

Dear Editor:

I am submitting the revised manuscript titled " Cellular targets in diabetic retinopathy therapy" for possible publication in World Journal of Diabetes as a review paper. We have revised the manuscript in accordance with the referee' comments. We have added more information about PPARs as potential target. In addition, we have incorporated a summary table to capture the targets discussed and we have treated to highlight the importance of the ocular drug discovery for diabetic retinopathy in the conclusion section. We think that the manuscript has been significantly improved and thank the referee for the valuable comments.

The manuscript will not be submitted for publication elsewhere until a decision has been made as to its acceptability for the World Journal of Diabetes. Co-authors have read the revised manuscript and agreed to submission to the World Journal of Diabetes.

My co-authors and I thank you for considering our manuscript.

Sincerely,

Ángel Ortega.

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Reviewer comments:

*1. " this reviewer suggests the authors include a discussion on PPARs as they fit with the topic and are too important to leave out. A good place to tie them in may be when discussing WNT signaling, as it's known that PPAR agonism, for example, results in WNT signaling inhibition.."*

We thank the referee for the valuable comments on our manuscript. We have significantly revised and added a discussion on PPAR (from line 19- page 17 to line 2- page 18).

*2. " The authors should include graphics to help indicate how pathways discussed lead to disease and to illustrate places of intervention. Inclusion of such visuals would enhance the accessibility of this article tremendously. The authors should include a summary table/graphic towards the end to capture the targets discussed. Once again, this would be very helpful to the reader and will likely lead to a higher impact reference for researchers. The authors should include a section that expands upon the challenges associated with the targets proposed/covered"*

As the referee pointed out, the use of tables and graphics would be very helpful to the reader. We think that a summary table is more useful to visualize the different ocular alterations suffered in diabetes, cell targets, associated alterations and therapeutic approaches different from current treatments, for this reason we have prepared the table 1 and added two paragraphs in page 18, lines 3-8 and page 18 lines 28-30; page 19 lines 1-4

*3. " a section highlighting the challenges of ocular drug discovery in general is warranted. Is it possible for these targets to be accessed via systemic administration to alleviate complications with current approaches?"*

We have extended the conclusion about the main role of the discovery of treatments without side effects and of easy administration capable of preventing the development of the pathology.

*4. " Please proofread carefully, a number of typos and sentence structure errors are scattered throughout."*

We have corrected spelling errors and sentence structure errors throughout the manuscript.