

Dear Editors and Reviewers:

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "Novel multiplex stool-based assay for detection of early-stage colon cancer in a Chinese population" (No. 73809). These comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our research. We have studied the comments carefully and have made correction which we hope meet with approval. The main corrections in the paper and the responses to the reviewer's comments are as follow:

**(1) Responds to the Reviewers' comments:**

***Reviewer #1:***

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: The topic of the study is fairly interesting, and its approach is correct. The manuscript is well written and structure, with and easily understandable and clear exposition. The results of this study could lead to its application in clinical practice, were they to be confirmed in future prospective multicenter studies. I encourage the authors to keep working on it. It would be interesting for the authors to reference other similar studies not based on a Chinese population.

**Response:** Many thanks for your positive comment. In this study, we identified a novel multiplex stool-based assay combining three stool DNA (sDNA) methylation biomarkers and fecal immunochemical test. Further validation in larger samples showed that it enabled the diagnosis of early-stage colon cancer (ECC) with high sensitivity and specificity throughout the colon. To our knowledge, this is the first study to focus on ECC screening in China. The limitations of our study should also be noted. For example, this was a single-center study, and the sample size was relatively small.

As a result, further demonstrations on a large-scale, prospective multicenter study are needed to conclusively evaluate the value of our assay. Actually, that's what we are working on, and it may take one year or two. When we finish this study, we will announce the results as soon as possible. In addition, as we indicated in the study, the reported screening efficacy of the same sDNA methylation biomarker varied greatly among studies, due to the different study populations (mainly the ethnic, geographic and dietary differences), inclusion criteria and levels of examination. In order to reduce the influence of these factors and to evaluate our study results objectively, we mainly cited the studies based on the Chinese population for comparison in the discussion section.

***Reviewer #2:***

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: This is an original study examining a novel multiplex stool-based assay for detection of early-stage colon cancer in the Chinese population. I do not have the molecular biology background to comment on the methodology but the validation of the test and its validation in this selected patient population appear sound. The paper is well written and the results are well displayed and tabulated. The discussion and conclusions are aligned with the findings.

**Response:** We sincerely appreciate this recognition of our research efforts. We will keep working on it. As stated above, we are presently organizing a multicenter study to prospectively evaluate the value of our assay. In addition, the revised manuscript has been edited for proper English language, grammar, punctuation, spelling, and overall style by one or more of the highly qualified native English-speaking editors (American Journal Experts). We hope the language now is acceptable.

**(2) Responds to the Editors' comments:**

## **1. Science editor**

This is an interesting study that about using multiplex stool-based assay for detection of early-stage colon cancer (ECC), which may have important implications in clinical practice is verified in future larger-scale studies. It is well-written and organized.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade B (Very good)

## **2. Company editor-in-chief**

I have reviewed the Peer-Review Report, the 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. Before final acceptance, uniform presentation should be used for figures showing the same or similar contents; for example, "Figure 1Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...". Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file. Please 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:** Special thanks to you for your hard work. We have carefully revised the manuscript, including the tables and figures, according to your good suggestions. In addition, the manuscript has also been revised by someone with expertise in technical English editing (American Journal Experts). We hope that the revised version will meet with your approval.

Once again, thank you very much for your comments and suggestions.

Looking forward to your reply.

Yours sincerely,

Erjiang Tang