

2020/4/22

World Journal of Diabetes

Lian-Sheng Ma, Founder and Chief Executive Officer

Baishideng Publishing Group Inc

Re: Invited review manuscript for World Journal of Diabetes

Dear Mr. Ma and Reviewers,

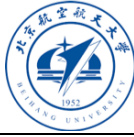
Thanks very much for taking your time to review this manuscript. We really appreciate all your positive and constructive comments and suggestions on our manuscript entitled “A review of gut microbiota observations: in context of diabetes.” (Manuscript NO: 55090). We have studied comments carefully and have made correction which we hope meet with approval. Please find our itemized responses in below and our revisions in the re-submitted files.

1. Response to comment:

In this review the authors have summarised the current evidence about the role of gut microbiota to diabetes mellitus. Though the review is interesting and timely, the authors need to propose whether there could occur any other mechanisms of action (other than what they have discussed) on the role of gut microbiota in DM. For instance, is microbiota is just a bystander or the cause or result of the DM. The relationship between gut microbiota and SCFAs and vagal to be need to be added to the review. Mice that do not have gut microbiota (germ free mice) have altered incidence of diabetes. This needs to be discussed. A table giving the products produced by the gut microbiota and their actions need to be given for easy understanding. The authors are advised to see the following publication to get a full idea about gut microbiota and accordingly modify their review. *Physiol Rev* 90: 859–904, 2010

Response:

We are very grateful to the reviewer’s suggestion. We have added other reported mechanisms and enriched those discussions in the re-submitted manuscript. We also wrote a summary to explain our views in more detail.



“The gut microbiota has long been regarded as a virtual organ of human metabolic activity^[58], and its metabolic activity interacts with insulin resistance and diabetes. Gut microbial metabolites can affect host physiological functions.” (page 16)

“It can be foreseen that the gut microbiota will be used not only as a biomarker for diabetes, but also as a target for potential therapeutic treatments.” (page 25)

Considering the Reviewer’s suggestion, we have supplemented the potential role of SCFA in activating the vagal nerve in diabetes, which can also bring more thoughts to the readers.

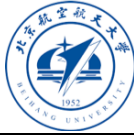
“On the other hand, SCFAs activates the vagal afferent neurons, which establish a connection between the intestinal information and the brain. This connection has been proved to play a role in controlling human feeding behavior, which also raises new considerations for the potential mechanism of SCFAs to increase the risk of diabetes by controlling human feeding behavior and selection of dietary response^[70].” (page 19)

According to the comments of reviewers, we made a more detailed supplementary explanation on the changes of insulin resistance in germ-free mice.

“It is important to note that previous research indicated that when mice do not have gut microbiota (germ-free mice) they also have lower body fat and insulin resistance than conventionalized (CONV-D) mice, and the tolerance of insulin and glucose in germ-free mice was higher than that observed in routinely fed mice. This study also opened up the exploration of many potential mechanisms in the past decade^[29].” (page 11)

It is really true as a Reviewer suggested that we were missing a Table, so we added Table 1 (A summary of products of gut microbiota and their mechanism of action) at the end of the re-submitted manuscript for easy understanding.

2. Response to comment:



This study tried to review the relationship between human gut microbiota and diabetes in the literatures. It has been found that a close association between gut microbiota and diabetes. Diet is a crucial regulator of intestinal flora. The anti-diabetic drugs may influence the intestinal flora. The fecal bacteria transplantation from insulin-sensitive donors can result in a significant improvement in insulin sensitivity with increased abundance of butyrate-producing bacteria. Generally, this is an interesting review. It may help develop future promising therapeutic interventions for diabetes. One suggestion is it will be much better if authors can further address the roles of gut microbiota in diabetic pathogenesis.

Response:

We are grateful for the suggestion. In the revised manuscript, we supplement the deficiencies of the previous mechanism by adding two other microbial metabolites (Bile acids and Branched-Chain Amino Acids). (page 20) At the same time, a table is added at the end of the paper to make it easier for readers to understand.

We acknowledge the reviewer's comments and suggestions very much, which are valuable in improving the quality of our manuscript.

Thank you for considering this manuscript for publication in **World Journal of Diabetes**. Looking forward to hearing from you.

Sincerely,

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