Reviewer's report

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

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Reviewer: Ilse Daehn

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Chen et al. demonstrate that S1PR2 antagonism can prevent high glucose induced endothelial dysfunction associated with fission and dysfunction of mitochondria. They suggest that RhoA/ROCK1/Drp1 signaling pathway links S1PR2 and mitochondrial fission in high glucose treated endothelial cells. The experimental system is well defined, the experimental approach is adequate, however, some concerns need to be addressed:

Main concerns

Authors block S1PR2 and demonstrate benefits, particularly in mitochondrial function, in HG treated endothelial cells. However they need to demonstrate that S1P is indeed secreted by the cells under high glucose conditions and acting in paracrine manner. A time course would possibly justify the duration of HG exposure (72hr, which seems very long considering intervention was only for 30 minutes if I understand correctly)

The discussion is very superficial and basically reiterates the results without discussing them in the context of diabetes and its complications. Authors also need to discuss the potential mechanism driving S1P secretion and the possible implications for blocking it.

Is the cell death mechanism apoptosis? Ann/PI does not discriminate other forms of cell death. Caspase 3 should be measured.
Please confirm that you have included your review in the 'Comments to Author' box?
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