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Round 1

Dear Editor:

Thank you for your letter in which you encouraged us to revise our manuscript submitted to *World of Diabetes* entitled “Identification of hub genes associated with *Helicobacter pylori* infection and type 2 diabetes mellitus: A pilot bioinformatics study” (Manuscript NO: 88359).

Thank you for the reviewers’ comments and editor’s suggestions. These comments will greatly enhance the quality of this manuscript. The issues you reminded us were carefully performed. We have listed our responses point by point. We also addressed these issues in the highlighted revision.

We would like to thank the editor and the reviewers for your critical comments and recommendations that have greatly improved the quality of this paper. We deeply hope our responses are satisfactory. If you have further questions, please do not hesitate to let us know by the E-mail. Thank you again for your consideration and we await a favorable response to the revision.

Reviewer 1:

1. The English need improvement since there are some grammatical and syntax errors in the manuscript. For example

- in line number 56, the words “the less” may be as “less”;
- in line number 71, “in immune” as “in the immune”;
- in line number 72, “that H. pylori” as “H. pylori”;
- in line number 140, “intersection” as “the intersection”;
- in line number 224, “was expressed” as “were expressed”;
- in line number 233, “was lower” as “were lower”;
- in line number 249, “highest” as “the highest”;
- in line number 295, “state in” as “state of”;
- in line number 310, “to treat” as “treatment of”;
- in line number 333, “may involve” as “may be involved”;
- in line number 334, “experiment” as “the experiment”.

The grammar mistakes which are not mentioned here are also to be checked and corrected properly.

Response: Thank you very much for your helpful suggestions. We have revised the grammatical and syntax errors in the revised manuscript. The manuscript was also revised by American Journal Experts and we have uploaded the certificate in the revised manuscript.

2. There are some typing mistakes as well, and authors are advised to carefully proof-read the text. For example

- in line number 60, the words “control on” may be as “control in”;
- in line number 93, “tissues samples” as “tissue samples”;
- in line number 157, “bioinformatics based” as “bioinformatics-based”;
- in line number 167, “ethnics” as “ethics”;
- in line number 233, “H. pylori infected” as “H. pylori-infected”;
- in line number 288, “factor alpha” as “factor-alpha”;
- all over the manuscript, “H. pylori associated” as “H. pylori-associated”;
- in line number 306, “individual” as “individuals”;
- in line number 313, “cell mediated” as “cell-mediated”. The typos not mentioned here are also to be checked and corrected properly.

Response: Thank you very much for your helpful advice. We have revised the typos according to your advice in the revised manuscript.

3. Check the abbreviations throughout the manuscript and introduce the abbreviation when the full word appears the first time in the abstract and the remaining part of the manuscript (For example, Differentially expressed genes (DEGs), Gene Ontology (GO), protein-protein interaction (PPI), etc.). Make a word abbreviated in the article that is repeated at least three times in the text, not all words to be abbreviated.

Response: Thank you very much for your wonderful suggestion. We have revised the abbreviations and listed the abbreviations used in this paper in the revised manuscript.

4. The full form of the species should be given when the first time appears in both the

abstract and in the remaining part of the manuscript and it should be followed by only the first letter of the genus (For example, *Helicobacter pylori* when the first time appear and followed by *H. pylori*).

Response: Thank you very much for your helpful advice. We have revised in the revised manuscript.

5. The introduction part appears less informative about *Helicobacter pylori* and type 2 diabetes, thus this section should be indicated as detailed to understand the manuscript in clear since the main objectives is focused on *Helicobacter pylori* and type 2 diabetes.

Response: Thank you very much for your wonderful suggestion. We have revised the introduction section accordingly.

6. The authors may cite recent prevalence or incidence data *Helicobacter pylori* and type 2 diabetes and it should be at-least of 2023 since the authors have cited only up to 2022.

Response: Thank you very much for your helpful suggestion. We have cited recent references in the revised manuscript.

7. The genus and species name should be italic all over the manuscript (*Helicobacter pylori* or *H. pylori*).

Response: Thank you very much for your helpful advice. We have checked all the manuscript thoroughly and revised accordingly.

8. The table and figure legends should be improved and a proper footnote should be given. All legends should have enough description for a reader to understand the tables and figures without having to refer back to the main text of the manuscript. For example, the necessary abbreviations should be given (DEGs, HbA1c, etc.,).

Response: Thank you very much for your helpful suggestion. We have revised the table and figure legends accordingly.

Thank you very much for your help again for improving our manuscript quality.

Reviewer 2:

The authors identified five hub genes that indicated that chronic inflammation caused by *H. pylori* infection is involved in diabetes mellitus by comprehensive analysis. It is interesting to note that all these genes correlate with immunity, including B cells, CD8⁺ T cells, macrophages, neutrophils and DCs. The results had been confirmed by RNA expression analysis in gastric tissue from *H. pylori*-infected diabetic patients. Further analysis of the detailed mechanism is needed using animal experiments in the future. Although there are issues such as small sample size as described in the paper, additional experiments or major modifications are not necessary.

Response: Thank you very much for your appreciation. We are now doing the animal experiments and hope to present the results in the near future.

Science editor:

The manuscript has been peer-reviewed, and it is ready for the first decision.

Response: Thank you very much and we have revised according to editors' and reviewers' advice.

Company editor-in-chief:

1. Before its final acceptance, please provide and upload the following important documents: Biostatistics Review Certificate, a statement affirming that the statistical review of the study was performed by a biomedical statistician.

Response: Thank you very much and we have uploaded the Biostatistics Review Certificate in the revised manuscript.

2. Institutional Review Board Approval Form or Document, the primary version (PDF) of the Institutional Review Board's official approval, prepared in the official language of the authors' country.

Response: Thank you very much for your suggestion and we have uploaded the signed Institutional Review Board Approval Form in the revised manuscript.

3. The quality of the English language of the manuscript does not meet the requirements of the journal. Before final acceptance, the author(s) must provide the English Language Certificate issued by a professional English language editing company. Please visit the following website for the professional English language editing companies we recommend: <https://www.wjgnet.com/bpg/gerinfo/240>.

Response: Thank you very much your helpful suggestion. We have uploaded the language certificate in the revised manuscript.

4. Before final acceptance, uniform presentation should be used for figures showing the same or similar contents; for example, "Figure 1 Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...". Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor. In order to respect and protect the author's intellectual property rights and prevent others from misappropriating figures without the author's authorization or abusing figures without indicating the source, we will indicate the author's copyright for figures originally generated by the author, and if the author has used a figure published elsewhere or that is copyrighted, the author needs to be authorized by the previous publisher or the copyright holder and/or indicate the reference source and copyrights. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2023.

Response: Thank you very much your suggestion. We have revised the figure legends and confirmed that all figures are original. We also uploaded the PPT in the revised manuscript.

5. Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

Response: Thank you very much your helpful suggestion. We have re-edited the tables accordingly.

6. Please upload the approved grant application form(s) or funding agency copy of any approval document(s).

Response: Thank you very much and we have uploaded the approved grant application form in the revised manuscript.

Round 2

Reviewer 1:

1. There are some grammatical, alignments and typographical errors noted in the manuscript and it should be thoroughly checked and corrected throughout the manuscript. For example, the words “province hospital” may be as “Province Hospital”; “establishment of” as “the establishment of”; “between expression” as “between the expression”; “gene gene” as “gene-gene”; “postload” as “post load”; “t test” as “t-test”; “neutrophil mediated” as “neutrophil-mediated”; “heparin binding” as “heparin-binding”; “that expression” as “that the expression”; “19 downregulated” as “19 were downregulated”; “in development” as “in the development”; “in recognition” as “in the recognition”; “on KEGG” as “on the KEGG”; “formation of” as “the formation of”; “validated expression” as “validated the expression”; “to be coregulated” as “was coregulated”; “infection related” as “infection is related”; “T2DM remains” as “T2DM remain”; “In the future” as “In future”; “will investigating” as “will be investigating”.

Response: Thank you very much for your helpful suggestion. We have revised the manuscript according to your suggestion.

2. This suggestion is not carried out properly and it should be rectified (Check the abbreviations throughout the manuscript and introduce the abbreviation when the full word appears the first time in the abstract and the remaining part of the manuscript) For example, the authors used both forms alternatively for “Differentially expressed genes (DEGs)”. This types of corrections need to be checked all over the manuscript.

Response: Thank you very much for your helpful suggestion. We have revised the manuscript according to your suggestion.

3. This suggestion is not carried out properly and it should be rectified. The full form of the species should be given when the first time appears in both the abstract and in the remaining part of the manuscript and it should be followed by only the first letter of the genus (For example, *Helicobacter pylori* when the first time appear and followed by *H. pylori*).

Response: Thank you very much for your helpful advice. We have revised according to your suggestion.

4. This suggestion is not carried out properly and it should be rectified. The genus and species name should be italic all over the manuscript (*Helicobacter pylori* or *H. pylori*) For example, in core tip it is not carried out and also the same should be checked all over the manuscript.

Response: Thank you very much for your helpful advice. We have revised and checked in the revised manuscript. Thank you very much again for the help in improving our manuscript quality.

Reviewer 2:

It has been appropriately amended and requires no further revision.

Response: Thank you very much for the help in improving our manuscript quality.