Author’s response to reviews

Title: Effects of concentration of amyloid β (Aβ) on viability of cultured retinal pigment epithelial cells

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Author’s response to reviews:

Dr. Guangde Tu
BMC Ophthalmology

Re: Ms. Ref. No.: BOPH-D-18-00556R1

February 15, 2019

Dear Dr. Tu,

Thank you for your comments and suggestions on our manuscript (BOPH-D-18-00556). We have revised our manuscript according to these comments.

The responses and changes are written in red fonts.

Reviewer 1

The rationale for the choice of AB-40 instead of 42 is stated in the rebuttal. These statements in the rebuttal should be incorporated into the Introduction (with more detail than exists in the current version). We believe that the 1-40 form is also very important. For example, Liu et al. demonstrated that NF-κB/RelA activation was enhanced in RPE cells after the stimulation of Aβ1-40 (Exp Eye Res. 2014 Oct;127:49-58). In addition, Sun et al. showed that intravitreally injected Aβ1-40 mice develop AMD-like pathologic changes (Cell Death Dis. 2017 Oct...
These findings suggested that Aβ1-40 plays important roles in the pathogenesis of AMD. As we mentioned, we believe that high concentrations of Aβ are important for the pathogenesis of AMD. Compared to other forms of Aβ, the concentration of Aβ1-40 is the highest among the different forms of Aβ (Invest Ophthalmol Vis Sci. 2010 Mar;51(3):1304-10.). That is why we chose Aβ 1-40 for this study. We have added comments and references about why the Aβ 1-40 was used in this study in the Discussion section.

Answer: We have added more text on Aβ 1-40 and references on why Aβ 1-40 was used in this study in the Introduction (Background) section.

Pg 19 lines 14-17: The sentence ('This represents atrophy....') represents an unjustified leap! This is an in vitro study, as indicated earlier. That statement is unjustified, and not supported. Please remove.

Answer: We have removed this sentence from the Discussion section.

Pg 20 lines 27-30: 'Cross talk between RPE cells and choroidal cells' has not been investigated here. The sentence 'But cross talk between the RPE cells and choroidal cells has not been conclusively determined.' needs revision or re-wording.

Answer: We have revised this sentence.

Reviewer #2

The study is solely based on in vitro approach in which RPE culture is the main target. Although RPE dysfunction is crucial in the pathogenesis of AMD, choroidal endothelial cells may also play an important role. It would be interesting to dissect the potential role of Ab in the cross talk between RPE and choroidal endothelial cells particularly with the increased VEGF expression by Ab.

- There was no real functional assessment of RPE, instead the study focused on molecular changes. It would be interesting of the investigators considered studying, RPE barrier or phagocytic function.

Answer: We have revised this sentence as suggested.

We thank the reviewers for the helpful comments and hope that we have now produced a more balanced and better account of our work.

Sincerely,
Nahoko Ogata, MD, PhD