

PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

Manuscript NO: 62628

Title: The Malfunction of Outer Retinal Barrier and Choroid in the Occurrence and Progression of Diabetic Macular Edema

Reviewer's code: 05691230

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Portugal

Author's Country/Territory: Romania

Manuscript submission date: 2021-01-13

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-01-13 22:38

Reviewer performed review: 2021-01-29 20:06

Review time: 15 Days and 21 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

A review focusing on the role of the outer retinal barrier in diabetic macular edema is of utmost importance. However, the paper does not focus just on this topic but rather on retinal and choroidal biomarkers in diabetic retinopathy. Either the content or the title and purpose should be changed. It features the most biomarkers on this topic, but some specifications should be addressed and some changes are necessary:

RPE-PR complex: the findings of a thickened RPE in diabetic patients may also be a consequence of impaired glycogen metabolism and accumulation inside the RPE in diabetic patients as shown in this paper (<https://pubmed.ncbi.nlm.nih.gov/24458975/>)

Choroidal thickness (CT) in patients with DR. This is a highly unreliable variable and multiple studies show different results. Better studies should be cited. The conclusion of this section shows that CT does not seem to be a good biomarker. There is a thorough review about this (<https://pubmed.ncbi.nlm.nih.gov/27545332/>)

In patients **Choroidal vascular index (CVI)** in patients with DM. There are more important references regarding CVI in DR, namely <https://pubmed.ncbi.nlm.nih.gov/28988899/> that performed a volumetric analysis. There are also studies analyzing CVI after treatment with anti-VEGF, like <https://pubmed.ncbi.nlm.nih.gov/29492689/>. I would recommend adding this paper using indocyanine angiography showing early areas of choroidal hypoperfusion in DR, years before the recent studies with OCT (<https://pubmed.ncbi.nlm.nih.gov/9727518/>)

A section about the use of OCT-A to evaluate the outer RBB is important. <https://pubmed.ncbi.nlm.nih.gov/30810284/>

Laboratory studies that studied the outer BRB should be included. Several times along the text it is stated that the outer BRB separates the neural retina from the underlying choriocapillaris. In fact, the outer BRB separates the retinal pigmented epithelium (which is not considered part of the neural retina) from the underlying



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choriocapillaris.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Author's Country/Territory: Romania

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Reviewer chosen by: Han Zhang (Part-Time Editor)

Reviewer accepted review: 2021-02-27 12:21

Reviewer performed review: 2021-03-02 03:26

Review time: 2 Days and 15 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The manuscript fills publication criteria