Format for ANSWERING REVIEWERS

July 10, 2021

Dear Editor:

Please find enclosed the edited manuscript in Word format (file name: 66044-Supplementary-Material-revision.docx).

Title: Dysbiosis of the duodenal microbiota as a diagnostic marker for pancreaticobiliary cancer

Author: Mitsuru Sugimoto, Kazumichi Abe, Tadayuki Takagi, Rei Suzuki, Naoki Konno, Hiroyuki Asama, Yuki Sato, Hiroki Irie, Ko Watanabe, Jun Nakamura, Hitomi Kikuchi, Mika Takasumi, Minami Hashimoto, Tsunetaka Kato, Ryoichiro Kobashi, Takuto Hikichi, and Hiromasa Ohira

The manuscript has been revised according to the reviewers' suggestions:
1 The format has been updated.

2 Revisions have been made according to the reviewers' suggestions.

Reviewer 1: Authors reported the correlation between the human microbiota and malignant gastrointestinal diseases and investigated the efficacy of the duodenal microbiota for diagnosing pancreaticobiliary cancers. The results showed that the combining Clostridium cluster XVIII and CA19-9 levels were 91.7% sensitivity and 71.4% specificity for pancreaticobiliary cancer diagnosis. However, the authors should screen to more cases to confirm the clinical values of Clostridium cluster XVIII compared with CA19-9 levels; Figure 2 and Figure 4 should be deleted.

Response: First, thank you very much for reviewing our manuscript. We revised our manuscript according to your comment. We agree with your point that only a small number of patients were involved in this study. However, based on the *Clostridium* cluster XVIII data, the average value of the malignant group was 4.5%, and that of the benign group was 1.5%. A total of thirty patients were needed to achieve an α error of 5% and a β value of 0.2. When *Clostridium* cluster XVIII was the main outcome, the minimum necessary sample size was secured. We have addressed this point in the limitation section (Lines 286-289).

Thank you for comments about Figure 2 and Figure 4. We have removed these figures and related parts.

Science Editor: Evaluation Report of First Decision Name of journal: World Journal of Gastroenterology Manuscript NO: 66044 Title: Dysbiosis of the duodenal microbiota as a diagnostic marker for pancreaticobiliary cancer.

Response: Thank you for reviewing our manuscript. We have revised the manuscript according to your comments.

1 Scientific quality: The manuscript is a basic study for evaluating the efficacy of the duodenal microbiota for diagnosing PB Ca. The combination of Clostridium cluster XVIII and CA19-9 levels showed 91.7% sensitivity and 71.4% specificity for diagnosing PB Ca. The topic is within the scope of the WJG.
(1) Classification: Grade C
(2) Summary of the Peer-Review Report: Authors reported the correlation between the human microbiota and malignant gastrointestinal diseases and investigated the efficacy of the duodenal microbiota for diagnosing pancreaticobiliary cancers. The results showed that the combining Clostridium cluster XVIII and CA19-9 levels were 91.7% sensitivity and 71.4% specificity for pancreaticobiliary cancer diagnosis. However, the authors should screen to more cases to confirm the clinical values of Clostridium cluster XVIII compared with CA19-9 levels; Figure 2 and Figure 4 should be deleted.

Response: We have revised our manuscript according to the reviewer's comments. Details of the related revisions are described above.

(3) Format: There are 7 tables and 4 figures. There are some capitalization errors in Table 1. Additionally, authors should provide the abbreviations in Table 6.

Response: We apologize for these errors. We have corrected the capitalization errors in Table 1 and added a description of the abbreviations to Table 6.

(4) References: A total of 67 references are cited, including 10 references published in the last 3 years (2018 – now).
(5) Self-cited references: There is no self-cited references.
(6) References recommendations: The authors have the right to refuse to cite improper references recommended by the peer reviewer(s), especially those published by the peer reviewer(s) him/herself (themselves). If the authors find the peer reviewer(s) request for the authors to cite improper references published by him/herself (themselves), please send the peer reviewer's ID number to editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately.

Response: Thank you for reviewing our manuscript.

2 Language evaluation: Classification: Grade B. A certificate for proficiency in English language was provided.

Response: Thank you for evaluating the quality of the English.

3 Academic norms and rules: The authors provided the Biostatistics Review Certificate, the Institutional Animal Care and Use Committee approval, and the Institutional Review Board Approval Form. The authors have not provided the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement forms. No

academic misconduct was found by the Google search.

Response: Thank you for this comment. We will submit the necessary documents.

4 Supplementary comments: This manuscript was an invited manuscript. The topic has not previously been published in the WJG.

Response: Thank you for this comment. This study focuses on new diagnostic methods for pancreaticobiliary cancer.

5. Issues raised:
1) The number of enrolled patients were too low.

Response: Thank you for this comment. We agree that only a small number of patients were involved in this study. However, based on the *Clostridium* cluster XVIII data, the average value of the malignant group was 4.5%, and that of the benign group was 1.5%. A total of thirty patients were needed to achieve an α error of 5% and a β value of 0.2. When *Clostridium* cluster XVIII was the main outcome, the minimum necessary sample size was secured. We have addressed this point in the limitation section (Lines 286-289).

2) The authors did not provide original pictures. Please provide the original figure files. Please prepare and arrange the figures using PowerPoint to ensure that arrows or text portions can be reprocessed by the editor.

Response: Thank you for this comment. We have revised the figures and arranged them in PowerPoint as suggested.

3) The "Article Highlights" section is missing. Please add the "Article Highlights" section at the end of the main text (and directly before the References).

Response: Thank you for this comment. We have added an "Article Highlights" section.

6 Re-Review: No
7 Recommendation: Conditional acceptance of transfer to another BPG journal (as Editor-in-chief recommend). Reviewer gave the Grade C only.

Response: Thank you for providing us an opportunity to revise the manuscript.

Sincerely,
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