

Dear Editor,

We are submitting the revised version of the Manuscript NoNO: 68279 (Invited manuscript No. 05382324) entitled “ Dental mesenchymal stromal/stem cells in different microenvironments - implications in regenerative therapy ”, authors: Ivana Okić Đorđević, Hristina Obradović, Tamara Kukolj, Anđelija Petrović, Slavko Mojsilović, Diana Bugarski, Aleksandra Jauković

All suggestions made by reviewers were addressed and corrections/modifications in the text were made.

All significant changes in the manuscript text were marked yellow, and deletions and single word grammar/spelling corrections were not marked. Detailed response to reviewers is also submitted.

We are grateful for all the suggestions and comments given by reviewers, which helped us to improve the quality of our work. We hope that the revised version of the manuscript will be acceptable for publication in World Journal of Stem Cells.

Best regards,
Ivana Okić Đorđević

We are thankful to the Reviewers for the observations made. According to the concerns of the Reviewers and recommendation of Editorial team, we revised the manuscript. Comments appointed by the Reviewers were addressed and related changes in the manuscript and figures were adjusted. We hope that the new version of the manuscript would be more suitable for acceptance in World Journal of Stem Cells.

Reviewer #1:

Relating to reviewer #1 editorial comment 1, to add line's number.

Answer: Appreciating the comment, we modified the manuscript as suggested.

Editorial comment 2, the references are sometimes very old.

Answer: The authors fully acknowledge the Reviewer's suggestion. New references are added- reference No. 6, 19 and 30.

Editorial comment 3, Page 5, paragraph 2: MSCs exist in many fetal tissues as well.

Answer: This sentence is corrected in the manuscript and changes marked yellow (page 5, line 18).

Editorial comment 4, Page 6, line 7 needs a reference.

Answer: The authors thank Reviewer #1 for this observation. The appropriate reference No 11 was added in manuscript.

Although figure 1 is interesting, the authors need to illustrate more figures mostly on the functions MSCs.

Answer: Authors appreciate this suggestion. New figures on MSCs and dental MSCs functions are added.

Editorial comment 5, Concerning the immunoregulatory aspect of MSCs, the authors have mentioned that the mechanism behind their function is not elucidated. This is not quite true. Please refer to these recently published reference to build up this section. (PMIDs: 33344453, 32669116, 33303019, 30359308).

Answer: The authors are thankful to the reviewer #1 for this comment. This section in the introduction was rewritten, and referred to suggested reference (reference No 13) (page 6, lines 10- 13).

Editorial comment 6, Regarding the role of hypoxia and inflammation on MSC's osteogenic and adipogenic capacities, the authors have only mentioned different published results in recent years. Please discuss what you think about these controversial results? In general author's viewpoint is missing in this manuscript.

Answer: Authors appreciate Reviewer's observation. Authors' thoughts on contradictory results regarding the effects of hypoxia and inflammation on dental MSCs and general viewpoint were written in Conclusion. All the changes/modifications in the text were marked yellow (page 21, lines 11-22)

Reviewer #2:

Relating to reviewer #2 editorial comment 1, to prepare one more table (table 2) to introduce how the inflammatory factors regulate the regenerative potential of human dental mesenchymal stem cells.

Answer: Authors thank the reviewer #2 for the suggestion. The authors have revised the manuscript and added one more table.

Reviewer #3:

Relating to reviewer #3 editorial comment: A very interesting and well-written manuscript in an emerging and hot topic in biomedical research. The article covers the most important topics on the role of different environments on dental mesenchymal stromal/stem cells and its implications in regenerative therapy.

Answer: Authors are very thankful to the reviewer for this comment.

We hope that the new revision of the manuscript would be more suitable for acceptance in World Journal of Stem Cells.

Sincerely

Ivana Okić Đorđević