

*World Journal of Diabetes*. Manuscript # **NO: 63482**

Title: **Clinical significance of serum miR-129-5p in patients with diabetes mellitus presenting macrovascular complications**

Dear *World Journal of Diabetes*.,

We appreciate the constructive criticisms/suggestions from the Editor and the Reviewers regarding our manuscript entitled “Clinical significance of serum miR-129-5p in patients with diabetes mellitus presenting macrovascular complications”, which we are resubmitting for consideration of publication in *World Journal of Diabetes*. We have addressed the issues and comments presented by the reviewers and believe these changes significantly enhanced our study.

**Response to Reviewer 1:**

This is an interesting study regarding early identification of diabetic macrocomplications via a novel biomarker. The topic is of interest and the results are of relevance. I would recommend accepting this manuscript for publication. There are some typographic errors. There are very long sentences. To improve readability, consider breaking this into multiple sentences. The authors are encouraged to proof-read thoroughly the text before resubmission. English must be excellent. The authors have chosen very strong references. The article is well-understandable, sentences are clear and concise. Notable strengths of the paper are the detailed and exhaustive figure legends. All results from the study are put into perspective and placed the study at a coherent position considering the bibliography.

**Reply:** Thank you very much for your suggestion and advice. The revised manuscript has been proofread by *Editage* (Receipt code # OYHEZ\_48), a professional editing service provider (a verification letter has been listed in the supplemental files), and we believe that the language and structure of the manuscript are improved and easily understandable.

**Response to Reviewer 2:**

The author's purpose of the investigation is very interesting, I would recommend the suggestions described below: Abstract should be quantitative as possible for rapid comparison with others studies, referring for instance to the percentage of the increase (how much?). Avoid imprecise terms such significantly higher, but how much? 2-fold? 50% regarding the control?. The paper includes only a few references from the last 3

years. Thus, the authors should perhaps include from 2019, 2020 and 2021, papers in the field particularly about new approaches and recent applications in the field. The results are globally not properly described. The authors should first describe in a quantitative manner the data before jump to conclusions. Avoid imprecise terms such as significant higher, but how much? Was the data validated by statistical analysis? Therefore there is no need to refer that the values were “significant”. However, the quantitative information about the “significant” decrease (or increase) is fundamental. The data should be described first. The reader should visualize the data after a correct description. Discussion should be more assertive and concise and should follow the order of presentation of the paper. Eventually, it could be divided in sections with titles highlighting the major topics analyzed in the paper .The conclusion should resume partial and then global conclusions and also with perspectives for future research.

**Reply:** Thanks for your suggestion. In the revised manuscript (the red marks are representative of the newly revised text), we have made the corresponding changes.

### **Response to Reviewer 3:**

The idea of the research is novel but the authors used unsuitable tests to analyze data, also materials and methods are deficient, and the manuscript needs extensive language editing.

**Reply:** Thank you very much for your suggestion and advice. The revised manuscript has been proofread by *Editage* (Receipt code # OYHEZ\_48), a professional editing service provider (a verification letter has been listed in the supplemental files), and we believe that the language and structure of the manuscript are improved and easily understandable..

### First comment.

Extensive language editing is mandatory, many sentences need rephrasing as in page 4 (In the morning, 5 ml peripheral blood of healthy controls or DM patients was extracted after fasting for 8–10 h. These peripheral blood were coagulated for 2h, then centrifuge at 3500 rpm at 4 °C for 30 minutes. The upper serum was collected and stored at - 80 °C until use.)

**Reply:** Thank you for this suggestion. We have made the appropriate changes in the Page 4 line 117-120 of the revised manuscript, and included the following text (the red marks are representative of the newly revised text):

Fasting venous blood samples (5 mL) were collected from all participants. After standing for 2 h, samples were centrifuged at 3500 rpm for 20 min 4 °C; the obtained serum samples were transferred to freshly sterilized tubes and immediately stored at –80°C.

Second comment.

In statistical analysis the authors used Student's t tests to evaluate the different expression of serum miR-129-5p, but the correct is to use ANOVA to compare the quantitative variables between three groups.

**Reply:** In the revised manuscript (Page 5 line 133-137), we have made the appropriate changes, and included the following text (the red marks are representative of the newly revised text):

Statistical analyses were performed using GraphPad Prism 5.0 (GraphPad Software, Inc., San Diego, CA, USA) and SPSS 18.0 (IBM Corp., Chicago, IL, USA). Student's t-test and one-way analysis of variance (ANOVA) were employed to evaluate the differential expression of serum miR-129-5p between patient groups and the healthy control group. Pearson's correlation coefficient was utilized to analyze the correlation between two indicators. The relationship between clinical factors and miR-129-5p expression was estimated using the Chi-square test. Receiver-operating characteristic (ROC) curve analysis was performed using the SigmaPlot suite 13.0 software. Results with  $p < 0.05$ ,  $p < 0.01$ , or  $p < 0.001$  were deemed statistically significant.

In page 7, the authors mentioned (Correlations between the expression levels of serum miR-129-5p and clinical factors in DMCs were analyzed use a chi-square test) while the chi-square test is not used for correlation

**Reply:** Sorry for our negligence. In the revised manuscript (Page 8 line 187), we have made the corresponding changes, and included the following text (the red marks are representative of the newly revised text):

Based on the median serum level of miR-129-5p, patients with DM presenting DMCs were divided into **high- and low-level groups**. **The relationship** between the expression levels of serum miR-129-5p and clinical factors in DMCs was analyzed using the Chi-square test.

Third comment.

In material and methods, the authors didn't mentioned the types of macrovascular complications and they were diagnosed.

**Reply:** Thanks for your suggestion. we have added the corresponding description in the material and methods of revised manuscript (**Page 19 line 596-611**), and included the following text (the red marks are representative of the newly revised text):

We added the diagnose of types 2 diabetic macrovascular complications in material and methods (We use the most common clinical non-invasive examination—B-mode ultrasound to diagnose patients with T2DM combined with macrovascular disease. When T2DM patients with carotid intima thickening and atherosclerotic plaque appear on B-ultrasound examination, it is considered that T2DM with macrovascular disease.)

**Response to Science Editor:**

1 Scientific quality: The manuscript describes a case control study (Not a Frontier) of the clinical significance of serum miR-129-5p for macrovascular complications in patients with diabetes mellitus. The topic is within the scope of the WJD. (1) Classification: Two Grades B and Grade D; (2) Summary of the Peer-Review Report: This is an interesting study regarding early identification of diabetic macrocomplications via a novel biomarker. The topic is of interest and the results are of relevance. The questions raised by the reviewers should be answered; (3) Format: There are 3 tables and 2 figures; (4) References: A total of 30 references are cited, including 8 references published in the last 3 years; (5) Self-cited references: There are 7 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](mailto:editorialoffice@wjgnet.com). The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately. 2 Language evaluation: Classification: Two Grades B and Grade C. No language editing certificate was provided. 3 Academic norms and rules: The authors didn't provide the Biostatistics Review Certificate, the Institutional Review Board Approval Form, and the written informed consent. No academic misconduct was found in the Bing search. 4 Supplementary comments: This is an invited manuscript. The study was supported by National Natural Science Foundation of China, China Postdoctoral Science Foundation, Research Program of Hunan Health Commission, China, and the Youth Fund of Xiangya Hospital. The topic has not previously been published in the WJD. 5 Issues raised: (1) The language classification is Grade C. Please visit the following website for the professional English language editing companies we recommend: <https://www.wjgnet.com/bpg/gerinfo/240>; (2) The "Author Contributions" section is missing. Please provide the author contributions; (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) PMID and DOI numbers are missing in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout; (6) The "Article Highlights" section is missing. Please add the "Article Highlights" section at the end of the main text; and (7) Please provide the Biostatistics Review Certificate, the Institutional Review Board Approval Form, and the written informed consent, and other related ethic documents. 6 Recommendation: Conditional acceptance.

**Reply:** Thanks for your comment. We made the appropriate changes in the revised manuscript.

Thank you so much for your input into helping us improving this paper.

Sincerely,  
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