

Dear Prof. Lian-Sheng Ma,

Thank you for your letter and the reviewers' comments on our manuscript (Manuscript NO: 63304). We have studied reviewers' comments carefully. According to the reviewers' detailed suggestions, we have made a careful revision on the original manuscript. All revised portions are highlighted in yellow in the revised manuscript which we would like to submit for your kind consideration.

With many thanks and best wishes.

Jing Liu

Shantou University Medical College

The main corrections are in the manuscript and the responds to the reviewers' comments are as follows point-to-point (the replies are marked in blue).

To Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Reply: Thank you again for your positive comments and valuable suggestions to improve the quality of our manuscript. We have revised the manuscript accordingly with tracked changes. And the manuscript has been polished by an English-native speaker with biological background.

Specific Comments to Authors:

1 Title. Does the title reflect the main subject/hypothesis of the manuscript? YES

Reply: Thank you again for your positive comments. According to the Guidelines and Requirement for Manuscript Revision in *World Journal of Gastroenterology*, we revise the title to less than 18 words.

2 Abstract. Does the abstract summarize and reflect the work described in the manuscript? YES

Reply: Thank you again for your positive comments.

3 Key words. Do the key words reflect the focus of the manuscript? YES

Reply: Thank you again for your positive comments.

4 Background. Does the manuscript adequately describe the background, present status and significance of the study? YES

Reply: Thank you again for your positive comments.

5 Methods. Does the manuscript describe methods (e.g., experiments, data analysis, surveys, and clinical trials, etc.) in adequate detail? YES

Reply: Thank you again for your positive comments.

6 Results. Are the research objectives achieved by the experiments used in this study? What are the contributions that the study has made for research progress in this field? YES This study supports the protective function of MUC2 in CRC. Moreover, the more secreted MUC2 in CRC patients indicates the impaired intestinal mucosal barrier.

Reply: Thank you again for your positive comments.

7 Discussion. Does the manuscript interpret the findings adequately and appropriately, highlighting the key points concisely, clearly and logically? Are the findings and their applicability/relevance to the literature stated in a clear and definite manner? Is the discussion accurate and does it discuss the paper's scientific significance and/or relevance to clinical practice sufficiently? YES, YES, YES

Reply: Thank you again for your positive comments.

8 Illustrations and tables. Are the figures, diagrams and tables sufficient, good quality and appropriately illustrative of the paper contents? Do figures require labeling with arrows, asterisks etc., better legends? 1) In Figure 3, the data described in Low/High expression does not correspond with the data described in Table 1. 2) More detailed legends are needed in all figures and tables

Reply: Thank you again for your professional comments and valuable suggestions. In dealing with Figure 3, the authors accidentally reversed the data of cancer tissue and normal tissue, leading to that the data described in Low/High expression does not correspond with the data described in Table 1. We are very sorry for our negligence to make such mistake and corrected Figure 3 accordingly. According to the reviewer's professional suggestions, we revised the legends for the figures and tables and added more details to make them readable and clear, in Page 21-28.

9 Biostatistics. Does the manuscript meet the requirements of biostatistics? YES

Reply: Thank you again for your positive comments.

10 Units. Does the manuscript meet the requirements of use of SI units? YES

Reply: Thank you again for your positive comments.

11 References. Does the manuscript cite appropriately the latest, important and authoritative references in the introduction and discussion sections? Does the author self-cite, omit, incorrectly cite and/or over-cite references? YES, NO

Reply: Thank you again for your positive comments.

12 Quality of manuscript organization and presentation. Is the manuscript well, concisely and coherently organized and presented? Is the style, language and grammar accurate and appropriate? YES

Reply: Thank you again for your positive comments.

13 Research methods and reporting. Authors should have prepared their manuscripts according to manuscript type and the appropriate categories, as follows: (1) CARE Checklist (2013) - Case report; (2) CONSORT 2010 Statement - Clinical Trials study, Prospective study, Randomized Controlled trial, Randomized Clinical trial; (3) PRISMA 2009 Checklist - Evidence-Based Medicine, Systematic review,

Meta-Analysis; (4) STROBE Statement - Case Control study, Observational study, Retrospective Cohort study; and (5) The ARRIVE Guidelines - Basic study. Did the author prepare the manuscript according to the appropriate research methods and reporting? YES

Reply: Thank you again for your positive comments.

14 Ethics statements. For all manuscripts involving human studies and/or animal experiments, author(s) must submit the related formal ethics documents that were reviewed and approved by their local ethical review committee. Did the manuscript meet the requirements of ethics? YES This manuscript found the protective function of MUC2 in CRC. Moreover, the more secreted MUC2 in CRC patients indicates the impaired intestinal mucosal barrier. The author concluded that MUC2 in intestinal tissues might play a protective role in the intestine and could be used as an indicator to evaluate the prognosis of CRC patients. Because the finding that serum MUC2 concentration is positively related to advanced tumor stage and distant metastasis, whether the secreted MUC2 can aggravate the condition of CRC and what's the mechanism would be interesting.

Reply: Thank you again for your positive comments. And we revised the manuscript according to your professional comments and valuable suggestions. We believe that the revised article will meet the criteria of *World Journal of Gastroenterology*.

To Editorial Office's Comments:

(1) To Science editor:

1 Scientific quality: The manuscript describes a retrospective study of the diverse expression pattern of MUC2 in cancer tissues and serum of colorectal cancer patients indicates its mechanism related to the intestinal mucosal barrier. The topic is within

the scope of the WJG. (1) Classification: Grade B; (2) Summary of the Peer-Review Report: The authors reported the protective function of MUC2 in CRC. However, the questions raised by the reviewer should be answered; and (3) Format: There are 5 tables and 5 figures. (4) References: A total of 23 references are cited, including 12 references published in the last 3 years; (5) Self-cited references: There are 2 self-cited references. The self-referencing rates should be less than 10%. Please keep the reasonable self-citations that are closely related to the topic of the manuscript, and remove other improper self-citations. If the authors fail to address the critical issue of self-citation, the editing process of this manuscript will be terminated; and (6) References recommend: The authors have the right to refuse to cite improper references recommended by peer reviewer(s), especially the references published by the peer reviewer(s) themselves. If the authors found the peer reviewer(s) request the authors to cite improper references published by themselves, please send the peer reviewer's ID number to the editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately.

Reply: Thank you again for your professional comments and valuable suggestions. Specifically, to (2), we have revised the manuscript and answered the reviewer's question accordingly in Page 21-28; to (5), a total of 23 references were cited in the study, and 2 self-cited references less than 10% are necessary for the article. One self-citation (Reference 12) is responsible for the methods conducted in our lab and another one (Reference 18) is a review for demonstrating the characteristics of mucins.

2 Language evaluation: Classification: Grade B.

Reply: Thank you again for your positive comments.

3 Academic norms and rules: The authors provided the Biostatistics Review Certificate, the Institutional Review Board Approval Form, and written informed consent. No academic misconduct was found in the Bing search.

Reply: Thank you again for your positive comments.

4 Supplementary comments: This is an invited manuscript. The study was supported by 6 grants. The topic has not previously been published in the WJCC.

Reply: Thank you again for your positive comments.

5 Issues raised: (1) The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s); (2) The authors did not provide original pictures. 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; and (3) The “Article Highlights” section is missing. Please add the “Article Highlights” section at the end of the main text; 6 Recommendation: Conditional acceptance.

Reply: Thank you again for your professional comments and valuable suggestions. We uploaded the funding agency copy of approval documents. To provide the original figures, we prepared and arranged the figures using PowerPoint, and uploaded this file accordingly. We have added the “Article Highlights” section at the end of the main text accordingly.

(3) To Company editor-in-chief:

I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Gastroenterology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office’s comments and the Criteria for Manuscript Revision by Authors.

Reply: Thank you again for your professional comments and valuable suggestions. We have revised the manuscript according to the reviewer's and Science editor's suggestions and comments and marked the changes with yellow highlight.