

Dear reviewer,

Thank you very much for your valuable comments. We will answer them one by one:

1. In Abstract, what does MSS stand for?

This is our negligence, we did not write the full name of MSS. MSS stands for microsatellite stability, which we have added to the abstract. Thank you very much for your reminder.

2. In immunochemistry, how is the IOD value measured?

Thank you for reading it so carefully, but we are sorry that we did not write clearly. In the final image analysis part of immunohistochemistry, three high power visual fields were randomly selected for image acquisition, and the image quantitative analysis was carried out with Image-Pro Plus 6.0 software. The average optical density of each protein was finally expressed by IOD value. We have also added this part to the “methods” section.

3. In this report, what TNM classification was used? UICC?

Thank you for reminding us. In our article, TNM classification was indeed made according to the Seventh Edition of TNM classification criteria issued by the Union for International Cancer Control (UICC). We have also added this part to the “methods” section.

4. About the reduction of inflammation, is there a possibility that the influence of other drugs contributed?

Neither of the two groups was given other drugs before operation, so we think we can rule out the effects of other drugs.

5. Are there any differences of the overall survival, and CRC recurrence between Control group and Treatment group?

We will follow up on the impact of the overall survival and recurrence of colorectal cancer patients in the control group and treatment group. Thank you for this question.

6. In the “GQD reduced inflammation” section, authors described “Meanwhile, compared with the control group and pre-treatment group, GQD significantly reduced the level of 5-HT in the post-treatment”. However, the value of 5-HT is not

significantly different between control and post-treatment in Figure 2F.

This is our fault. We are very sorry for the mistake in writing. We have revised it in the manuscript.

7. How should we interpret Figure 6? Did the carcinogenic gut microbiota increase in post treatment data?

Figure 6 shows KEGG functional enrichment of differential genes of gut microbiota between the pre-treatment and post-treatment groups. The results showed that the functional differences of gut microbiota mainly included energy metabolism, immune system, nervous system and cancer. The bar chart shows the function of genes enrichment, not the abundance of gut microbiota.

8. In page 14, line 10, the authors described “their activation state may be changed.”. Are there any methods to investigate the activation of NK and Treg cell? If you can't, it's okay.

With regard to the activation of NK cells, their killing ability can be detected after culture in vitro. However, the activation of Treg cells may be related to many types, and different types may have different effects. In our follow-up series of studies, we will also pay attention to the activation state of these immune cells and add some tests.

9. In page 16, line 15-16, a next sentence “the abundance of harmful bacteria such as *Escherichia coli*, *Bacteroides fragilis*, and *Fusobacterium nucleatum* increased,” is written. Therefore, harmful bacteria increased in the post-treatment because the abundance of Bacteroidetes was increased?

We are sorry that's not what we meant. What is said here is that there are changes in the gut microbiota of most patients with colorectal cancer, which is reflected in the increase in the abundance of some harmful bacteria such as *Escherichia coli*, *Bacteroides fragilis*, and *Fusobacterium nucleatum* and the decrease in the abundance of beneficial bacteria. In our study, the abundance of Bacteroidetes was increased, while the abundance of Firmicutes, Proteobacteria and Verrucomicrobia was decreased in the post-treatment group. While at the genus level, we found that compared with pre-treatment group *Bacteroides*, *Akkermansia* and *Prevotella* were

enriched and the abundance of Megamonas and Veillonella was decreased in the post-treatment group.

10. Do you need the paragraph starting with a sentence “Many scientists ...” in page 17? Discussion part is long. If you need the paragraph, you don’t have to remove the paragraph.

Thank you for your advice. However, our discussion is indeed a bit long, and according to your suggestion, we have reduced this paragraph.

11. In page 18, line 12-13, “In this study, the abundance of Akkermansia of patients with CRC after taking GQD was increased”. Is there a figure of the result?

Yes, figure 5F showed that the abundance of Akkermansia of patients with CRC after taking GQD was increased, which was represented by a light brown bar.