

To Editor-in-Chief, Assistant Editor and Guest Editor, *World Journal of Stem Cells*

Subject: Revised Version of Manuscript NO: 82589

Messina, March 17th, 2023

Dear Professors,

Manuscript NO: 82589, entitled “**The Human Retinal Secretome: a Cross Link between Mesenchymal and Retinal Cells**” by Luigi Donato et al. has now been significantly revised, and therefore I kindly resubmit it for your attention.

All changes in the manuscript were made by using the track changes mode in MS Word.

Attached to the present letter there is an annotated version and un-annotated version of the revised manuscript.

Here are the answers to the comments made by reviewer point by point:

REVIEWER 1

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: The authors of this review summarized the features of MSC mesenchymal stem cell (MSC) and the features of MSC secretome. They also highlighted a significant role of MSC secretome in immunomodulation and Central Nervous System Pathologies. Additionally, they further elucidate the features of retinal cells and retinal pigmented epithelium (RPE) cell secretome and retinal diseases. Moreover, the authors discuss delineated the importance of the “cross-talk” between mesenchymal stem cells and retinal cells, focusing on common/induced secreted factors, during experimental therapy for retinal diseases. The topic of the review is significant and the manuscript is organized well enough. However, my major criticism is that the manuscript is mainly a description of words, and lacks a summary with tables or figures. Therefore, it is suggested to add a table or figure in the manuscript. I have some special comments and concerns that can be considered by the authors as follows:

1. In vivo, in vitro should be written in Italics throughout the text.

We have corrected the Italics when required, thanks.

2. Phrase abbreviation, human bone marrow-derived mesenchymal stem cells (hBMSCs) changed to human BMSCs will be good. Please check all the full names and abbreviations.

We have checked the abbreviation through the whole text, thanks.

3. Figure 1 is not mentioned in the text.

We added the reference to Figure 1 within the text, thanks.

4. It is suggested that the authors make a table to summarize the key molecules of mesenchymal secretome derived from different cell types in the treatment and regeneration of retinal cells.

We added the Table 1 which summarizes the key molecules of mesenchymal secretome derived from different cell types in the treatment and regeneration of retinal cells.

REVIEWER 2

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: This manuscript arouses considerable interest especially towards the concept of immunomodulation and cross talk that the secretome develops. Congratulations to the authors.

Thank you very much for your comments.

Thank you for your kind attention, and I trust the paper is now in a suitable form for publication.
Yours sincerely

Dr. Simona Alibrandi

Department of Biomedical and Dental Sciences and Morphofunctional Imaging, Division of Molecular Genetics and Preventive Medicine, University of Messina, Messina, Italy