

Dear editor-in-chief and reviewers,

We would like to thank you for providing us with an opportunity to adequately address reviewer's comments for our manuscript, entitled "Fecal microbial biomarkers along with MT-sDNA improve the diagnostic accuracy in colorectal cancer(**Manuscript NO: 84686**)" for further consideration for publication in the World Journal of Gastrointestinal Oncology.

We have taken each of the reviewers' comments into careful consideration. Below this cover letter, we address each of the comments individually.

We hope you find the revised manuscript acceptable for publication in The World Journal of Gastrointestinal Oncology, but would be pleased to have the opportunity to make further amendments, if required. Thank you once again for your consideration.

Best regards,

Yours sciencereally,

Hanlu Gao Ph.D.

Reviewer #1: Dear Associate Editor Thank you for sending me the article entitled "Fecal microbial biomarkers along with MT-sDNA improve the diagnostic accuracy in colorectal cancer" for review. This trial evaluated the association between some genera of intestinal microbiome, tumor markers and MT-sDNA with colorectal cancer. They showed a positive correlation between MT-sDNA, CEA and AFP with intestinal microbiome. Moreover, eight biomarkers including 6 genera of gut microbiota, MT-sDNA and CEA showed a prominent sensitivity and specificity for the CRC prediction. There are some comments as the followings:

1-Please do not use abbreviations like MT-sDNA in the abstract.

We feel great thanks for your professional review work on our article. We fixed this error by adding the full English name when the abbreviation first appeared.

2-Since cirrhosis affect the AFP level, please define if subjects with cirrhosis were excluded from the study.

Thank your for pointing this out. Subjects with cirrhosis were included in the exclusion criteria.

3-Please define the criteria for selection of healthy subjects. Was colonoscopy performed in the controls? Were subjects with colorectal polyps excluded from control group?

Thank you for your interest in our research. We defined the criteria for selection of healthy subjects. The colonoscopy was performed in the controls. Subjects with colorectal polyps were excluded from control group.

4-Considering the role of environment in gut microbiome, please clarify why only educational status was evaluated in this trial. I think some other important sociodemographic variables (residency in rural-urban area, monthly income...) and food patterns should be matched in the trial arms. These shortages could be addressed in as the limitations of study.

Thank you for your good suggestion. Education status in this study was a confounding factor and was used as a control variable in correlation analysis.

As you mentioned, some environmental factors such as diet style, frequency and lifestyle may affect intestinal flora, but relevant investigation and research have not been carried out in this study, so it cannot be analyzed and discussed. With reference to your suggestions, we have explained the deficiencies in the study.

Reviewer #2: It is an interesting review, recent publications should be added and discussed ie Cancers (Basel). 2022 Dec 28;15(1):192.

Thanks a lot for your interest in our article. We include the article you recommended in the paper as reference 5.