral disc degeneration

Journal Editor-in-Chief/Associate Editor/Editorial Board Member: Shengwen Calvin Li

Country/Territory: United States

Editorial Director: Jin-Lei Wang

Date accepted review: 2023-10-28 19:10

Date reviewed: 2023-10-29 05:20

Review time: 10 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	language polishing	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Major revision

JOURNAL EDITORIAL BOARD COMMENTS TO AUTHORS

Comment: Mini-review should be sharp, focused, and straightforward to the point. However, neither the themes nor the problems surfaced upon reading the current manuscript. The authors did not address the comments by all the peer-reviewers: They did not follow the point-to-point format or understand what they were being asked about – The authors simply listed their own points without referencing the original peer-review reports, demonstrating no respect for those peer-review reports. Nor did they address the questions and critiques. Thus, the revision did not improve clarity. EIC specific comments: 1)The current version of the manuscript did not thoroughly analyze the literature and develop novel themes. Nor did the authors point out the problems and offer any specific solutions. Instead, the authors blended the facts from different sources without defining the boundaries of scientific terminology. For example, The authors did not take up the peer-reviewer critiques to revise their title: “How to enhance the ability of mesenchymal stem cells to alleviate



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intervertebral disc degeneration," to reflect their content. 2) Another example of blended facts in a compound concept is "MSCs," as reviewer 1 specifically pointed out: "2-Despite similar phenotypes and the common mechanisms of tissue regeneration, the source of MSCs can play a crucial role in their therapeutic effects. Studies have shown that diversity in the microenvironment of MSCs and, subsequently, the expression of different genes lead to differences in their function and behavior. So, it has been suggested that tissue-matched MSCs may increase the efficacy of their regenerative effects." 3) No specific connection was found between the text and the abstract: e.g., "The current aim of stem cell therapy is to replace the aged and metamorphosed cells in the ID and to increase the content of the extracellular matrix" (Abstract) did not connect to the main text. The second example: "The treatment of disc degeneration with stem cells has achieved good efficacy, with an efficacy rate of almost 70%, and the current challenge is how to improve this efficacy" (abstract), did NOT flow into deeply elaborating the statement in the main text. Third example: "Here, we reviewed current treatments for disc degeneration and summarize studies on stem cell vesicles, enhancement of therapeutic effects when stem cells are mixed with related substances, and improvements in the efficacy of stem cell therapy by adjuvants under adverse conditions (abstract)." What did they mean "enhancement of effects?" How much did the authors enhance from 70% to what percentage of effects? Any follow-up elaboration? Fourth example: "The new approaches and ideas for stem cell treatment of disc degeneration" - How did the authors define "new approaches?" 4) Neither logical nor scientific: "Intervertebral discs (IDs) have a complex structure with a unique internal environment. They contain nucleus pulposus cells, fibrous rings, and extracellular matrix (ECM)[1-4], which are in a dynamic balance of self-renewal." How did such elements in a dynamic balance of self-renewal? [Introduction]. 5) The authors did not give any transition and jumped into "this balance of secreting exosomes and vesicles, mixing other substances to promote their differentiation into nucleus pulposus cells." If IDs can be in a dynamic balance of self-renewal, why bother doing these? 6) Again, the authors jumped starting "METABOLITES AND MSCS, " "gel-loaded MSCS," or "GEL-LOADED MSCS" or "CIRCULAR RNA AND EXOSOMES" or "MSC MIXTURE" or "STIMULATION INDUCTION WITH MSCS" - backtracked to "HARSH ENVIRONMENT OF THE ID." None of these sections came with setting up, unfolding, and conclusion, but randomly crawling around different concepts. 7) "FUTURE DIRECTIONS FOR STEM-CELL-BASED THERAPY" did not envision anything novel but regurgitating what was said before. So, in its conclusion. 8) Neither Figure 1 nor Figure 2 offer any specific information concerning the topic, as it was too superficial and generic, not as expected from the expert's review. 9) Many grammar errors crawled across the pages to obscure its logic. E.g., "Here, we reviewed current treatments for disc degeneration and summarize studies on stem cell vesicles, enhancement of therapeutic effects when stem cells are mixed with related substances, and improvements in the efficacy of stem cell therapy by adjuvants under adverse conditions (abstract)."



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Name of journal: World Journal of Stem Cells

Manuscript NO: 86992

Title: How to enhance the ability of mesenchymal stem cells to alleviate intervertebral disc degeneration

Journal Editor-in-Chief/Associate Editor/Editorial Board Member: Carlo Ventura

Country/Territory: Italy

Editorial Director: Jin-Lei Wang

Date accepted review: 2023-10-27 10:52

Date reviewed: 2023-10-29 10:41

Review time: 1 Day and 23 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	language polishing	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Major revision

JOURNAL EDITORIAL BOARD COMMENTS TO AUTHORS

This is an interesting Minireview, presenting and discussing relevant findings related the onset and progression of intervertebral disk degeneration (IDD), a major and widespread degenerative disorder with severe impact on the life quality. I noticed some incongruence in the cited literature. For instance, at page 6, "The combination of heat-sensitive decellularized ECM hydrogels with adipocyte-derived MSC exosomes does not damage the therapeutic activity of MSCs. The heat-sensitive dECM@exo hydrogel system produces gelation in situ to help MSCs differentiate into nucleus pulposus cells and maintains the content of ECM. This hydrogel also creates a suitable environment for the proliferation and differentiation of nucleus pulposus cell [22]". The cited reference "Pretreatment of nucleus pulposus mesenchymal stem cells with appropriate concentration of H₂O₂ enhances their ability to treat intervertebral disc degeneration. Stem Cell Res Ther 2022; 13: 340 [PMID: 35883157 DOI: 10.1186/s13287-022-03031-7]" only reports the use of hydrogels in the



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introduction section, but the study per se is not meant to assess the hydrogel effect on the investigated context. Nevertheless, the paper reported in the Minireview as reference [22] cites in its introduction section two papers (refs, 21 and 22: 21. Xing H, et al. Injectable exosome - functionalized extracellular matrix hydrogel for metabolism balance and pyroptosis regulation in intervertebral disc degeneration. *J Nanobiotechnol.* 2021;19(1):264. <https://doi.org/10.1186/s12951-021-00991-5>. 22. Zeng Y, et al. Injectable microcryogels reinforced alginate encapsulation of mesenchymal stromal cells for leak-proof delivery and alleviation of canine disc degeneration. *Biomaterials.* 2015;59:53–65. <https://doi.org/10.1016/j.biomaterials.2015.04.029>.) These references are more appropriate to be cited in this Minireview with regard to the hydrogel effect. Similarly, by reading ref 23 cited in the minireview (Hu Y, Tao R, Wang L, Chen L, Lin Z, Panayi AC, Xue H, Li H, Xiong L, Liu G. Exosomes Derived from Bone Mesenchymal Stem Cells Alleviate Compression-Induced Nucleus Pulposus Cell Apoptosis by Inhibiting Oxidative Stress. *Oxid Med Cell Longev* 2021; 2021: 2310025), I couldn't find any explicit experiment done with hyaluronic acid and platelet-rich hydrogels, nor any clear result on keratin gene expression as it is instead reported in the Minireview (page 6). Some more appropriate Reference supporting this statement should be cited in the Minireview. At page 8, please correct miRNA-cahama into miRNA-199a! Again at page 8, "Similarly, the combination of MSCs with in situ bioresorbable gel (dMD-001) produced the above therapeutic effects in IDD and was used after discectomy to prevent IDD. Similarly, when MSCs are combined with coenzyme Q10 for the treatment of most ID lesions, it reduces oxidative stress in the ID, inhibits degradation of nucleus pulposus cells, and steadily improves the efficacy of IDD treatment". These sentences don't report any reference in support! (These issues are not part of the study quoted as Ref 37 in the Minireview). Please, clarify and add specific related references. At page 11, please correct methanipine cross-linked into genipin-cross-linked.