

Dear Editors and Reviewers,

On behalf of my co-authors, I am re-submitting the revisions “miR-124 is upregulated in diabetic mice and inhibits proliferation and promotes apoptosis of high-glucose-induced β -cells by targeting EZH2”, for possible publication on the *World Journal of Diabetes*. The manuscript (Manuscript NO.79357, Basic Study) had been revised carefully responding to the reviewers' comments one by one, and the related questions had been carefully replied as following:

Reviewer #1:

Scientific Quality: Grade A (Excellent)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

Specific Comments to Authors: The manuscript entitled "miR-124 was upregulated in diabetic mice and inhibited proliferation and promote apoptosis of high glucose-induced β -cells by targeting EZH2" is a preclinical study that explores targeting of miR-124 and enhancer of zeste homolog 2 (EZH2) in pancreatic tissues of diabetic mice to inhibit apoptosis of the β -cells of pancreas. The overall comments to the authors is as follows: 1) What is the reference for using a Streptozotocin dose of 45 mg/kg to induce type-2 diabetes mellitus? 2) The authors considered a FBG above 16.7 mmol/L (300 mg/dL) as a cutoff for T2DM. This cutoff seems to be too high. Overall the results are extremely insightful and must be considered for publication.

Reply:

Thanks very much for the comments of the reviewers.

1) The dose of streptozotocin was referred to the related literature : Xiang Z, Xie H, Tong Q, Pan J, Wan L, Fang J, Chen J. Revealing hypoglycemic and hypolipidemic mechanism of Xiaokeyinshui extract combination on streptozotocin-induced diabetic mice in high sucrose/high fat diet by metabolomics and lipidomics. *Biomed Pharmacother* 2021; 135:111219 [PMID: 33433360 DOI:10.1016/j.biopha.2021.111219], which had been cited in the manuscript and included in the list of references.

And “a Streptozotocin dose of 45 mg/kg to induce type-2 diabetes mellitus” was also reported in the article of Ren et al [Ren Z, Yang Z, Lu Y, Zhang R, Yang H. Anti- glycolipid disorder effect of epigallocatechin-3- gallate on high- fat diet and STZ- induced T2DM in mice. *Mol Med Rep*. 2020 Jun;21(6):2475-2483. doi: 10.3892/mmr.2020.11041].

2) The FBG above 16.7 mmol/L (300 mg/dL) as a cutoff for T2DM was supported by the references [①Li D, Jiang C, Mei G, Zhao Y, Chen L, Liu J, Tang Y, Gao C, Yao P. Quercetin Alleviates Ferroptosis of Pancreatic β Cells in Type 2 Diabetes. *Nutrients*. 2020 Sep 27;12(10):2954. doi: 10.3390/nu12102954. ② Xu L, Li Y, Yin L, Qi Y, Sun H, Sun P, Xu M, Tang Z, Peng J. miR-125a-5p ameliorates hepatic glycolipid metabolism disorder in type 2 diabetes mellitus through targeting of STAT3. *Theranostics*. 2018 Nov 9;8(20):5593-5609. doi: 10.7150/thno.27425].

The reference had been added and highlighted in the manuscript.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: The original findings of this manuscript is that miR-124 is highly expressed in diabetic mice and HG-induced Min6 cell, miR-124 regulates insulin secretion, proliferation and apoptosis of islet β cells by targeting EZH2. The study used HE staining、Immunohistochemistry、Cell culture、ELISA、Flow cytometry、RT-qPCR、Western blot、Double luciferase reporter assay to verify their hypotheses. The title reflect the main hypothesis of the manuscript. The abstract and key words summarize and reflect the work. The background of this manuscript adequately describe the present status and describe methods in adequate detail. The research objectives achieved by the experiments used in this study. The discussion of this manuscript interpret the findings adequately and appropriately, but the limitations of the study should be more fully discussed.

Reply: Thanks for the comments of the reviewer. According to the suggestions from the reviewer, the limitation of the study had been added in the conclusion section of manuscript, and highlighted.

About the language quality: The revised manuscript had been sent to Charlesworth Author Services (<https://www.cwauthors.com/>) to polish the language of the manuscript. The manuscript had been revised according to the note of modification.

4 LANGUAGE POLISHING REQUIREMENTS FOR REVISED MANUSCRIPTS SUBMITTED BY AUTHORS WHO ARE NON-NATIVE SPEAKERS OF ENGLISH

As the revision process results in changes to the content of the manuscript, language problems may exist in the revised manuscript. Thus, it is necessary to perform further language polishing that will ensure all grammatical, syntactical, formatting and other related errors be resolved, so that the revised manuscript will meet the publication requirement (Grade A).

Authors are requested to send their revised manuscript to a professional English language editing company or a native English-speaking expert to polish the manuscript further. When the authors submit the subsequent polished manuscript to us, they must provide a new language certificate along with the manuscript.

Once this step is completed, the manuscript will be quickly accepted and published online. Please visit the following website for the professional English language editing companies we recommend: <https://www.wjgnet.com/bpg/gerinfo/240>.

Reply: The revised manuscript had been sent to a professional English language editing company(Charlesworth Author Services: <https://www.cwauthors.com/>) to polish the manuscript further. The manuscript had been revised according to the note

of modification, and the new language certificate along with the manuscript was also uploaded in the system.

5 ABBREVIATIONS

In general, do not use non-standard abbreviations, unless they appear at least two times in the text preceding the first usage/definition. Certain commonly used abbreviations, such as DNA, RNA, HIV, LD50, PCR, HBV, ECG, WBC, RBC, CT, ESR, CSF, IgG, ELISA, PBS, ATP, EDTA, and mAb, do not need to be defined and can be used directly.

The basic rules on abbreviations are provided here:

(1) Title: Abbreviations are not permitted. Please spell out any abbreviation in the title.

(2) Running title: Abbreviations are permitted. Also, please shorten the running title to no more than 6 words.

(3) Abstract: Abbreviations must be defined upon first appearance in the Abstract. Example 1: Hepatocellular carcinoma (HCC). Example 2: *Helicobacter pylori* (H. pylori).

(4) Key Words: Abbreviations must be defined upon first appearance in the Key Words.

(5) Core Tip: Abbreviations must be defined upon first appearance in the Core Tip. Example 1: Hepatocellular carcinoma (HCC). Example 2: *Helicobacter pylori* (H. pylori)

(6) Main Text: Abbreviations must be defined upon first appearance in the Main Text. Example 1: Hepatocellular carcinoma (HCC). Example 2: *Helicobacter pylori* (H. pylori)

(7) Article Highlights: Abbreviations must be defined upon first appearance in the Article Highlights. Example 1: Hepatocellular carcinoma (HCC).

Example 2: *Helicobacter pylori* (H. pylori)

(8) Figures: Abbreviations are not allowed in the Figure title. For the Figure Legend text, abbreviations are allowed but must be defined upon first appearance in the text. Example 1: A: Hepatocellular carcinoma (HCC) biopsy sample; B: HCC-adjacent tissue sample. For any abbreviation that appears in the Figure itself but is not included in the Figure Legend textual description, it will be defined (separated by semicolons)

at the end of the figure legend. Example 2: BMI: Body mass index; US: Ultrasound.

(9) Tables: Abbreviations are not allowed in the Table title. For the Table itself, please verify all abbreviations used in tables are defined (separated by semicolons) directly underneath the table. Example 1: BMI: Body mass index; US: Ultrasound.

Reply: The abbreviations had been revised and checked in the manuscript according to the requirements.

6 EDITORIAL OFFICE'S COMMENTS

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

(1) Science editor:

The manuscript has been peer-reviewed, and it's ready for the first decision.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade B (Very good)

Reply: The revised manuscript had been sent to a professional English language editing company (Charlesworth Author Services: <https://www.cwauthors.com/>) to polish the manuscript further. The language of the manuscript had been revised according to the note of modification, and the new language certificate along with the manuscript was also uploaded in the system.

And according to the comments of the reviewers, the manuscript had been revised and the queries had been replied one by one.

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Diabetes, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Before final acceptance, uniform presentation should be used for figures showing the same or similar contents; for example, "Figure 1 Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...". Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2022. Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the Reference Citation Analysis (RCA). RCA is an

artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: <https://www.referencecitationanalysis.com/>.

Reply: The decomposable Figures (all components are movable and editable) had been provided as a PowerPoint file. And according to the comments of the editors, the highlights of the latest research results had been supplemented and added in the manuscript.

Best regards,

Xiao-kai Duan