

August 20, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 12940-edited.doc).

Title: Stem cell therapy for retinal diseases

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Name of Journal: World Journal of Stem Cells

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We are thankful for the review of our manuscript and for consideration of possible publication in WJSC. We, by point-by-point responses below, will provide reviewers answers. We very much appreciate consideration of our manuscript.

Reviewer 1:

The authors review the present strategies in retinal therapies based on stem cell strategies. This subject has been reviewed recently by Ng et al World J Stem Cells (2014) 6(2):111-9, although the present review is focused on retinal degeneration, and therefore is timely. The review is clear and well written, although some aspects of the format could be improved.

It would be interesting to include tables summarizing the therapeutic strategies discussed and the clinical trials. **A table is now included – Table 1.**

In key words, the authors should use "Stargardt's disease" instead of only "Stargardt's". **OK**

When more than one reference is listed together, the authors should put them under the same brackets i.e. (1, 2) instead of (1) (2). **OK**

Page 5. Hemorrhagic. **OK**

Page 6. Outer segment. **OK**

Page 8. Phagocytosis. **OK**

It would be interesting to include the ligands of MerTK in the retina (Mol Cell Neurosci. 2006 33:96-108; Neuron. 2012 76(6):1123-32). **Prasad D**, Rothlin CV, Burrola P, Burstyn-Cohen T, Lu Q, Garcia de Frutos P, Lemke G. TAM receptor function in the retinal pigment epithelium. Mol Cell Neurosci 2006; **33**(1): 96-108

The statement was inserted in the text: *The RCS rat is used in disorders involving the RPE, including AMD^[9, 10]. RCS rats have a defect in the RPE MerTK gene. Genetic studies have demonstrated that Mer is essential for RPE function, and its lack results in inherited phagocytosis defect of the photoreceptor outer segment, progressive photoreceptor degeneration and retinal atrophy within 2 months of birth^[1, 4, 14, 15]. The MerTK gene encodes a transmembrane tyrosine kinase, that is expressed by the RPE, and plays a role in signal transduction pathway involved in the phagocytosis of rod outer segments^[10]. Prasad et al, in 2006, demonstrated the action of Mer, suggesting that the Protein S is a biologically relevant ligand^[15]. These changes could be prevented or reversed by RPE transplantation in the RCS rat^[2].*

Page 11 induction of photoreceptor damage (or damage of the photoreceptors). **OK**

Page 12 gestational. **OK**

Page 13 rhodopsin instead of rhodopsinin. **OK**

Page 14 promising instead of promissing. **OK**

Page. 15 enhance not enhace. **OK**

In the final conclusion of the review, it would be interesting to know the opinion of the authors on the closing of the NIH stem cell programm, as it included clinical trials on retinal pathologies. **OK**

Inserted: *Most ocular stem cell translational studies are at early stages. Additional sources of funding are therefore imperative to maintain the research programs and integrate these basic and preclinical discoveries and launch early phase clinical trials within the coming years. Although the recent controversy involving changes in strategy planning and funding of the Center of Regenerative Medicine (CRM), from the US NIH, studies of SC therapy for macular degeneration will not be affected.*

Reviewer 2:

This is well written manuscript and I recommended for publication. The manuscript have sufficient details about target disease of stem cells in Opnthalmology field and describes well about current situation stem cell therapy in this field . The writing is acceptable.

1 Format has been updated. Comments from reviewer **00608332** were completely accepted

2 Revision has been made according to the suggestions of the reviewer

- (1) Yes
- (2) Yes
- (3) Yes
- (4) Yes
- (5) Yes
- (6) Yes

3 References and typesetting were corrected

We are than kful for the reviewe rs' comments and we are po sitive that all comments will im prove the scientific quality of our manuscript.

Sincerely yours,

Bruno Diniz, MD, PhD.