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World Journal of Diabetes

Dear Professors Lu Cai, Michael Horowitz and Md. Shahidul Islam

Thank you for reviewing our manuscript titled “**Long-term effects of gestational diabetes mellitus on the pancreas of female mouse offspring**” with identification number 90707. We deeply thank the reviewers for their helpful and insightful comments. We have made all the changes suggested by the reviewer and Science Editor and described these changes on a point-by-point basis below. We have incorporated all the changes in the revised manuscript. We do believe these changes have significantly improved the manuscript and will broaden its impact.

Your support and interest in our manuscript are deeply appreciated as I understand how much time and effort it takes to review and edit submitted manuscripts. Thank you for your consideration of this manuscript for publication in the *World Journal of Diabetes*.

Sincerely,



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Ms. No: 90707

Title: Long-term effects of gestational diabetes mellitus on the pancreas of female mouse offspring

World Journal of Diabetes

Reply to Science Editor and Reviewer comments.

We would like to thank the Science Editor and the Reviewer for their thorough and helpful comments to further improve our manuscript. Accordingly, we have gladly modified our manuscript considering all suggestions made. Our statement of how we have responded to each of the comments/criticisms made (point-by point) is given below.

Reviewer's Comments to Author:

Reviewer 1

Comments to the Author

I was pleased to review your article and I have the following comments:

1. This study is interesting. Please explain the novelty of your study

Reply. We have rewritten the first paragraph of the discussion to properly address this point. *"This study reports for the first time that while adult offspring born from STZ-induced GDM do not exhibit alterations in body weight and glucose levels as compared to their age-matched respective controls [Muñoz-Islas E et al., 2012, they have significant alterations at a cellular level in their pancreas. These include an increased density of a subset of sensory and sympathetic nerve fibers innervating exocrine pancreatic tissue along with an enhanced vasculature and macrophage infiltration in the exocrine pancreas. It was also found that there is an increased vasculature within the islets in these adult offspring exposed to GDM".*

2. Please highlight the study limitation.

Reply. We have stated the limitations of the present study at the end of the Discussion as follows: *"The present study has some limitations. First, we recognize that while we found cellular alterations in the pancreatic tissue from adult offspring born from dams with GDM, there is a need to assess whether these anatomical changes are translated into functional alterations such as a higher propensity to develop and/or greater severity of metabolic diseases. Secondly, it is not possible to discern whether the increase in endomucin+ blood vessels [McDonald DM and PL Choyke, 2003] will result in changes in pancreatic blood flow. Third, while we observed an increase in the number of macrophages around acinar cells of offspring of GDM dams; it is unknown whether this macrophage infiltration will lead to altered production of pro-inflammatory and/or anti-inflammatory cytokines. Finally, we do recognize that these anatomical alterations were found at one time-point of life, however, it is warranted to determine when these changes start at and/or to assess whether they disappear with aging".*

3. English language edits are required

Reply. The Professor Christopher M. Peters from Wake Forest Medical Center, who is native English speaker, author of the manuscript and expert on immunohistochemistry, confocal microscopy. He has reviewed and edited the manuscript. We have added a letter to state it.

Editorial Office's comments

1) Science editor:

Specific comments

1. Please provide the filled conflict-of-interest disclosure form.

Reply. We have added the filled form.

2. Please provide the Figures cited in the original manuscript in the form of PPT. All text can be edited, including A, B, arrows, etc. With respect to the reference to the Figure, please verify if it is an original image created for the manuscript, if not, please provide the source of the picture and the proof that the Figure has been authorized by the previous publisher or copyright owner to allow it to be redistributed. All legends are incorrectly formatted and require a general title and explanation for each figure. Such as Figure 1 title. A: ; B: ; C: .

Reply. We have provided the Figures as stated.

3. 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 $fP < 0.01$.

Reply. We have adjusted the manuscript as indicated.

4. Please provide all fund documents [National Council for Humanities, Science and Technology of Mexico CONAHCyT (CB/2017-2018/A1-S-27869)].

Reply. We have provided the requested document.

5. The "Article Highlights" section is missing. Please add the "Article Highlights" section at the end of the main text (and directly before the References).

Reply. We have added the highlights at the end of the main text.

6. Please provide the PMID numbers and DOI citation numbers to the reference list and list all authors of the references. If there is no PMID or DOI, please provide the website address.

Reply. We have added the PMID and DOI citation numbers to the reference list.

2) Company editor-in-chief:

Specific comments

1. When revising the manuscript, it is recommended that the author 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 PubMed, or a new tool, the RCA, of which data source is PubMed. RCA is a unique artificial intelligence system for citation index evaluation of medical science and life science literature. 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/>, or visit PubMed at:

<https://pubmed.ncbi.nlm.nih.gov/>.

Reply. We have taken into consideration your recommendations.