Author’s response to reviews

Title: Role of colonic microbiota in the pathogenesis of ulcerative colitis

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Author’s response to reviews:

Dear Editors and Reviewers:

Thank you for your letter and for the reviewers’ comments concerning our manuscript entitled “Role of colonic microbiota in the pathogenesis of ulcerative colitis” (ID: BMGE-D-18-00313R1). 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 studied comments carefully and have made the correction which we hope to meet with approval. The revised portion is marked in red in the paper. The main corrections in the paper and the responds of the reviewers ‘comments are as flowing:
Responds to the reviewers’ comments:

Reviewer 1

1. The abstract mentions mouse model of UC but does not specify. please give these details.
Response: The details of the mouse model of UC in the abstract are as follows: The dextran sulfate sodium(DSS)-induced UC model was established by exposing mice to cycles of DSS. The details of the mouse model of UC have been added in the Methods, Results and Discussion sections and marked in red.

2. The INTRODUCTION is much too long. Please revise, shorten and enhance the focus of this section.
Response: Thank you for the advice. The INTRODUCTION has been revised and shortend.

3. The preparation of the inner mucous layer is not detailed (the methods only lists the scraping of the outer layer and the preparation of the remaining tissue).
Response: Details of the preparation of the inner mucous layer have been added in the Methods and marked in red (Line5 in “Isolation of intestinal content, an external mucus layer, and internal mucus layer” section).

4. The appropriate p values should be listed using a whole number or using a less than sign.
Response: The p values have been marked in red and revised as follows: The results showed that the DAI and body weight of model group differed significantly from the control group after time correction (F=168.66, P≤0.05; F=10.881, P≤0.05) (Line 4 in Results section).

5. How did the inflammatory process affect the mucous layers?
Response: All mucosal surfaces with their associated lymphoid structures are part of a common mucosal immune system or mucosa-associated lymphoid tissue. Each mucosal surface is covered by a layer of epithelium directly overlying loosely organized lymphoid tissue called the lamina propria. The epithelial layer is composed of one cell layer of columnar epithelium. These epithelial cells derive from the basal crypts and differentiate into villus or surface epithelium, goblet cells, and neuroendocrine cells (Paneth cells) that are involved in secretory functions. Overlying the epithelium is the glycocalyx composed of complex glycoproteins and mucins. This
mucous coat is an important physical barrier to potential pathogens, with organisms getting trapped and passed out in the stool. All mucosal sites have a mucus barrier that serves similar functions. The second level of physical protection is the epithelium itself. The third level of physical protection is the tight junctions joining adjacent enterocytes. The tight junction proteins, including occludin, claudins, and zonula occludens, are crucial for the maintenance of epithelial barrier integrity. These junctions are so tight that they prevent even small peptides from passing through. During inflammatory processes, these tight junctions can be disrupted, allowing free passage of luminal contents into the lamina propria. Specialized lymphocytes also reside in the epithelial layer situated on the basement membrane. And a significant body of evidence has highlighted the role of cytokines in the regulation of various tight junction proteins in a multitude of pathological conditions. Tumor necrosis factor-α (TNFα), interferon-γ (IFN-γ), and interleukins all are well-known for their indisputable role in the regulation of tight junction integrity. TNFα is a key player in the caveolin-1-mediated internalization of occludin, which elevates gut permeability; further, the overexpression of occludin alleviates the cytokine-induced increase in gut permeability. TNFα stimulation of the NFκB signal transduction pathway is another major mechanism involved in tight junction regulation. We have added some details about this question in the Discussion section and marked in red (Line 26-28 in the Discussion section).

6. The DISCUSSION is also way too long and should be shortened to enhance readability and focus.

Response: Thank you very much for the advice. The DISCUSSION section has been revised and shortend.

7. Most of the Figure/Tables titles/legends are inadequate (too short and don't provide adequate information). These should be enhanced to give more independence of these parts of the manuscript.

Response: More details have been given in the Figure legends and marked in red.

8. There are numerous errors of English word usage/grammar/language. These need correction.

Response: We are very sorry for our negligence of the errors of English word usage/grammar/language. We have made corrections and marked them in red.
Reviewer 2

1. The paper is well written and reports a very interesting plot. The study design is appropriate and skilled. Nevertheless, the discussion is too long and could be simplified to better focus on the topic.

Response: Thank you very much for the advice. The DISCUSSION section has been revised and shortened.

We tried our best to improve the manuscript and made some changes in the manuscript. These changes will not affect the content and framework of the paper. And here we did not list the changes but marked in red in the revised paper. We appreciate Editors/Reviewers’ warm work earnestly and hope that the correction will meet with approval.

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

Regards,

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