

Answers to the Editors and Reviewers

We are thankful the Editors and the reviewers for the opportunity to revise and improve our manuscript #: **67445**, entitled “**Retina stem cells, hopes and obstacles**”. We have complied with all the reviewers’ queries. We thank the Reviewers for their valuable suggestions, which have contributed to improve our manuscript. We hope that you will find it now suitable for publication in the World Journal of Stem Cells.

2 Peer-review report

Reviewer #1: In this review, the authors summarize the current findings of retina stem cells, including transplantation of stem cells into the eye to replace lost cells of retinal degeneration. Although this manuscript is interesting and well-documented, there are several issues that should be addressed in a revised manuscript. Comments:

1. The article reviewed the overview of stem cells, molecular regulation of stem cells, regeneration in the retina, different sources of retina stem cells and their potential risk. Thus, the reviewer thinks that the authors need to take an effort to improve logic and fluency in the manuscript. For example, the ‘INTRODUCTION’ and ‘Overview and Types of Stem Cells’ sections are not necessary, or these content can be briefly summarized into the ‘Preface’.

Answer: as recommended by the reviewer the Introduction, Overview and types of SC, have now been substantially reduced and included in the “Preface”.

Additionally, the reviewer suggests the authors may re-organize sections into the following subheadings: • Retinal Degeneration and Treatment • Stem Cells Therapy and Neural Regeneration • Stem Cells in Retinal Degeneration: Current Approaches • Therapeutic Efficacy and Mechanisms of Different Retina Stem Cells • Conclusions

Answer: we thank the reviewer by his/her recommendation. We have re-organized the manuscript into the suggested subheadings and deleted other subtitles.

2. A table used to briefly summarize the interventions of RSCs derived from different sources (RPCs, ESCs, PSCs, iPSCs, and MSCs, etc.) for treating retinal degeneration would be more helpful, especially including clinical trials.

Answer: as suggested by the reviewer, a new table (Table 1) showing the main interventions and clinical trials has been included in the new version of the MS.

3. The “Conclusion” section may be revised with some efforts. Please do not use subheading, but provide perspective or insights, and the content of ‘The pros and cons of current strategies for transplantation of SC in the retina’ summarized into several points would be better.

Answer: the “Conclusions” has been completely rewritten, as suggested by the reviewer.

4. Finally, if the Figures used or edited in this manuscript have been published elsewhere, the authors should obtain the permissions and correctly indicating the reference source and copyrights.

Answer: all the figures used are originals and made from scratch. Due to the requirement of WJSC to prepare all figures in Power point, we have now redesigned the previous version of the figures (1 to 5), which have been redone using Power point.

Additionally, Figure 4 was not cited in the text.

Answer: we apologize for the omission; former Figure 4 is the present Figure 5 and has been cited in the new version of the manuscript.

Reviewer #2: Manuscript: Retina stem cells, hopes and obstacles. The manuscript has provided a descriptive approach to several possible treatment

strategies for retina degeneration using different stem cells. The authors present the associated limitations as well as lack of evidence or studies. The manuscript is well written and instructive for a reader who wants to gain knowledge in the field. However, there are already published reviews that present the existing literature background in the field (e.g., Singh et al. 2019, Retinal stem cell transplantation: Balancing safety and potential). To avoid overlapping with the already published manuscript and make this manuscript original, the reviewer strongly recommends delving into the role of miRNA and lincRNA as future molecular targets since this topic is little explored and only mentioned in this manuscript.

Answer: we thank the reviewer by his/her recommendation. In the new version of the MS we have expanded the information on miRNAs and included a new section analyzing the roles of lincRNA as recommended.

The abstract summarized the review; nevertheless, the aim of the publication is completely missing. To provide the reader a better overview of the several stem cell types described and therapeutic efficacy achieved with the associated reference should be summarized in a table. Additionally, several references are missing in the whole manuscript (e.g., “However, humans have about 1011 neurons with different morphologies and multiple functions, making it nearly impossible to regenerate the brain as a whole.”)

Answer: as suggested by the reviewer, we have now rewritten the abstract to clearly indicate the aim of the manuscript. We have also added a new table (Table 1) summarizing the information regarding stem cell types and therapeutic efficacy, and included the missing references.

Minor comments: 1) Foreign words and only gene names should always be in italic (e.g., *in vivo*, *in vitro*, *et al.*) 2) There is inconsistency in the way of writing some abbreviations in the manuscript (e.g., SOX2, Sox2, SOX-2) 3) Abbreviation of BMP was clarified in the manuscript after the first used. 4) Several abbreviations used were not clarified (e.g., RPE and PHRs) or clarified twice (e.g., IL-6) 5) Several typos' mistakes (e.g., double spaces, double commas, missing period at the end of the sentence)

Answer: we apologize for the inconsistencies regarding gene names and abbreviations; we have now corrected them throughout the text, carefully checked and clarified abbreviations and corrected the typos.