

Reviewer response

25 November 2022

Manuscript (ID: 80776): Pancreatic β -cell dysfunction in type 2 diabetes: Implications of inflammation and oxidative stress

Dear Editor,

Thank you for the chance to consider the manuscript mentioned above. The manuscript has been revised, and we are grateful for the opportunity to submit it as an updated version for your consideration. We confirm that all reviewer concerns have been addressed. All changes are highlighted in red text throughout the revised version of the manuscript.

Reviewer 1 (Number ID: 03460306)

This is a review article regarding the implications of inflammation and oxidative stress on pancreatic beta cell dysfunction in T2D. The manuscript was easy to follow. However, there are several comments.

Thank you for the chance to consider the manuscript mentioned above. The manuscript has been revised, and we are grateful for the opportunity to submit it as an updated version for your consideration. We have updated the introduction to be show the uniqueness of our review, while also improving other relevant section (by adding a new section on the clinical relevance) and the conclusion. We further proof-read the manuscript to minimize any grammatical and spelling mistakes, hopefully it is now acceptable.

1. Literature search criteria and selection flow should be described in the manuscript.

Thank you for this important comment, and in agreement with the reviewer, a separate section has been added within the manuscript to describe literature search criteria. This section is highlighted in red and comes after the introduction.

2. The evidences in animal models and those in human studies are mixed in each section. They should be clearly distinguished and separately described.

Thank you for this important comment. Please note, for all sections described, in particular the markers of inflammation and oxidative stress, preclinical (animal) models are described first, to highlight the mechanistic insights involved relevant to β -cell dysfunction. Thereafter, a clinical section is added to indicate any clinical relevance, this way has been applied in all subheadings. Where there is limited clinical evidence, this fact is also mentioned.

3. The section regarding microbiota is too short and superficial. The link between microbiota and pancreatic islet inflammation should be more precisely described.

Thank you for this important comment, in agreement with the reviewer, we have decided to remove this section to not confuse the reader and enhance the quality of our manuscript.

4. In figure 2, the expression “type 1 diabetes/type 2 diabetes” is very confusing. The similarities and differences between T1D and T2D should be more clearly described.

Thank you for this comment, hence figure 2 has been revised, and the word “type 1 diabetes” has been removed because the whole manuscript/proposed mechanistic insight is based on type 2 diabetes.

5. Clinical relevance should be described. Please mention on the role of anti-oxidants and anti-diabetic agents in treatment of T2D.

Thank you for this important comment. Please note, we have revised the manuscript and added a new section (highlighted in red) entitled “5. Antidiabetics and other agents potentially regulate inflammatory markers to improve β -cell function”. This section is accompanied by its own relevant table describing clinical evidence from randomized controlled trials linking some of these discussed pathological markers with β -cell function. In addition, this section informs on the therapeutic effects of antidiabetic and other drugs relevant for affecting β -cell function.

6. Overall, the contents are not novel. The authors should describe the novelty of this review in the abstract and introduction.

Thank you for this important comment. Please note, we have revised the introduction (the last paragraph which is highlighted in red), to clearly highlight the uniqueness and

significance of the current study. This is also in line with adding a new section discussing, antidiabetics and other agents potentially regulate inflammatory markers to improve β -cell function.

Reviewer 2 (Number ID: 06323682)

In the current review Authors focused on " β -cell dysfunction in type 2 diabetes: Implications of inflammation and oxidative stress". Authors nicely narrated about the content However, I have few queries in the present review Molecular mechanisms related to Oxidative stress and inflammation is well known in type 2 diabetes.

Thank you for the chance to consider the manuscript mentioned above. The manuscript has been revised, and we are grateful for the opportunity to submit it as an updated version for your consideration. We have updated the introduction to be show the uniqueness of our review, while also improving other relevant section (by adding a new section on the clinical relevance) and the conclusion. We further proof-read the manuscript to minimize any grammatical and spelling mistakes, hopefully it is now acceptable.

I think novelty of the present content is missing.

Thank you for this important comment. Please note, we have revised the introduction (the last paragraph which is highlighted in red), to clearly highlight the uniqueness and significance of the current study. This is also in line with adding a new section discussing, antidiabetics and other agents potentially regulate inflammatory markers to improve β -cell function.

Authors may provide the clinical information related clinical studies explain the Inflammation and oxidative stress makers in table form (clinical studies published on oxidative and inflammatory markers association with the b-cellll dysfunction in type 2 diabetes patients).

Thank you for this important comment. Please note, we have revised the manuscript and added a new section (highlighted in red) entitled "5. Antidiabetics and other agents potentially regulate inflammatory markers to improve β -cell function". This section is

accompanied by its own relevant table describing clinical evidence from randomized controlled trials linking some of these discussed pathological markers with β -cell function. In addition, this section informs on the therapeutic effects of antidiabetic and other drugs relevant for affecting β -cell function.

Acknowledgement: it need to be correct "All author authors"

Thank you for this important comment. We corrected this error by removing the words "All author authors"

Gut microbiota and pancreatic β -cell dysfunction in type 2 diabetes. In this section authors should fill the gaps between Gut microbiome- beta dysfunction- Inflammation. I feel that there is much space to contact this in the article or Authors may remove the this part because it is diverting from the title.

Thank you for this important comment, in agreement with the reviewer, we have decided to remove this section to not confuse the reader and enhance the quality of our manuscript.