

Dear Lian-Sheng Ma,

I sincerely thank you for your prior acceptance of Manuscript NO: 81468 "Genetic heterogeneity of colorectal cancer and the microbiome" in World Journal of Gastrointestinal Oncology, and reviewers for objective and important comments. It was very interesting for me to work on this document. This topic is so vast, it covers a variety of aspects related to the role of the microbiome in the initiation and progression of colorectal cancer, that it is absolutely impossible to consider it within the framework of one article. For me personally, of particular interest are the mechanisms by which individual representatives of the intestinal microbiota can realize their carcinogenic potential. It is these mechanisms that I tried to cover in more detail in this review manuscript as the knowledge of these mechanisms opens up new possibilities for the prevention and treatment of colorectal cancer.

The manuscript has been re-verified by the professional editor, a certificate is attached.

Dear Editorial Board, due to comment of reviewer #1, I would like to change the title of the manuscript to "Gut microbiota, polyps and colorectal cancer" or "Gut microbiota and genetic heterogeneity of colorectal cancer". The first title more accurately reflects the content of the manuscript, as I planned from the outset to discuss the role of the microbiome in colorectal carcinogenesis. Unfortunately, I was unable to enter this title into the F6Publishing system. The system did not accept it, answering that such title already exists. I changed the title and again tried to enter it the system. This was repeated several times. As a result, I sent several variants of the title of the same manuscript to the system. On September 28, I wrote about this problem to Prof. Lian-Sheng Ma, President and Editor-in-Chief, Beijing Baishideng BioMed Scientific Co., Ltd., Founder and CEO. I don't know if it's possible to change the title now and will the titles "Gut microbiota, polyps and colorectal cancer" or "Gut microbiota and genetic heterogeneity of colorectal cancer" be appropriate.

In accordance with the comments of the reviewers, I made the following corrections to the manuscript:

Reviewer #1.

1. I asked the Editor of the World Journal of Gastrointestinal Oncology with a request to change the title of the manuscript to "Gut microbiota, polyps and colorectal cancer" or "Gut microbiota and genetic heterogeneity of colorectal cancer".

2. I discussed in more detail the possible causes of changes in the types of intestinal microorganisms in patients with colorectal cancer.
3. I discussed the differences in the immune system of the colon and small intestine in more detail.
4. An additional subchapter "Gut microbiota and immunity" has been added to the manuscript, which discusses in more detail the role of the gut immune system in colorectal carcinogenesis.

Reviewer #2.

1. I completely rewrote the introduction to match the subject of the manuscript.
2. The problem of genetic heterogeneity of the colorectal cancer in this manuscript is considered solely from the standpoint of the impact on genetic mutations of the intestinal microbiome. Unfortunately, the title of the manuscript is not entirely appropriate. In this regard, I asked the Editor of the World Journal of Gastrointestinal Oncology with a request to change the title of the manuscript to "Gut microbiota, polyps and colorectal cancer" or "Gut microbiota and genetic heterogeneity of colorectal cancer".
3. Unfortunately, the role of the microbiome in colorectal cancer heterogeneity is not well understood. This problem requires a detailed study, as I indicated in the conclusion.
4. I consider that the section of the manuscript "Mycobiome and progression of CRC" to be very important. But I agree that the section was written very superficially. I have discussed this issue in more detail.
5. The main goal of the manuscript is to discuss in detail the role of the gut microbiota in the initiation and progression of CRC. The question of the genetic heterogeneity of CRC is considered in the manuscript only from the standpoint of the possible involvement of the intestinal microbiome in these processes. I slightly changed the structure of the manuscript by adding new sections to it. I hope that in this form the manuscript retains its integrity.

Reviewer #3.

I sincerely thank the reviewer for the positive evaluation of my manuscript.

Best regards, Marina A Senchukova (ID 03270609), MD, PhD, professor of Oncology Department, Orenburg State Medical University