Dear Editor,

We greatly appreciate the reviewers' comments and suggestions. Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have revised the manuscript to provide a more scientifically sound article and have answered their questions here.

Reviewer #1

Q1: This is an interesting study, but I have a few comments: 1) I did not find any mention of the Phachyocytes phylum (listed in the Results chapter) in the publications; 2) Proteus is not a phylum, but a genus

A: Thank you very much for your timely correction of the language translation problem of this article. Your comments are very important for the accuracy of the language of this article. "*Phachyocytes* phylum" should be "*Firmicutes* phylum" here, "*Proteus*" should be "*Proteobacteria* phylum" here. All issues related to the translation of the above two languages in this article have been revised and corrected, and marked with highlighted text in yellow.

Q2: The design of the study is too complex, the flowchart is not presented.

A: Thank you very much for your suggestion. Your suggestions have played an important role in improving this article. We have produced a study design picture as Figure 1.

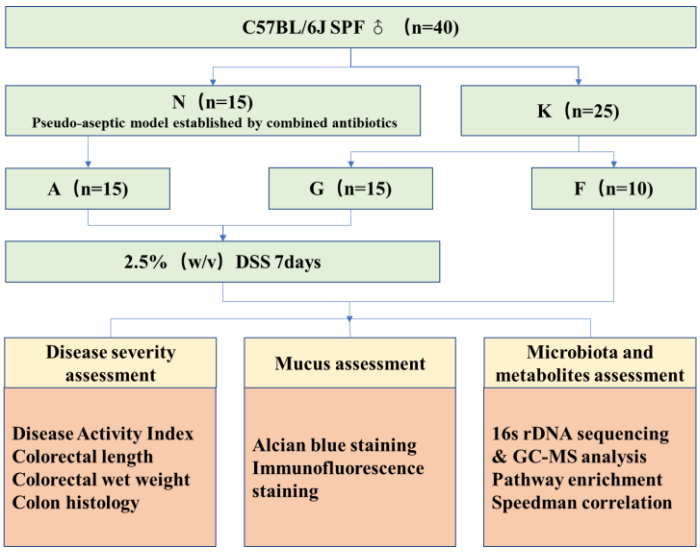

Figure 1. Study design

N: pseudo-aseptic group; K: blank group; A: microbiota$^-$ colitis group; G: microbiota$^+$ colitis group; F: blank group.

Q3: The number of examined animals in subgroups is too small to draw conclusions

A: Thank you very much for your comment. The small sample size was indeed a problem in our study. However, due to the limited funds, we have tried our best to set the maximum number of subgroup samples within the range of available funds. Our follow-up research will focus on this issue and increase the number of cases appropriately.

Q4: The aim of the study and the choice of experimental interventions are not clear: the authors claim they want to study ulcerative colitis, but describe the features of some colitis experimental models, but not in ulcerative colitis itself

A： We are grateful to the reviewer for this question. UC is a disease caused by multiple etiologies and the cause of the disease is not completely clear. All existing modeling methods cannot fully meet the pathophysiological changes of UC. At present, the animal experiments related to UC are all carried out with colitis as the UC model. Thus, our choice is based on the most recognized and common UC model in the world, and we will continue to pay attention to this issue, whether there is a more suitable UC model in the future.

Reviewer #2

Q1: In this study, the authors investigated the changes in intestinal microbiota and metabolites in mice with dextran sulfate sodium-induced colitis and the correlation between gut microbiota and metabolites. Overall, the study was well-designed and performed. Some minors are suggested. In the methods, the tools or website for 'Comparison of biological information for differential microbiota' should be listed.

A: Thank you very much for your comment. We have supplemented the website 'Comparison of biological information for differential microbiota' in Methods, as you suggested. Please see the yellow highlighted text in the Methods.

Q2: In the Discussion, some contexts such as ‘There are 10 to 100 trillion microorganisms in the human gastrointestinal tract, and in the past few decades, the impact of the gut microbiota on human health has received widespread interest from science and the general public.’ and ‘Different antibiotics selectively deplete different members of the microbiota…’. In contrast, more information should be discussed about the new bacterial and metabolite function in UC or colitis.

A: We are grateful to the reviewer for this question. Your suggestion is very helpful for deepening the content of the article. We have supplemented the discussion with more information on the new bacterial and metabolite function in UC or colitis as you suggested. Please see the highlighted text of yellow in the Discussion.

Q3: For MUC2, list the abbreviation at the first time.

A: Thank you very much for your suggestion. We have listed the full name and abbreviation of MUC2 when it first appeared. Please see the text highlighted in yellow in the Introduction.

Q4: Some letters or words in the figures are too small, such as Figure 4B. Figures could be separated at different slides/pages when providing the original images.

A: Thank you very much for your suggestion. At the same time, the magazine also put forward relevant requirements for this. The figures we have uploaded as required by the magazine are original images that can be edited in high definition. If the article is accepted, the figures will depend on the journal's typographic and layout requirements.

Reviewer #3

Q1: The article is of clinical interest. The research methods are up-to-date and consistent with the purpose of the article. The article is illustrated with a sufficient number of figures. The list of references contains up-to-date references. Comments: 1. It is recommended to add a figure with the study design.

A: Thank you very much for your suggestion. Your suggestions have played an important role in improving this article. We have produced a study design picture as Figure 1.

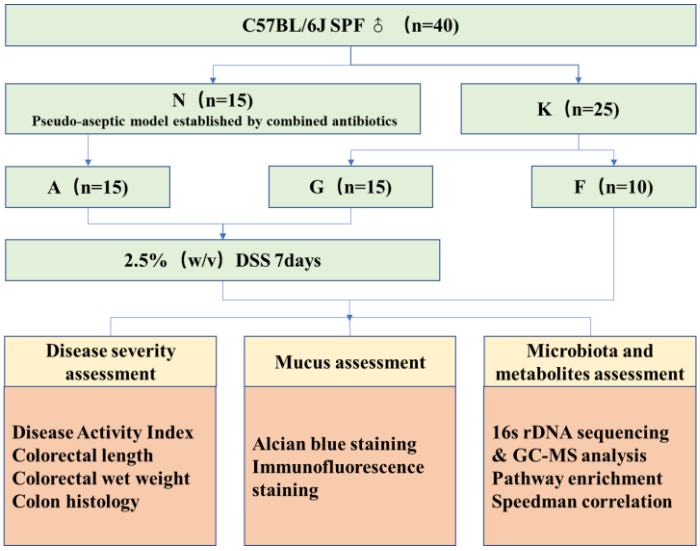

Figure 1. Study design

N: pseudo-aseptic group; K: blank group; A: microbiota$^-$ colitis group; G: microbiota$^+$ colitis group; F: blank group.

Q2: Was the effect of the antibiotics used evaluated on the intestinal epithelium? Could these antibiotics directly affect the expression of some key proteins involved in colitis? For example, treatment with metronidazole may affect goblet cell function and expression of some key proteins.

A: We are grateful to the reviewer for this question, it gave us a lot of inspiration in the future study. Regarding the effect of a specific antibiotic on key proteins associated with intestinal epithelial cells and colitis, it is a pity that our existing experiments do not yet answer this question, which is also the inadequacy of our research. We will design this aspect of the research content in subsequent experiments.

Q3: Was there antibiotic-associated diarrhea in mice in the pseudo-aseptic group? Could it have affected the acceleration of DSS elimination and the severity of colitis?

A: Thank you again for your question. First of all, from Figure 2B, it can be seen that pseudo-aseptic mice compared with mice in the non-intervention group had no statistical difference in body weight and no significant change in fecal traits, which can reflect from the side that there is no antibiotic-related diarrhea in the pseudo-aseptic group mice, and it will not affect or accelerate the severity of

DSS-induced colitis. Second, from Figures 3 and 4, it can be seen that the symptoms of colitis, disease activity, intestinal mucosal histological structure and mucus distribution in pseudo-aseptic mice are less than those in intestinal bacterial mice, if pseudo-aseptic mice already have antibiotic-associated diarrhea, then in the case of DSS administration, it should lead to diarrhea and other symptoms more serious, but this contradicts the results we found, so it is further proved that pseudo-aseptic mice should not have antibiotic-related diarrhea.

We appreciate for warm work of editors and reviewers earnestly, and hope that the correction will meet with approval. Once again, we are grateful for reviewers' comments and suggestions.