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PEER-REVIEW REPORT

Name of journal: *World Journal of Stem Cells*

Manuscript NO: 84485

Title: Factors affecting osteogenesis and chondrogenic differentiation of mesenchymal stem cells in osteoarthritis

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03079551
Position: Peer Reviewer
Academic degree: MD
Professional title: Doctor
Reviewer's Country/Territory: China
Author's Country/Territory: China

Manuscript submission date: 2023-03-17

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-03-20 10:00

Reviewer performed review: 2023-03-20 11:20

Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No creativity or innovation

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Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The differentiation function of MSCs plays an important role in the treatment of OA. This review is the first time to report the factors that may affect the differentiation direction of MSCs in the treatment of OA, and provide guidance for more accurate regulation when MSC therapy is applied in the future. However, there are still some issues with this article that need to be addressed. 1. It is suggested that authors adjust the writing order in the introduction, such as introducing the current treatment of OA, and then discussing the current research progress of MSCs. 2. It is recommended that authors use tables to summarize the specific mechanisms of action of factors affecting the differentiation direction of MSCs. 3. Several reviews have been published on the influencing factors of MSCs differentiation, and the authors seem to have missed some important factors, such as scaffold materials and bFGF.

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Reviewer's code: 03550490
Position: Peer Reviewer
Academic degree: PhD

Professional title: Honorary Research Fellow

Reviewer's Country/Territory: Malaysia

Author's Country/Territory: China

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Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-03-18 16:50

Reviewer performed review: 2023-03-24 16:03

Review time: 5 Days and 23 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [Y] Grade C: Fair [ ] Grade D: No creativity or innovation

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Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Peng at al has summarized the factors influencing osteogenesis and chondrogenic differentiation of MSCs. To make it more specific to OA, as authors planned to, a few issues should be addressed. Major: 1. Authors mentioned the following in the core tips: differentiation function of MSCs also plays an important role in the treatment of diseases. This is also the purpose for writing this review article. Authors should write a section to support this statement. It is to convince the readers, besides paracrine effect, differentiation of MSCs also contribute to OA treatment. Suggest to include clinical data or animal modal to show MSC differentiate into osteocytes and chondrocytes in OA treatment. 2. As mentioned in the title, abstract and core tips, the focus of this manuscript is specific to OA. Authors should include more evidence/literature on the factors affecting the differentiation of MSCs for OA or OA microenvironment. I would like to emphasise that the keywords here are OA or OA microenvironment. Based on current manuscript, authors have mostly explained or elaborated on the factors affecting osteogenesis and chondrogenic differentiation of MSC in general or in vitro, but did not explain how the OA microenvironment plays a role in differentiation. Thus, for each

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section of the manuscript such as Mechanism of osteogenic and chondrogenic differentiation and Factors affecting differentiation (Oxygen concentration, Glucocorticoid, Sources of MSCs), please further explain the topics in relation to OA or OA microenvironment. Minor: 3. Suggest to draw a figure of mechanisms/interactions to show how these factors or signalling pathways affect the osteogenesis and chondrogenic differentiation. This is to summarize the section on 'Mechanism of osteogenic and chondrogenic differentiation of MSCs'. Authors could draw one for each differentiation. 4. Authors mentioned that by December 2022, 1141 clinical studies have been registered in clinicaltrials.gov. It is now March 2023. Therefore, the authors should update the figure to the latest.