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PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 65029

Title: Priming Strategies for Controlling Stem Cell Fate: Applications and Challenges in

Dental Tissue Regeneration

Reviewer's code: 00727943 Position: Peer Reviewer Academic degree: PhD

Professional title: Professor

Reviewer's Country/Territory: South Korea

Author's Country/Territory: China

Manuscript submission date: 2021-02-27

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-03-01 04:03

Reviewer performed review: 2021-03-01 10:54

Review time: 6 Hours

Scientific quality	[] Grade A: Excellent [Y] Grade B: Very good [] Grade C: Good [] Grade D: Fair [] Grade E: Do not publish
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) [Y] Accept (General priority) [] Minor revision [] Major revision [] Rejection
Re-review	[Y]Yes []No
Peer-reviewer	Peer-Review: [Y] Anonymous [] Onymous
statements	Conflicts-of-Interest: [] Yes [Y] No



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SPECIFIC COMMENTS TO AUTHORS

In this review article, the authors summarize the priming approaches of dental tissue-derived MSCs to improve the therapeutic effects of MSCs in dental tissue regeneration. The priming approaches include priming culture conditions, preconditioning by cytokines and growth factors, and genetic modification of MSCs. They summarized well not only the tremendous progress, but also challenges of the current approaches in the field. This article is acceptable for publication in World Journal of Stem Cells. There is no major comments, but some minor corrections need to be made in terms of English expressions, for example 'dental-derived MSC' should be 'dental tissue-derived MSC' in the second paragraph on page 5 and 'a sufficient number' should be 'a sufficient number of cells' in the last paragraph on page 7.



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Name of journal: World Journal of Stem Cells

Manuscript NO: 65029

Title: Priming Strategies for Controlling Stem Cell Fate: Applications and Challenges in

Dental Tissue Regeneration

Reviewer's code: 04738361 Position: Peer Reviewer Academic degree: PhD

Professional title: Director, Research Scientist

Reviewer's Country/Territory: France

Author's Country/Territory: China

Manuscript submission date: 2021-02-27

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-02-28 14:22

Reviewer performed review: 2021-03-02 10:13

Review time: 1 Day and 19 Hours

Scientific quality	[] Grade A: Excellent [Y] Grade B: Very good [] Grade C: Good [] Grade D: Fair [] Grade E: Do not publish
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	[Y] Yes [] No
Peer-reviewer	Peer-Review: [Y] Anonymous [] Onymous
statements	Conflicts-of-Interest: [] Yes [Y] No



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SPECIFIC COMMENTS TO AUTHORS

Manuscript ID65029 reviews different priming approaches to increase MSC regenerative and immunomodulatory activities. In general, this manuscript is very well organized and comprehensive. It covers most of the essential aspect of MSC biology. The text is fluid, however, it lacks some more descriptive figures on priming subjects. Although this manuscript is very interesting, the following points need to be clarified. * In the introduction, the authors have mentioned the MSC capacity of differentiation. However, recent studies demonstrate their potential to differentiate into an even larger range of cell types such as endothelial cells and especially hepatocytes which makes them even more interesting in the field of regenerative medicine. The following article could help you to build up this section. (PMID: 32033595 and PMID: 29763649) * In Figure 1, for demonstrating the immunoregulatory function of MSCs, the authors have depicted only macrophages. MSC ability to control T cells have been discussed more extensively than * concerning TNFa priming: very recent publications demonstrate the strong involvement of the TNF-TNFR2 singling pathway and not TNF-TNFR1 in MSC regenerative and immunomodulatory effects. This includes their pro-angiogenic function, the suppression of T cells, induction of Tregs, and changing their T cell cytokine production pattern. Moreover, TNFR2 expression were corelated with NF-kB which is also mentioned by the authors to be essential after TNF pre-treatment. The following articles cover this important aspect since the main focus of this review is on priming effects. (PMID: 33344453, PMID: 32669116, PMID: 33303019) * One of the crucial mechanisms of action of MSC immunoregulatory function is via induction of The authors did not discuss this point. Moreover the coverage on T cell suppression is very poor and needs more attention.



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PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 65029

Title: Priming Strategies for Controlling Stem Cell Fate: Applications and Challenges in

Dental Tissue Regeneration

Reviewer's code: 05818999 Position: Peer Reviewer Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: China

Manuscript submission date: 2021-02-27

Reviewer chosen by: Ya-Juan Ma

Reviewer accepted review: 2021-03-12 05:14

Reviewer performed review: 2021-03-30 09:58

Review time: 18 Days and 4 Hours

Scientific quality	[] Grade A: Excellent [] Grade B: Very good [Y] Grade C: Good [] Grade D: Fair [] Grade E: Do not publish
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) [] Minor revision [Y] Major revision [] Rejection
Re-review	[Y]Yes []No
Peer-reviewer	Peer-Review: [Y] Anonymous [] Onymous
statements	Conflicts-of-Interest: [] Yes [Y] No



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SPECIFIC COMMENTS TO AUTHORS

The present manuscript entitled "Priming Strategies for Controlling Stem Cell Fate: Applications and Challenges in Dental Tissue Regeneration" was examined. The author reviewed many studies that were published in the regulation of MSCs that are summarized in the manuscript. After careful evaluation, some suggestions are listed below and this manuscript still needs to upgrade. 1. The manuscript rarely refer to the tissue regeneration, thus, it doesn't correspond to the question very well. 2. Towards the regulation of MSCs, chemical and physical factors also play very vital roles besides biological agents. Therefore, I think it is better to supplement the related research work.

3. This review lack of the personal perspective of the authors. 4. There are some grammar mistakes, for example, the tense problems, and it is necessary to improve the written English.