Author's response to reviews

Title: Osteogenic Differentiation of Dental Pulp Stem Cells under the Influence of Three Different Materials

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Author's response to reviews: see over
Dear Chief Editor.

Submitted is the reviewed version of the manuscript entitled “Osteogenic Differentiation of Dental Pulp Stem Cells under the Influence of Three Different Materials”, after doing the requested adjustments. I would like to thank you as well as your reviewer board for taking the time considering this manuscript, hoping that the review process finds it acceptable for publication in your esteemed journal.

Response to the editor:
Thank you for your comment, all points raised were adjusted/clarified:

- **Regarding the selection of DPSCs and EMD:** It is explained in the introduction the importance of use of proper cell populations and select a signaling molecule that help control them. The reason for the use of *dental pulp stem cells* is further explained, however, regarding *EMD*, the objective of the study was to compare the effect of all the three materials on cellular osteogenic differentiation, for selection of the best signaling material for future regenerative applications. As explained in the introduction, EMD has long been utilized for periodontal regeneration, as well as the more recent material: PDGF-BB. However, the new test material in this study was *MTA*. The rationale for selection of each material is discussed in the introduction. Meanwhile, in the results, EMD has consistently gave superior results in all evaluated aspects, and accordingly, suggested as a material with good regenerative potential. This was further clarified in the conclusion, as well as further evaluation of the MTA and PDGF was suggested.

- References are updated

- The paper has already received professional editing by the agency recommended by the journal “Edanz Group”. The invoice and payment confirmations are attached with this email
Response to Reviewer 1 (Professor Gianpaolo Papaccio).

Dear Prof. Papaccio:

Thank you for your valuable comments.

- Regarding the methodology: I agree that periodontal regeneration involves reconstruction of multiple tissue types, which requires complex cellular events including migration, mitogenesis, differentiation…etc. However, since this is a limited in vitro study, only certain aspects were measured: the osteogenic potential of the selected materials, in order to identify the best material which may assist hard tissue formation, including bone as well as cementum. Further in vivo studies with histologic evaluations are required to better document the overall regeneration process influenced by those materials.

- For the references. More updated articles were utilized. The suggested references were also added (no. 3 and 23). Please note that stem cell therapy and periodontal regeneration are very active topics, with so many papers evaluating different aspects. In this manuscript, only few articles were selected to represent different areas and support the presented ideas in an attempt to be as much clear and concise as possible.

Response to Reviewer 2: (Dr. Piero Antonio Zecca)

Dear Dr. Zecca:

Thank you very much for your positive encouraging comments. The results were slightly reduced as per your recommendation; however, we believe that further reduction may hide the results of many steps already mentioned in the materials and methods section. Additionally, the results are already divided into two sections: “Cell isolation and characterization” and “material application”. The latter is further subdivided into “ALP staining” and “Alizarin Red S staining”

Sincerely yours,
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