

Dear Editors and Reviewers:

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "Profilin-1 is involved in macroangiopathy induced by advanced glycation end products (AGEs) via vascular remodeling and inflammation" (ID:67684). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. The main corrections in the paper and the responds to the reviewer's comments are as following:

Responds to the reviewer's comments:

Reviewer #1: Previous studies have shown that Diabetic macroangiopathy is the leading cause of morbidity and mortality in diabetic patients. After strict blood glucose and risk factors control, the incidence of diabetic vascular complications has not decreased. Based on previous studies on vascular lesions in patients with diabetes and AS, this study made bold assumptions: 1. The plasma levels of profilin-1 and RAGE in patients with coronary heart disease complicated with diabetes were significantly higher than those in patients with CAD alone. 2. AGEs can up-regulate the expression of profilin-1 in aorta or cultured VSMCs, causing vascular remodeling and VSMCs proliferation. 3. Profilin-1 may be involved in AGEs-induced inflammation and vascular remodeling through the JAK2/STAT3 pathway. Then, through clinical studies, cell experiments and animal experiments, the above hypothesis is verified, and the conclusion can properly summarize the data provided by this study. And it is expected to make profilin-1 a promising therapeutic target for the prevention of diabetes mellitus associated with vascular damage. The team's future research could be: 1. To develop a targeted drug against profilin-1, and further verify whether profilin-1 can truly become a new target for the prevention and treatment of diabetes secondary to AS with vascular injury. 2. Further study of profilin-1 on the exact molecular mechanism of AGE-induced vascular lesions.

Response:

There are minor language defects for grammar, sentence structure,

word usage, spelling, capitalization, punctuation, format, and general readability about our manuscript, which has been solved by a professional English language editing company providing an English Language Certificate.

All abbreviations have been defined when they appear the first time in title, running title, abstract, key words, core tip, article highlights, figures, tables and main text.

Science editor: 1 Scientific quality: The manuscript describes a basic study of the Profilin-1 involved in macroangiopathy induced by AGEs via VSMCs proliferation and proatherogenic mediators expression. The topic is within the scope of the WJD. (1) Classification: Grade C; (2) Summary of the Peer-Review Report: The authors through clinical studies, cell experiments and animal experiments, the above hypothesis is verified, and the conclusion can properly summarize the data provided by this study. And it is expected to make profilin-1 a promising therapeutic target for the prevention of diabetes mellitus associated with vascular damage; (3) Format: There are 3 tables and 7 figures; (4) References: A total of 50 references are cited, including 12 references published in the last 3 years, references 28 and 39 are same; (5) Self-cited references: There are 3 self-cited references. The self-referencing rates should be less than 10%. Please keep the reasonable self-citations (i.e. those that are most closely related to the topic of the manuscript) and remove all other improper self-citations. If the authors fail to address the critical issue of self-citation, the editing process of this manuscript will be terminated; and (6) References recommendations: The authors have the right to refuse to cite improper references recommended by the peer reviewer(s), especially references published by the peer reviewer(s) him/herself (themselves). If the authors find the peer reviewer(s) request for the authors to cite improper references published by him/herself (themselves), please send the peer reviewer's ID number to editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately. 2 Language evaluation: Classification: Grade B. 3 Academic norms and rules: The authors provided and the Institutional Review Board Approval Form. Written informed consent was waived. The authors should provide the Biostatistics Review Certificate, the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement, Institutional Animal Care and Use Committee Approval Form, and fill out The ARRIVE Guidelines with page

numbers. No academic misconduct was found in the Bing search. 4 Supplementary comments: This is an unsolicited manuscript. The study was supported by National Natural Science Foundation of China, Xiangya Eminent Doctor Project, Natural Science Foundation of Hunan Province, and Fund for Health Care in Hunan Province. The topic has not previously been published in the WJD. 5 Issues raised: (1) The “Author Contributions” section is missing. Please provide the author contributions; (2) The “Core Tip” section is missing. Please add the core tip; (3) The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s); (4) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor; (5) The “Article Highlights” section is missing. Please add the “Article Highlights” section at the end of the main text; and (6) please don't include any *, #, †, §, ‡, ¥, @....in your manuscript; Please use superscript numbers for illustration; and for statistical significance, please use superscript letters. Statistical significance is expressed as $aP < 0.05$, $bP < 0.01$ ($P > 0.05$ usually does not need to be denoted). If there are other series of P values, $cP < 0.05$ and $dP < 0.01$ are used, and a third series of P values is expressed as $eP < 0.05$ and $fP < 0.01$. 6 Recommendation: Conditionally accepted.

Response:

- (1) References 28 and 39 are same: we have deleted reference 39, and a total of 49 references have been edited by Auto-Analyser.
- (2) There are 3 self-cited references and the self-referencing rates is less than 10%.
- (3) The Biostatistics Review Certificate, the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement, Institutional Animal Care and Use Committee Approval Form and The ARRIVE Guidelines with filled out page numbers have been uploaded in the Revision Files.
- (4) The “Author Contributions”, “Core Tip” and “Article Highlights” sections have been added in our revised manuscript.
- (5) The approved grant application forms of National Natural Science Foundation of China, Natural Science Foundation of Hunan Province, and

Fund for Health Care in Hunan Province have been uploaded in the Revision Files.

(6) We have prepared the figures and tables using a PowerPoint or Word document, and uploaded it.

(7) There isn't any *, #, †, §, ‡, ¥, @...in our manuscript, and for statistical significance, we have replaced * and # with superscript letters.

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 its final acceptance, the author(s) must provide the Chinese version of the ethical approval document. Before final acceptance, the author(s) must provide the English Language Certificate issued by a professional English language editing company. Please visit the following website for the professional English language editing companies we recommend: <https://www.wjgnet.com/bpg/gerinfo/240>.

Response:

(1) The Chinese version of the ethical approval document has been uploaded in the Revision Files.

(2) The English language problems have been issued by a professional English language editing company recommended by you and the English Language Certificate also has been uploaded in the Revision Files.

We appreciate for Editors and Reviewers' warm work earnestly, and hope that the correction will meet with approval.

Once again, thank you very much for your comments and suggestions.

Thank you and best regards.

Yours sincerely,

Dr. Mei-Fang Chen

Telephone: 86-0731-89753050

E-mail: meifang121@sohu.com