

Reviewer #1

The above manuscript is a well-planned and executed study. However, the results are based on the bioinformatics analysis. If authors pick a few genes and validated them in the cohort samples it will give more meaning full. Further, it is not sure whether it is type 2 diabetes or Type 1 diabetes. In my opinion, this CD4 immune cell infiltration may be related to the immune cell infiltration in type 2 diabetes. Table 1 may represent the pathways specific gene labeling is more important to make the readers more understandable. The figure was not clear may be authors may improve while proofreading.

R. Thanks for the comments. We updated the title and keywords to figure out our disease is type 2 diabetes mellitus. We added the description for the gene in the revised Table 1. We uploaded the clear Figures.

Reviewer #2

This article idea focuses on one of the important hall marks in the pathogenesis of diabetes mellitus. So, the idea of this work is promising and is considered as a new sight in management of diabetes mellitus. Thanks for the authors for creating such innovative study. However, I suggest the following recommendations regarding the manuscript as follows: 1. General notes: -Replace the word diabetes all over the manuscript either with diabetes mellitus and or type 2 diabetes mellitus to discriminate it from diabetes insipidus. -Add the full name for all the abbreviated words all over the manuscript while they were firstly mentioned e.g., IRE1, Mfn2, PPIs.....to be clear for the readers. 2. Title. -Add the model of the study to the title. -Specify that it was carried out in Type 2 diabetes mellitus. 3. Abstract. The abstract summarizes and reflects the work described in the manuscript but: -Write the full name for the abbreviated words as they are 1st mentioned such as GSEA, GSVA and CD4+to be clear for the readers. 4. Key words. The key words reflect the general idea of the manuscript but still ambiguous. So, it is better to be use more specific words. 5. Introduction. The manuscript adequately describes the background, present status and significance of the study but: -Avoid repetition: remove "or raised blood glucose",..... in the following sentence (Hyperglycaemia, or raised blood glucose,.....). -Add a reference to "In 2019, diabetes was the direct cause of 1.5 million deaths according to the data from World Health Organization". -It is better to replace these prevalence data with recent ones as DM is a common disease and you can easily cite more recent research articles regarding it more than 2014 and 2019. 6. Methods. The manuscript describes methods (e.g., experiments, data analysis, surveys, and clinical trials, etc.) in adequate details. 7. Results. The research objectives achieved by the experiments used in this study and the study could greatly contribute to the research progress in this field. 8. Discussion. The manuscript interprets the findings adequately and appropriately, highlighting the key points concisely, clearly, and logically. The findings and their applicability/relevance to the literature were stated in a clear and definite manner. The discussion is accurate and discusses the paper's scientific significance and relevance to clinical practice sufficiently. 8 Illustrations and tables. The figures, diagrams, and tables were sufficient, in good quality and appropriately illustrative of the paper contents. 9 Biostatistics. The manuscript meets the requirements of biostatistics. 11 References. -It is better to cite more recent important and authoritative references in the introduction and discussion sections as the most recent references was in 2021. So, kindly update the references 12 Quality of manuscript organization and presentation. The manuscript is well, concisely, and coherently organized and presented. The style, language and grammar are accurate and appropriate. Finally, many regards to the editors and authors for their great effort.

R. Thanks for the comments. We replaced the word diabetes all over the manuscript either with diabetes mellitus or type 2 diabetes mellitus to discriminate it from diabetes insipidus. We added the full name of all the abbreviated words all over the manuscript while they were first mentioned to be clear for the readers. We changed the Title to "Comprehensive analysis of endoplasmic reticulum stress-related mechanisms in type 2 diabetes mellitus". We updated the Key Words to "Endoplasmic reticulum stress; type 2 diabetes mellitus;

biomarkers; memory CD4+ T cells". We removed "or raised blood glucose" in our revised manuscript to avoid repetition. We used the latest references to update the prevalence data. Finally, we cited more recent important and authoritative references in the introduction and discussion sections.