

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 67394

Title: Recombinant Angiopoietin-Like Protein 4 Attenuates Intestinal Barrier Structure and Function Injury after Ischemia/Reperfusion.

Reviewer's code: 05532596

Position: Peer Reviewer

Academic degree: MD

Professional title: Assistant Professor, Consultant Physician-Scientist

Reviewer's Country/Territory: Mexico

Author's Country/Territory: China

Manuscript submission date: 2021-04-24

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-05-15 12:21

Reviewer performed review: 2021-05-20 04:13

Review time: 4 Days and 15 Hours

Scientific quality	[<input checked="" type="checkbox"/>] Grade A: Excellent [<input 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] Grade E: Do not publish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 checked="" type="checkbox"/>] Accept (High priority) [<input type="checkbox"/>] Accept (General priority) [<input type="checkbox"/>] Minor revision [<input 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



**Baishideng
Publishing
Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

SPECIFIC COMMENTS TO AUTHORS

First i would like to compliment the authors, as their work offers valuable information on the use of rh ANGPTL4 in the preservation of the intestinal barrier structure and it's function. Review: The manuscript is very well written and organized. Nonetheless there are a few typos in the manuscript that need to be corrected before publication. line 51: "Almost recently, studies indicated patients who suffered coronavirus disease 2019 (COVID-19) associated with intestinal hypoperfusion which may further deteriorate barrier dysfunction and acute lung injury by a positive feedback mechanism". Change to: Almost recently, studies indicated patients who suffered coronavirus disease 2019 (COVID-19) associated with intestinal hypoperfusion which may further deteriorate barrier dysfunction and acute lung injury by a positive feedback mechanism Line 269: "intestinal mucusal", change to: intestinal mucosal Line 351: "lessons the autophagy" change to: lessens the autophagy Line 357: "oxidatation" change to: oxidation. Line 432: "induction of autpophagy" change to: induction of autophagy Line 495: "rhANGPTL4 can lesson I/R injury", change to: rhANGPTL4 can lessen I/R injury. I recommend this manuscript for publication.

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Name of journal: World Journal of Gastroenterology

Manuscript NO: 67394

Title: Recombinant Angiopoietin-Like Protein 4 Attenuates Intestinal Barrier Structure and Function Injury after Ischemia/Reperfusion.

Reviewer's code: 03475142

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Assistant Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: China

Manuscript submission date: 2021-04-24

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-05-12 16:55

Reviewer performed review: 2021-05-23 10:11

Review time: 10 Days and 17 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" 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

The manuscript was reviewed for publication in the journal. The manuscript was designed to evaluate whether rhANGPTL4 may protect intestinal barrier breakdown induced by I/R. The results obtained showed that rhANGPTL4 can lesson I/R injury by preserving intestinal barrier structure and function. It is the reviewer's opinion that the manuscript is easy to follow. However, it appears that there are a couple of concerns in the manuscript.

- 1) Recombinant human ANGPTL4 was used in a rat model of intestinal I/R in the study. How about the similarity compared to rat ANGPTL4? The authors used 28 mg/kg body of rhANGPTL4. Is this concentration based on the previous study? The authors should discuss the issue.
- 2) Intestinal mucosal barrier function was assessed by mucosal-to-serosal clearance of FITC-conjugated dextran (FD-4) in everted intestinal ileal sacs incubated ex vivo. How long incubated? What is the concentration of FD-4? The intestinal I/R model (60 minutes of ischemia followed by 240 minutes of reperfusion) appears to be severe. Is the assessment of intestinal permeability appropriate for the intestinal I/R model? The authors should explain/discuss the issue.
- 3) Figure 2A needs scale bar. Intestinal scores were also shown in Figure 2. Each score should be shown as a dot spot in different groups. Also, different statistical analysis should be considered.
- 4) The authors have assessed the effects of rhANGPTL4 on the apoptosis and autophagy induced by intestinal I/R. After all, which effect is much important? The authors should discuss the issue.
- 5) Figure 7A needs scale bar. The effects of si Angptl4 and rh Angptl4 were shown in Figure 7 and Figure 8, respectively. How about the effect of rh Angt4 on H/R-induced si-ANGPTL4 cells? The authors should discuss the issue.
- 6) Figure 9 showed that rhAngptl4 restored the VE-cadherin in HUVECs after H/R and VE-cadherins level. Is there any reason for the experiment? How about the role of VE-cadherin in the rat study? The authors should explain the



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7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
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issue. 7) In abstract, line 7: radio-induced? In abstract, line 13: VE-cad were significantly increased after intestinal I/R. No data of VE-cad in vivo study? In manuscript and figure, si Angptl4 or siANGPTL4 and rhANGPTL4 or rhAngptl4 were used.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Reviewer's code: 05532596

Position: Peer Reviewer

Academic degree: MD

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Reviewer's Country/Territory: Mexico

Author's Country/Territory: China

Manuscript submission date: 2021-04-24

Reviewer chosen by: Han Zhang (Online Science Editor)

Reviewer accepted review: 2021-06-29 18:40

Reviewer performed review: 2021-06-29 18:45

Review time: 1 Hour

Scientific quality	<input checked="" type="checkbox"/> Grade A: Excellent <input 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 checked="" type="checkbox"/> Accept (High priority) <input 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

First i would like to compliment the authors for their work. The manuscript is suitable for publication.