

Cover Letter

Dear Editor and Reviewer,

Firstly, thank you for the great comments. The manuscript (70046) was made revision according to each comment from the reviewers. The following steps outlined below were fulfilled during the revision and re-submission.

Please check the responses of each point. All the revisions were tracked in the revised manuscript and also pointed in the reply to reviewer's comments in this letter.

Thank you for consideration of the revised manuscript.

Sincerely,

Ming Yang, PhD

University of Missouri-Columbia

1 MANUSCRIPT REVISION DEADLINE

We request that you submit your revision in no more than 14 days. Please note that you have only two chances for revising the manuscript.

Response: The revised manuscript will be submitted before due time.

2 PLEASE SELECT TO REVISE THIS MANUSCRIPT OR NOT

Please login to the F6Publishing system at <https://www.f6publishing.com> by entering your registered E-mail and password. After clicking on the "Author Login" button, please click on "Manuscripts Needing Revision" under the "Revisions" heading to find your manuscript that needs revision. Clicking on the "Handle" button allows you to choose to revise this manuscript or not. If you choose not to revise your manuscript, please click on the "Decline" button, and the manuscript will be WITHDRAWN.

Response: A revision was made according to all the reviewers' comments.

3 SCIENTIFIC QUALITY

Please resolve all issues in the manuscript based on the peer review report and make a point-by-point response to each of the issues raised in the peer review report. Note, authors must resolve all issues in the manuscript that are raised in the peer-review

report(s) and provide point-by-point responses to each of the issues raised in the peer-review report(s); these are listed below for your convenience:

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: *In this letter, the authors commented briefly on O'Neill's review article. Interestingly, you summarized clinical trials evaluating diagnostic methods or biomarkers for PC in a table. However, in paragraph 2, I suggest you simplify the characteristics of PC and insert a summary on the limitations of clinical application of multi-biomarker panel. My other questions are shown below: 1. In line 45: Do you mean "less common endocrine cancers"? 2. In line 58: Is the term "benign pancreatic benign disease" correct here? 3. In line 73: It is "Table 1". 4. In table 1, some statements lack necessary references.*

Response: The authors appreciated the great comments from the reviewer. Each comment was addressed and tracked in the manuscript. Here are the details:

In paragraph 2, a summary of limitations of clinical application of multi-biomarker panel was added in lines 78-81 (end of paragraph two).

Other questions: 1. exocrine corrected to endocrine; 2. Corrected to benign pancreatic disease; 3. Table 3 corrected to Table 1; 4. All the clinical trials with results have been added references, other recruiting clinical trials only with the titles of trials.

Reviewer #2:

Scientific Quality: Grade A (Excellent)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: *This very interesting paper contains important recent data of diagnostic biomarkers for pancreatic cancer. please check the proper formatting for LETTER TO THE EDITOR of this journal.*

Response: The authors thank the reviewer's great suggestion. The format of the letter was modified according to the format style of WJG.

Reviewer #3:

Scientific Quality: Grade E (Do not publish)

Language Quality: Grade A (Priority publishing)

Conclusion: Rejection

Specific Comments to Authors: This letter describes what is well known to anyone involved in the treatment of pancreatic cancer and a list of past and current clinical studies regarding tumor markers for pancreatic cancer. I am afraid to say that there is little novel information to be added in this field, so that this letter would not be worthy of publication in World Journal of Gastroenterology.

Response: Thanks to this point. In this letter, the authors summarize some latest clinical trials information about the diagnostic markers that could be potential application in the future. It provides very valuable information for scientists who studying pancreatic cancer but other areas, and a summary review information helps to quickly attain the knowledge for young scientists and clinicians.

Reviewer #4:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: This letter represents a supplement to the original review. There are 2 comments to the authors. First, the authors demonstrated "PC consists of two main subtypes, including more common exocrine cancers and less common exocrine cancers". Please check the latter less common one is endocrine cancers. Second, the NCT00899158 was completed in 2008, there was no study published yet? Please check.

Response: The authors appreciated the great effort and suggestion of the review. 1. The typo error exocrine was corrected to endocrine. 2. The authors double checked the trial NCT00899158, there is no study published yet and no results posted until searching date August 7, 2021.

4 LANGUAGE POLISHING REQUIREMENTS FOR REVISED MANUSCRIPTS SUBMITTED BY AUTHORS WHO ARE NON-NATIVE SPEAKERS OF ENGLISH

As the revision process results in changes to the content of the manuscript, language problems may exist in the revised manuscript. Thus, it is necessary to perform further language polishing that will ensure all grammatical, syntactical, formatting and other related errors be resolved, so that the revised manuscript will meet the publication requirement (Grade A).

Authors are requested to send their revised manuscript to a professional English language editing company or a native English-speaking expert to polish the manuscript further. When the authors submit the subsequent polished manuscript to us, they must provide a new language certificate along with the manuscript.

Once this step is completed, the manuscript will be quickly accepted and published online. Please visit the following website for the professional English language editing companies we recommend: <https://www.wjgnet.com/bpg/gerinfo/240>.

Response: The English was checked using one of the suggested companies. A certification was submitted associated with the manuscript.

5 ABBREVIATIONS

In general, do not use non-standard abbreviations, unless they appear at least two times in the text preceding the first usage/definition. Certain commonly used abbreviations, such as DNA, RNA, HIV, LD50, PCR, HBV, ECG, WBC, RBC, CT, ESR, CSF, IgG, ELISA, PBS, ATP, EDTA, and mAb, do not need to be defined and can be used directly.

The basic rules on abbreviations are provided here:

(1) Title: *Abbreviations are not permitted. Please spell out any abbreviation in the title.*

(2) Running title: *Abbreviations are permitted. Also, please shorten the running title to no more than 6 words.*

(3) Abstract: *Abbreviations must be defined upon first appearance in the Abstract. Example 1: Hepatocellular carcinoma (HCC). Example 2: Helicobacter pylori (H. pylori).*

(4) Key Words: *Abbreviations must be defined upon first appearance in the Key Words.*

(5) Core Tip: *Abbreviations must be defined upon first appearance in the Core Tip. Example 1: Hepatocellular carcinoma (HCC). Example 2: Helicobacter pylori (H. pylori)*

(6) Main Text: *Abbreviations must be defined upon first appearance in the Main Text. Example 1: Hepatocellular carcinoma (HCC). Example 2: Helicobacter pylori (H. pylori)*

(7) Article Highlights: *Abbreviations must be defined upon first appearance in the Article Highlights. Example 1: Hepatocellular carcinoma (HCC).*

Example 2: Helicobacter pylori (H. pylori)

(8) Figures: *Abbreviations are not allowed in the Figure title. For the Figure Legend text, abbreviations are allowed but must be defined upon first appearance in the text. Example 1: A: Hepatocellular carcinoma (HCC) biopsy sample; B: HCC-adjacent tissue sample. For any*

abbreviation that appears in the Figure itself but is not included in the Figure Legend textual description, it will be defined (separated by semicolons) at the end of the figure legend. Example 2: BMI: Body mass index; US: Ultrasound.

(9) Tables: *Abbreviations are not allowed in the Table title. For the Table itself, please verify all abbreviations used in tables are defined (separated by semicolons) directly underneath the table. Example 1: BMI: Body mass index; US: Ultrasound.*

Response: The abbreviations were checked.

6 EDITORIAL OFFICE'S COMMENTS

Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

(1) Science editor:

1 Scientific quality: The invited manuscript describes "Diagnostic biomarkers for pancreatic cancer: an update". The topic is within the scope of the WJG. (1) Classification: Grade E, Grade A, Grade B, and Grade C; (2) Summary of the Peer-Review Report: (03674268): The authors commented briefly on O'Neill's review article. Interestingly, you summarized clinical trials evaluating diagnostic methods or biomarkers for PC in a table. However, in paragraph 2, I suggest you simplify the characteristics of PC and insert a summary on the limitations of clinical application of multi-biomarker panel. My other questions are shown below: 1. In line 45: Do you mean "less common endocrine cancers"? 2. In line 58: Is the term "benign pancreatic benign disease" correct here? 3. In line 73: It is "Table 1". 4. In table 1, some statements lack necessary references. (03474273): This letter represents a supplement to the original review. There are 2 comments to the authors. First, the authors demonstrated "PC consists of two main subtypes, including more common exocrine cancers and less common exocrine cancers". Please check the latter less common one is endocrine cancers. Second, the NCT00899158 was completed in 2008, there was no study published yet? Please check. (03455028): This very interesting paper contains important recent data of diagnostic biomarkers for pancreatic cancer. please check the proper formatting for LETTER TO THE EDITOR of this journal. (03252941): This letter describes what is well known to anyone involved in the treatment of pancreatic cancer and a list of past and current clinical studies regarding tumor markers for pancreatic cancer. I am afraid to say that there is little novel information to be added in this field, so that this letter would not be worthy of publication in World Journal of Gastroenterology. (3) Format: There are 1 tables and 0 figures; (4) References: A total of 16 references are cited, including 14 references published in the last 3 years; (5) Self-cited references: There are 1 self-cited reference; (6) References

recommendations: The authors have cited proper references. 2. Language evaluation: Classification: Grade A, Grade B, Grade A, and Grade B. 3 Academic norms and rules: NA. 4 Supplementary comments: This is an invited manuscript. The authors declare no conflict of interest. The topic has not previously been published in the WJG. 5 Issues raised: NA. 6. Re-Review: Required. 7 Recommendation: Conditional acceptance

(2) 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.

Response: Thank you for the comments. The manuscript was revised according to all the reviewers' comments. English of revised manuscript was checked with suggested company, and all the revision was tracked in the manuscript. The manuscript was formatted according to the editorial officer suggestion.

7 STEPS FOR SUBMITTING THE REVISED MANUSCRIPT

Step 1: Author Information

Please click and download the Format for authorship, institution, and corresponding author guidelines, and further check if the authors names and institutions meet the requirements of the journal.

Step 2: Manuscript Information

Please check if the manuscript information is correct.

Step 3: Abstract, Main Text, and Acknowledgements

(1) Guidelines for revising the content: Please download the guidelines for Original articles, Review articles, or Case Report articles for your specific manuscript type (Letter to the Editor) at: <https://www.wjgnet.com/bpg/GerInfo/291>. Please further revise the content your manuscript according to the Guidelines and Requirements for Manuscript Revision.

(2) Format for Manuscript Revision: Please update the format of your manuscript according to the Guidelines and Requirements for Manuscript Revision and the Format for Manuscript

Revision. Please visit <https://www.wjgnet.com/bpg/GerInfo/291> for the article type-specific guidelines and formatting examples.

(3) Requirements for Article Highlights: If your manuscript is an Original Study (Basic Study or Clinical Study), Meta-Analysis, or Systemic Review, the “Article Highlights” section is required. Detailed writing requirements for the “Article Highlights” can be found in the Guidelines and Requirements for Manuscript Revision.

Step 4: References

Please revise the references according to the Format for References Guidelines, and be sure to edit the reference using the reference auto-analyser.

Step 5: Footnotes and Figure Legends

(1) Requirements for Figures: Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file, and submit as “**70046-Figures.pptx**” on the system. The figures should be uploaded to the file destination of “Image File”.

(2) Requirements for Tables: Please provide decomposable Tables (in which all components are movable and editable), organize them into a single Word file, and submit as “**70046-Tables.docx**” on the system. The tables should be uploaded to the file destination of “Table File”.

Step 6: Automatically Generate Full-Text Files

Authors cannot replace and upload the “Manuscript File” separately. Since we only accept a manuscript file that is automatically generated, please download the “Full Text File” or click “Preview” to ensure all the contents of the manuscript automatically generated by the system are correct and meet the requirements of the journal. If you find that there is content that needs to be modified in the Full-Text File, please return to the corresponding step(s), modify and update the content, and save. At this point, you then have to click the “Save & Continue” button in Step 5 and the F6Publishing system will automatically regenerate the Full-Text File, and it will be automatically stored.

Step 7: Upload the Revision Files

For all required accompanying documents (listed below), you can begin the uploading process via the F6Publishing system. Then, please download all the uploaded documents to ensure all of them are correct.

- (1) 70046-Answering Reviewers**
- (2) 70046-Audio Core Tip**
- (3) 70046-Conflict-of-Interest Disclosure Form**
- (4) 70046-Copyright License Agreement**
- (5) 70046-Approved Grant Application Form(s) or Funding Agency Copy of any Approval Document(s)**
- (6) 70046-Non-Native Speakers of English Editing Certificate**
- (7) 70046-Video**
- (8) 70046-Image File**
- (9) 70046-Table File**
- (10) 70046-Supplementary Material**

If your manuscript has supportive foundations, the approved grant application form(s) or funding agency copy of any approval document(s) must be provided. Otherwise, we will delete the supportive foundations.

If your manuscript has no “Video” or “Supplementary Material”, you do not need to submit those two types of documents.

Response: The revised manuscript was submitted according to the above seven steps, with all the documents including (1) to (4), and (6), (9).

8 COPYRIGHT LICENSE AGREEMENT

All authors should accept and sign the Copyright License Agreement (CLA), following the link sent in individual emails to each author. After all authors have accepted and signed their respective CLA, the Corresponding Author is responsible for downloading the signed CLA by clicking on the “Download” button in the CLA page, re-storing it as “PDF”, and then uploading it to the file destination of “Copyright License Agreement”. If any of the authors do not accept to sign the CLA, the manuscript will not be accepted for publication.

Response: Copyright was signed and uploaded.

9 CONFLICT-OF-INTEREST DISCLOSURE FORM

Please click and download the fillable ICMJE Form for Disclosure of Potential Conflicts of Interest (PDF), and fill it in. The Corresponding Author is responsible for filling out this form. Once filled out completely, the Conflict-of-Interest Disclosure Form should be uploaded to the file destination of 'Conflict-of-Interest Disclosure Form'.

Response: The Conflict-of-Interest Disclosure Form was signed and uploaded.

Best regards,

Ming Yang