

16-May-2021

Dear Editors,

We would like to thank the reviewers for their thoughtful and constructive comments regarding our manuscript. We have carefully read through the comments from reviewers. To fully address reviewers' questions and comments, we have revised our manuscript accordingly. Revised portions are highlighted in red in the manuscript. The point-by-point responses to the reviewers' comments are listed as follows.

Reviewer 1:

Comments to the Author

The authors aimed to discuss epigenetic mechanisms, including noncoding RNAs, histone modifications, and DNA methylation and research progress in modulating cell fate determination of DPSCs. In fact, it has become clear that the epigenetic layer of regulation plays an essential role in pulp-dentin regeneration based on DPSCs, and has great potential in RE, which is also discussed in the proposed review. The manuscript is addressing an interesting point. The structure of the manuscript appears adequate and well divided in the sub-paragraphs. The study is easy to follow but some issues should be improved before publication.

Response: Thank you very much for your affirmation. The issues raised are addressed as follows.

1) The manuscript needs moderate English change and grammar correction. Please also check typos thorough the text.

Response: We appreciate reviewer's concern to improve our manuscript. We have carefully checked the sentences and typos in our manuscript according to your suggestions. The manuscript has been revised by a native English speaker. The certificate document has been provided as well. We hope the revised manuscript could be up to the standard.

2) PDPSCS, SHEDS AND THEIR CHARACTERISTICS section: Will be useful to the reader to add some interesting literature describing regenerative potentialities and translational applications of dental-derived stem cells (please see and briefly discuss: PMID: 29445404; PMID: 33101420; PMID: 31696459; PMID: 30008608; PMID: 29254292) as well some main molecular mechanism including stemness properties (PMID: 31002142; PMID: 30840286).

Response: Thanks for raising this comment. We have carefully read through the articles suggested by reviewer. The corresponding contents to describe regenerative potentialities and translational applications of dental-derived stem cells have been added in 1st paragraph of section "PDPSCS, SHED AND THEIR CHARACTERISTICS", and the corresponding contents for main molecular mechanism including stemness properties have been added in "PDPSCS, SHED AND THEIR CHARACTERISTICS" section, which are highlighted in red in the manuscript.

3) Conclusion Section: This paragraph required a general revision to eliminate redundant sentences and to add some "take-home message".

Response: Thanks for your suggestion. We have modified the "CONCLUSION" section and highlighted in red accordingly.

Editorial Office:

Comments to the Author

1 Scientific quality: The manuscript describes a review of the epigenetic regulation of dental pulp stem cells and its potential in regenerative endodontics. The topic is within the scope of the WJP. (1) Classification: Grade C; (2) Summary of the Peer-Review Report: The manuscript is addressing an interesting point. The structure of the manuscript appears adequate and well divided in the sub-paragraphs. However, some issues should be improved.

Response: Thank you very much for your affirmation. The issues raised are addressed as follows.

References: A total of 145 references are cited, including 1 reference published in the last 3 years; (5) Self-cited references: There are 5 self-cited references. The self-referencing rates should be less than 10%. Please keep the reasonable self-citations that are closely related to the topic of the manuscript, and remove other improper self-citations. If the authors fail to address the critical issue of self-citation, the editing process of this manuscript will be terminated;

Response: We appreciate reviewer's concern to improve our manuscript. Strictly speaking, there is only one reference "PMID:28880717" that can be counted as self-sited, we cited this article to address that bivalent histone modifications on the same promoter can facilitate rapid activation of certain genes. I wonder if you refer to the other 4 self-cited references as "PMID:25069920, PMID:29294297, PMID:32936965, PMID:29028630", these references did belong to the same affiliation (State Key Laboratory of Oral Diseases & National Clinical Research Center for Oral Diseases, West China Hospital of Stomatology, Sichuan University), however, they are from a different research group and there is no interest related. These four references are essential to address our topics.

Issues raised: The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s).

Response: We feel sorry for this mistake. We have uploaded the approved grant application form(s) or funding agency copy of any approval document(s) accordingly in the system.

We have carefully read through and addressed the reviewer and Editorial Office's comments. We hope our responses could address reviewer and Editorial Office's concern and our revised manuscript now is appropriate for publication in *World Journal of Stem Cells*.

Sincerely,

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