PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes
Manuscript NO: 93578
Title: Intestinal GLP-1: A new player associated with impaired counterregulatory responses to hypoglycaemia in type 1 diabetic mice
Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed
Peer-review model: Single blind
Reviewer’s code: 03830173
Position: Editorial Board
Academic degree: MD, PhD
Professional title: Associate Professor, Doctor
Reviewer’s Country/Territory: Croatia
Author’s Country/Territory: China
Manuscript submission date: 2024-03-01
Reviewer chosen by: AI Technique
Reviewer accepted review: 2024-04-05 10:40
Reviewer performed review: 2024-04-05 11:11
Review time: 1 Hour

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<tr>
<th>Scientific quality</th>
<th>[ ] Grade A: Excellent</th>
<th>[ ] Grade B: Very good</th>
<th>[ ] Grade C: Good</th>
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<td></td>
<td>[ ] Grade D: Fair</td>
<td>[ ] Grade E: Do not publish</td>
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<tr>
<th>Novelty of this manuscript</th>
<th>[Y] Grade A: Excellent</th>
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<td>[ ] Grade D: No novelty</td>
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<th>Creativity or innovation of this manuscript</th>
<th>[Y] Grade A: Excellent</th>
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SPECIFIC COMMENTS TO AUTHORS
Dear Authors, I have read your manuscript with great interest. It is a very comprehensive basic study covering endocrine and paracrine changes in response to hypoglycemia (recurrent and occasional) in T1DM mice model. In specific, the role of GLP-1 and GLP-1R expression in intestinal cells as a response to two distinct hypoglycemia settings was covered. The results suggest the importance of GLP-1 in the development of hypoglycemia unawareness. The mentioned findings have enormous clinical relevance; in specifics related to the use of GLP-1RA in type 1 DM patients and their potential to influence the endocrine response to hypoglycemia. As a clinician I would be very interested in the findings in human studies. In specifics; I would like to know if the authors have results on responses to hypoglycemia in the 2 experimental hypoglycemia mouse models regarding the time of day- i.e. nocturnal hypoglycemia. And if yes, to comment it in the Manuscript.
Name of journal: World Journal of Diabetes

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Title: Intestinal GLP-1: A new player associated with impaired counterregulatory responses to hypoglycaemia in type 1 diabetic mice

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 02461627

Position: Peer Reviewer

Academic degree: PhD

Professional title: Professor

Reviewer’s Country/Territory: United Arab Emirates

Author’s Country/Territory: China

Manuscript submission date: 2024-03-01

Reviewer chosen by: Ming Fan

Reviewer accepted review: 2024-05-14 02:21

Reviewer performed review: 2024-05-21 01:23

Review time: 6 Days and 23 Hours

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SPECIFIC COMMENTS TO AUTHORS
The manuscript entitled “Intestinal GLP-1: a new player associated with impaired counter regulatory responses to hypoglycemia in type 1 diabetic mice” showed an increased level of expression of intestinal GLP-1 and GLP-1R in DH5 mice. Authors then demonstrated that consecutive excess of intestinal GLP-1 weakened the sympathetic-adrenal reflex, leading to dysfunction of the adrenal counter-regulation during hypoglycemia. In addition, expression of GLP-1R in islet cells and levels of plasma active GLP-1 were significantly increased in the DH5 group. Authors finally demonstrated that in model mice the intestinal GLP-1 during recurrent hypoglycemia hindered the secretion of the counter-regulatory hormone glucagon via the endocrine pathway. One major concern is the lack of in vitro validation to provide a more detailed insights into the mechanism. Other comments • Rigorous proofreading is needed. • An abbreviation list should be added. One example, what does “DH” refer to? • Animal research ethics approval is missing. The cited “SCXK (Lu) 20200001” does not seem to be an approval number. • The manuscript does not have an abstract. • Uncropped gels of the western blots should be provided as supplementary document. • Abbreviations list
should be added. • Images in fig 2A are not quite representative of the otherwise clear quantified effects. Replace with more representative images. • References should be enriched and updated with more diversified investigations that discuss relevant pathways in greater depth.
RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Reviewer’s code: 02461627

Position: Peer Reviewer

Academic degree: PhD

Professional title: Professor

Reviewer’s Country/Territory: United Arab Emirates

Author’s Country/Territory: China

Manuscript submission date: 2024-03-01

Reviewer chosen by: Li Li

Reviewer accepted review: 2024-06-06 13:55

Reviewer performed review: 2024-06-06 14:07

Review time: 1 Hour

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<td>[ ] Grade D: No creativity or innovation</td>
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<tr>
<td>Scientific significance of the conclusion in this manuscript</td>
<td>[ ] Grade A: Excellent</td>
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<tr>
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<td>[ ] Grade A: Priority publishing</td>
<td>[ ] Grade B: Minor language polishing</td>
<td>[ ] Grade C: A great deal of language polishing</td>
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<tr>
<td>Conclusion</td>
<td>[ ] Accept (High priority)</td>
<td>[ ] Accept (General priority)</td>
<td>[ ] Minor revision</td>
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<td>Peer-reviewer statements</td>
<td>Peer-Review: [ ] Anonymous</td>
<td>[ ] Onymous</td>
<td>Conflicts-of-Interest: [ ] Yes</td>
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**SPECIFIC COMMENTS TO AUTHORS**
This reviewer's comments have not been sufficiently addressed.
RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Reviewer’s Country/Territory: Croatia

Author’s Country/Territory: China

Manuscript submission date: 2024-03-01

Reviewer chosen by: Li Li

Reviewer accepted review: 2024-06-09 17:38

Reviewer performed review: 2024-06-10 18:30

Review time: 1 Day

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Scientific significance of the conclusion in this manuscript

[ ] Grade A: Excellent  [Y] Grade B: Good  [ ] Grade C: Fair
[ ] Grade D: No scientific significance

Language quality

[ Y] Grade A: Priority publishing  [ ] Grade B: Minor language polishing  [ ] Grade C: A great deal of language polishing  [ ] Grade D: Rejection

Conclusion

[ ] Accept (High priority)  [Y] Accept (General priority)
[ ] Minor revision  [ ] Major revision  [ ] Rejection

Peer-reviewer statements

Peer-Review: [ Y] Anonymous  [ ] Onymous
Conflicts-of-Interest: [ ] Yes  [Y] No

SPECIFIC COMMENTS TO AUTHORS
The Authors have addressed the raised comments, which improved the Manuscript quality.