Reviewer's report

Title: S1PR2 antagonist ameliorate high glucose-induced fission and dysfunction of mitochondria in HRGECs via regulating ROCK1

Version: 0 Date: 17 Jan 2019

Reviewer: Orestes Foresto-Neto

Reviewer's report:

In the present study, human glomerular endothelial cells were pretreated with the S1PR2 antagonist JTE-013 or the ROCK1 inhibitor Y27632, and exposed to a high-glucose milieu to investigate whether the S1PR2/ROCK1 plays a role in modulating mitochondrial morphology and function. The Authors showed that High glucose induced mitochondrial damage and endothelial dysfunction. Although interesting, the following points represent flaws, and need to be addressed:

Major

- In figure 1A and 3B, although the overall mitochondrial shape seems to be restored by the JTE-013 or Y27632 treatments, the low magnification pictures provided by the Authors make it difficult to observe the mitochondria cristae morphology. Larger magnification pictures would be helpful to elucidate whether the mitochondria are undergoing loss of cristae or are not. Better quality images should be provided for the figures 1D and 3D as well. The pictures provided do not match the graphs.

- In abstract: I suggest to the Authors to change "diabetic kidney disease" by "high glucose milieu" in Conclusion. The data provided do not support this conclusion.

- Authors should provide data regarding the mitochondrial outer membrane potential in the different groups (e.g. using tetramethylrhodamine ethyl ester dye). It would be helpful to understand the real role of the S1PR2/ROCK1 in harming the mitochondria integrity.
Minor

- Page 1, line 3 - lysophospholipid not "lysphospholipid".

- What was the software used to perform the statistical analysis?

- Figure 2D is not convincing. The RhoA WB provided does not match the graph.

- In page 12 "Moreover, the increased levels of cell permeability and apoptosis were markedly reduced and the level of migration was significantly elevated in the HG+JTE-013 group compared to the HG-treated group..", please review this sentence.

- The English quality sometimes undermines the understanding of the text.

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