

## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Diabetes*

**Manuscript NO:** 82020

**Title:** Characterization of gut microbial and metabolite alterations in faeces of Goto Kakizaki rats using metagenomic and untargeted metabolomic approach

**Provenance and peer review:** Unsolicited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 06131948

**Position:** Peer Reviewer

**Academic degree:** PhD

**Professional title:** Doctor, Teacher

**Reviewer's Country/Territory:** Russia

**Author's Country/Territory:** China

**Manuscript submission date:** 2022-12-02

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2022-12-02 09:15

**Reviewer performed review:** 2022-12-07 14:34

**Review time:** 5 Days and 5 Hours

|                           |   |
|---------------------------|---|
| <b>Scientific quality</b> | <input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good<br><input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish            |
| <b>Language quality</b>   | <input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing<br><input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection |
| <b>Conclusion</b>         | <input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority)<br><input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection             |
| <b>Re-review</b>          | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No   |

|                                     |   |
|-------------------------------------|---|
| <b>Peer-reviewer<br/>statements</b> | Peer-Review: [ <input checked="" type="radio"/> ] Anonymous [ <input type="radio"/> ] Onymous |
|                                     | Conflicts-of-Interest: [ <input type="radio"/> ] Yes [ <input checked="" type="radio"/> ] No  |

## **SPECIFIC COMMENTS TO AUTHORS**

Diabetes mellitus is a global problem of modern medicine, so a better understanding of its pathogenesis is an urgent task. This article analyzes the fecal microbiota in rats with a model of diabetes mellitus. Comments: 1. The introduction is too short. It would be helpful to supplement it with data on the importance of the gut microbiota to diabetes mellitus. 2. The study compared the gut microbiota in rats of different lines. However, the microbiota may have had differences even before the development of diabetes. It would be interesting to understand how the gut microbiota changes in GK rats as diabetes progresses. It might be possible to use 2 groups of GK rats in which the microbiota would be assessed at different times.

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**Peer-review model:** Single blind

**Reviewer's code:** 06403983

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

**Reviewer's Country/Territory:** Japan

**Author's Country/Territory:** China

**Manuscript submission date:** 2022-12-02

**Reviewer chosen by:** AI Technique

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|---------------------------|--|
| <b>Scientific quality</b> | <input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good<br><input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish                                     |
| <b>Language quality</b>   | <input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/><br><input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection |
| <b>Conclusion</b>         | <input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority)<br><input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection                                      |
| <b>Re-review</b>          | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No  |

|                                     |   |
|-------------------------------------|---|
| <b>Peer-reviewer<br/>statements</b> | Peer-Review: [ <input checked="" type="checkbox"/> ] Anonymous [ <input type="checkbox"/> ] Onymous |
|                                     | Conflicts-of-Interest: [ <input type="checkbox"/> ] Yes [ <input checked="" type="checkbox"/> ] No  |

## SPECIFIC COMMENTS TO AUTHORS

Recent research suggests that both humans as well as animal models of Type 2 Diabetes Mellitus (T2DM), such as Goto-kakizaki (GK) rats, exhibit dysbiosis of the gut microbiota and that this characteristic microbiota imbalance contributes to the development of T2DM. In addition, research shows that undesirable shifts in metagenome and microbiota associated metabolite production may negatively impact glucose and insulin homeostasis. The original manuscript under review entitled; 'Characterization of the gut microbial and metabolite alterations in the faeces of GK rats by a metagenome and untargeted metabolomics approach,' aimed evaluate the gut microbial and metabolite alterations in GK rat faeces based on metagenome and untargeted metabolomics. Although this manuscript is overall well structured and aims to better understand the gut microbiota and associated metagenome and metabolite structure of GK rats, the manuscript fails to show novelty/innovation in the context of the wider research field of T2DM and diabetes. In addition the clinical implications/applicability of results to humans are not adequately provided nor are the limitations relating translatability to humans. Lastly, background of the research to date regarding T2DM and the microbiota and associated metabolites in both humans and animals as well mechanistic insight regarding some of the results showing significant differences are not addressed appropriately. Firstly, the authors should sufficiently summarise and highlight key findings in the literature to date regarding T2DM and gut microbiota and metabolites in both animals and humans in the background, clearly showing the gaps in the literature and how this study aims to fill them and stating their hypothesis. In doing this, points of novelty of the study can then be provided -

obviously the gut microbiota, metagenome and metabolite structure in GK rats has not been widely studied. Importantly the study needs to also demonstrate how these findings are applicable/translatable to humans and clinical implications (in the conclusion). Perhaps authors could touch on that in characterising the gut microbiota in GK rats and interpreting this against the wider findings in the literature to date, identification of certain species of microbiota and metabolites implicated in T2DM may help to lead to more personalised interventions and treatments that target the structure of the gut microbiota, metagenome and metabolites and how this then interacts with and influences aspects of metabolic health related to T2DM. Lastly, results such as the as the lower body weight seen in the final weeks in GK mice - (and HOMA-B) and the impact that these findings may have on the gut microbiota results should be discussed.

## RE-REVIEW REPORT OF REVISED MANUSCRIPT

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**Academic degree:** PhD

**Professional title:** Doctor, Teacher

**Reviewer's Country/Territory:** Russia

**Author's Country/Territory:** China

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**Reviewer chosen by:** Han Zhang

**Reviewer accepted review:** 2023-01-05 07:22

**Reviewer performed review:** 2023-01-07 07:31

**Review time:** 2 Days

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|---------------------------|---|
| <b>Scientific quality</b> | <input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good<br><input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish            |
| <b>Language quality</b>   | <input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing<br><input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection |
| <b>Conclusion</b>         | <input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority)<br><input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection             |
| <b>Peer-reviewer</b>      | Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous   |



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statements

Conflicts-of-Interest: [ ] Yes [Y] No

## SPECIFIC COMMENTS TO AUTHORS

The authors made changes to the article that improved its quality.