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May 7th, 2020, Valladolid, Spain

Dear reviewer, Dear Science Editor,

Please find below a relation of the changes that have now been introduced in the manuscript "Stem cell-based approaches: possible route to hearing restoration?", in accordance with your reviews. I do thank you for your comments that have no doubt improved the quality of the manuscript. I hope this is now considered acceptable for publication in the *World Journal of Stem Cells*.

Thank you.

Yours sincerely,

A handwritten signature in black ink, appearing to read 'Beatriz Durán-Alonso', with a long horizontal flourish extending to the right.

María Beatriz Durán-Alonso

All the elements required in the First Section of Writing Requirements have now been introduced: Title, Running Title, Author's information (including ORCID number), Corresponding Author's information, Abstract, Key Words, Core Tip. These were missing in the previous version of the manuscript, as pointed out by the Science Editor; I do apologize for this mistake. All these data are now found in pages 1-4 of the revised version of the manuscript.

In accordance with the comments by the Reviewer, three figures have now been added to the manuscript, to guide the reader through the main aspects that are discussed in this review:

- Figure 1 summarizes some of the most important considerations regarding the use of exogenous cells as donor cells for the replacement of damaged cochlear cell types; a short paragraph has been added to the text (lines 28-35) to introduce this figure:

When considering the implantation of exogenous cells into the cochlea, a wide range of factors must be taken into account that have an important effect on the fate of the implanted cells and ultimately determine treatment outcome. Considerations such as the type of exogenous cells, their differentiation status and potential to differentiate towards other cell types, the selected route of implantation and the host micro-environment all play key roles in the survival and integration of the implanted cell population within the host tissue (Figure 1).

- Figure 2 is an overview of the various types of exogenous cells that have been tested and a brief account of the main results that have been obtained with these cells, their advantages and shortcomings. A sentence in lines 443-446 introduces this figure.

Summarizing what has been discussed above, a number of exogenous cell types have been evaluated for their potential to replace damaged cells in the adult mammalian cochlea, in a quest for a promising approach to hearing restoration. Some of these results are summarized in Figure 2.

- Figure 3 summarizes some of the questions raised by current studies with regard to the presence of putative progenitor cells in the adult mammalian cochlea. Lines 522-528 have been added to the text that introduce Figure 3.

The identification of a progenitor cell population in the cochlea and elucidating the reasons why these cells appear unable to regenerate the damaged tissue would be of the utmost importance; these progenitors would constitute an ideal cell source for regeneration therapies, placed at the appropriate location, and would override some of the main hurdles encountered by approaches that rely on the use of donor cells from exogenous sources (Figure 3).

The legends corresponding to Figures 1-3 can be found at the end of the manuscript, in page 37 (lines 1016-1037). These legends have also been added to the Powerpoint file that contains the three figures.

