

21.08.2024

Dear Editor,

Thank you very much for your work in revising our paper submitted as an Editorial to *World Journal of Diabetes*.

Title: Targeting neuronal PAS domain protein 2 and KN motif/ankyrin repeat domains 1: Advances in type 2 diabetes therapy

Authors: Chun-Han Cheng, Wen-Rui Hao, Tzu-Hurng Cheng

Manuscript NO: 99387

We would like to thank the Reviewer for providing comments regarding our manuscript.

Peer-review report(s). Authors must resolve all issues in the manuscript that are raised in the peer-review report(s) and provide point-by-point responses to each of the issues raised in the peer-review report(s):

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors:

In this editorial article, the functions of NPAS2 and KANK1 in type 2 diabetes (T2D) were examined. Their potential as therapeutic targets and their role in β -cell dysfunction, along with the implications for novel therapeutic approaches, were highlighted. The study's understanding of cellular processes and gene regulation provides encouraging avenues for enhancing T2D management through focused therapies. I have the following comments for authors: 1) The topic is important in the research on diabetes; insert a figure that illustrates that. It is recommended that the figure also explain the role of Kanki and their relationship. 2) The language is fine with the exception of three notices: please remove one comma from the first page, line 7, the word new from the first line of the introduction, and replace "for" with "to" on line 7, page 5. The introduction is recommended to be changed as follows: The ongoing fight against type 2 diabetes (T2D) has recently gained momentum with discoveries about the genetic and molecular underpinnings of this widespread disease. A pivotal study by Yin et al. in the *World Journal of Diabetes* has highlighted the significance of the transcription factor NPAS2 (neuronal PAS domain protein 2) and its downstream target KANK1 (KN motif and ankyrin repeat domain 1) in the dysfunction of pancreatic β -cells, a key event in the development of T2D [1]. Since β -cell dysfunction is central to T2D pathogenesis, a deeper understanding of these regulatory mechanisms is crucial for advancing therapeutic approaches. NPAS2 is a component of the circadian clock system, influencing various physiological processes, including glucose metabolism [2]. Its role in β -cell

function and insulin secretion has opened new avenues for diabetes research. The study by Yin et al. demonstrates how NPAS2 modulates KANK1 expression, thereby affecting the structural and functional integrity of β -cells. KANK1 plays a critical role in maintaining cell adhesion and cytoskeletal dynamics, which are essential for β -cell function [3]. The interaction between KANK1 and focal adhesion proteins influences the stability and organization of microtubules and actin filaments, thereby impacting insulin secretion [4]. Changes in KANK1 expression can cause disruption in these processes, which can result in β -cell malfunction and accelerate the development of type 2 diabetes. The purpose of this editorial is to place these findings within the larger framework of diabetes research. We can gain a better understanding of NPAS2 and KANK1's potential influence on upcoming T2D treatment approaches by investigating their complex pathways. Yin et al.'s work emphasises how crucial it is to focus on these molecular pathways to maintain β -cell function and enhance diabetic outcomes. The last part of conclusion is recommended to be changed as follows: Utilizing these molecular connections, new therapeutic approaches that specifically improve β -cell resilience can be created. These genetic and molecular interactions should be further investigated in the future, with an emphasis on how they might be altered to provide more precise and potent T2D treatments. As we learn more about the NPAS2-KANK1 pathway and its wider effects, the possibility of developing novel therapies that profoundly enhance the quality of life for people with type 2 diabetes grows. This strategy has the potential to not only maintain β -cell function but also to create all-encompassing plans for improved diabetes control [5, 6].

Reply:

We would like to express our sincere gratitude for your thoughtful and constructive feedback on our editorial article. Your insights have been invaluable in helping us refine and improve our manuscript. We have carefully addressed each of your comments as follows:

1. Figure Inclusion:

We agree that a figure illustrating the functions and relationship between NPAS2 and KANK1 in type 2 diabetes (T2D) will enhance the clarity of the manuscript. As per your suggestion, we have added a figure that visually represents the role of NPAS2 in regulating KANK1 and how these interactions influence β -cell dysfunction, which is central to the development of T2D. This figure is designed to provide readers with a clear understanding of the topic's importance in diabetes research.

2. Language Revisions:

We have made the minor language corrections you suggested:

Removed the comma from the first page, line 7.

Deleted the word "new" from the first line of the introduction.

Replaced "for" with "to" on line 7, page 5.

3. Introduction Revision:

Thank you for the suggested revision to the introduction. We have updated the introduction according to your recommendations, which has strengthened the manuscript's focus on the relevance of NPAS2 and KANK1 in the pathogenesis of T2D and the potential for targeted therapies. The revised introduction now better highlights the importance of these molecular pathways in maintaining β -cell function and advancing diabetes treatment.

4. Conclusion Revision:

We have also incorporated your suggested revisions to the conclusion. The updated conclusion emphasizes the potential for new therapeutic strategies that enhance β -cell resilience through the targeted modulation of NPAS2 and KANK1 pathways. It underscores the significance of further research into these molecular interactions to develop more precise and effective treatments for T2D.

We believe these revisions have significantly improved the manuscript and aligned it with your valuable suggestions. We hope that the revised version meets your expectations and look forward to your feedback. Thank you once again for your thorough review and constructive suggestions.

Editorial Office's comments. Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are provided below:

(1) Science Editor:

1 Scientific quality: The authors submitted an editorial of the new insights in type 2 diabetes therapy.

(1) Classification: Grade B;

(2) Summary of the Peer-Review Report: The manuscript needs to be supplemented with images, language polished, and the introduction and conclusion modified. The questions raised by the reviewers should be answered;

(3) References recommendations: The reviewer didn't request the authors to cite improper references published by him/herself.

(4) Manuscript Type: After verification, the manuscript type is "Editorial".

2 Specific comments

(1) Country/Territory of origin: China

(2) The language classification is Grade B. Please provide the latest Language certificate after Return the Manuscript to Author for Revision. Please visit the following website for the professional English language editing companies that we recommend: <https://www.wjgnet.com/bpg/gerinfo/240>.

(3) Manuscript Title:

The title should not include any abbreviations.

(4) Policy of allowing co-first authors and co-corresponding authors who made equal contribution to a manuscript

(<https://www.wjgnet.com/bpg/GerInfo/310>).

Please do not use abbreviations for the keywords (e.g., Ulcerative colitis, not UC).

(5) Reference numbers in the main text.

The name of the author(s) of a reference is listed in the sentence, the reference number should be placed immediately after the author(s) of the reference.

Example: Mandal et al[8] proposed that retractor aponeurosis disinsertion is the most likely cause of congenital low lid entropion.

(6) The author(s) must add a table/figure to the manuscript. There are no restrictions on the figures (color, B/W) and tables.

3 Recommendation: Conditional acceptance.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade B (Very good)

Reply:

Thank you for your comprehensive feedback and the conditional acceptance of our manuscript. We appreciate the guidance provided, and we have carefully addressed each of your comments as follows:

1. Scientific Quality and Revisions

We have made the necessary revisions to enhance the manuscript based on the reviewer's suggestions:

- **Images and Figures:** We have supplemented the manuscript with a figure that illustrates the roles of NPAS2 and KANK1 in type 2 diabetes, highlighting their interaction and impact on β -cell dysfunction.
- **Language Polishing:** The manuscript has undergone further language polishing, and we have made minor corrections as recommended by the reviewer.
- **Introduction and Conclusion:** Both the introduction and conclusion have been revised to better reflect the significance of NPAS2 and KANK1 in type 2 diabetes therapy and to align with the reviewer's suggestions.

2. Language Certificate:

- We have arranged for a professional English language editing service, and provided the latest Language Editing Certificate upon the return of the manuscript.

3. Manuscript Title and Keywords:

- **Title:** We have revised the manuscript title to eliminate abbreviations, in compliance with your guidelines. The new title is: "Targeting neuronal PAS domain protein 2 and KN motif/ankyrin repeat domains: Advances in type 2 diabetes therapy."
- **Keywords:** We have ensured that the keywords do not include any abbreviations, as requested.

4. Reference Formatting:

- We have ensured that all reference numbers in the main text are placed immediately after the authors' names when mentioned, in accordance with the journal's citation style.

5 Figures and Tables:

- A figure has been added to the manuscript, providing a visual representation of the critical points discussed. This inclusion aligns with the recommendation to enhance the manuscript's comprehensibility.

We appreciate your recommendation for conditional acceptance and have worked diligently to address all the points raised. We hope these revisions meet the journal's standards and look forward to your feedback. Thank you for your consideration.

(2) Company Editor-in-Chief:

本篇手稿有一个好的同行评议意见。请科学编辑继续送同行评议人。谢谢！

Reply:

尊敬的主编，感谢您对我们手稿的审阅和宝贵意见。我们很高兴得知手稿获得了良好的同行评议意见，并感谢您安排进一步的同行评议。我们已根据审稿人的反馈进行了一系列修订，包括图表的添加、语言的润色以及引言和结论的修改。我们希望这些修改能够提高手稿的质量，并期待您的进一步指导。再次感谢您和科学编辑的帮助与支持！

Through the F6 release system, we have uploaded the following files:

- (1) 99387-Manuscript File
- (2) 99387-Answering Reviewers
- (3) 99387-Audio Core Tip
- (4) 99387-Conflict-of-Interest Disclosure Form
- (5) 99387-Copyright License Agreement
- (6) 99387-Approved Grant Application Form(s) or Funding Agency Copy of any Approval Document(s)
- (7) 99387-Non-Native Speakers of English Editing Certificate
- (8) 99387-Video
- (9) 99387-Image File
- (10) 99387-Table File
- (11) 99387-Supplementary Material
- (12) 99387-Similarity Report Generated by iThenticate
- (13) 99387-Checklist for Authors to Revise a Manuscript

Thank you again for publishing our manuscript in *World Journal of Diabetes*.

Yours sincerely,

Tzu-Hung Cheng