

Peer Review File

Article information: <https://dx.doi.org/10.21037/aes-21-17>

Reviewer 1:

Comments:

This review addresses the use of the amniotic membrane for the treatment of AMD. The review is well written and easy to follow. They have searched Pubmed database for keywords like "amniotic membrane" and "AMD". Additional articles were selected based on reference lists on included studies.

1. I would suggest to add references from Ben M'Barek et al (2017 and 2020) as it is the first studies using hAM as a substrate for RPE cells derived from human pluripotent stem cells even if the indications are not AMD but retinitis Pigmentosa. It shows the feasibility of using this substrate in retinal diseases and a clinical trial is in progress.

Reply 1:

Dear Reviewer,

Thanks for the suggestion, however, what has been investigated in the studies of Ben M'Barek et al has been more on the role of this layer as a substrate for cell transport into the sub-retinal space and the role of this layer per se has not been evaluated. However, we have added the most relevant content to this title in the text.

Changes in the text:

"It has been disclosed that RPE cell sheets on human amniotic membrane transplanted into the eyes has some advantages compared to injection RPE cell suspension into the vitreous cavity. Secreting more growth factors and cytokines makes RPE cells more resistant to oxidative damage that can lead to cell death. The human amniotic membrane also acts like Bruch membrane which is damaged in some types of ARMD. These may be the reasons for better visual acuity in this group of eyes.(35)"

Reviewer 2:

Comments:

This manuscript has aimed at reviewing the suitability of amniotic membranes on the therapy of age-related macular degeneration (AMD). While the idea is interesting, the manuscript contains some concerns. Please, find detailed comments below.

1. It should be clearly stated in the Introduction/Background to which form of age-related macular degeneration (AMD) amniotic membrane therapy is intended.

Reply 1:

Dear reviewer,

I appreciate you mentioning the points you highlighted. We stated many times in the text that the early form of the disease does not need treatment. However, for clarity, when it is necessary, we also mentioned the type of disease in the text.

2. Many large topics remain very superficial. For example the summary of AMD mechanisms is succinct and in order to show the efficacy of amniotic membranes. Mechanisms should be opened in more detail and then point out how amniotic membrane regulates them.

Reply 2:

Considering that this disease pathophysiology and the mechanisms of amniotic membranes are not fully understood and according to the structure of this article, the related topics that fall within the scope of the article but are not beyond it are divided among the sections. Nonetheless, we added a few points regarding this disease's mechanism.

Changes in the text:

"Role of the RPE & Bruch membrane in ARMD"

3. The manuscript would greatly benefit from language revision by a native English speaker.

Reply 3: I did it.

4. Attention should be paid also to terminology; for example, RPE cells are not included in the central nervous system.

Reply 4: we checked and edit this point.

5. Moreover, the text is partially list-like and references are missing. All facts/claims/mentions must be equipped with proper references.

Reply 5: All items that need reference, checked.