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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 62970

Title: Fecal microbiota transplantation ameliorates experimental colitis via gut microbiota and T-cell modulation

Reviewer's code: 05402068
Position: Peer Reviewer
Academic degree: MD, MSc
Professional title: Doctor
Reviewer's Country/Territory: United States
Author's Country/Territory: China

Manuscript submission date: 2021-01-23
Reviewer chosen by: AI Technique
Reviewer accepted review: 2021-01-23 04:00
Reviewer performed review: 2021-01-23 04:09
Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

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SPECIFIC COMMENTS TO AUTHORS

This manuscript demonstrates that fecal microbiota transplantation ameliorates experimental colitis through the mechanism of regulating gut microbiota and activating T lymphocytes. This study combined the animal study together with differentially expressed genes analysis, which is scientifically adequate enough for its research purpose. It provides scientific value to the treatment of colitis by FMT. However, the language still needs some minor polishing before being accepted.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 62970

Title: Fecal microbiota transplantation ameliorates experimental colitis via gut microbiota and T-cell modulation

Reviewer's code: 04091933

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Associate Professor, Senior Researcher

Reviewer's Country/Territory: Russia

Author's Country/Territory: China

Manuscript submission date: 2021-01-23

Reviewer chosen by: Jin-Lei Wang

Reviewer accepted review: 2021-01-25 13:14

Reviewer performed review: 2021-01-27 20:33

Review time: 2 Days and 7 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

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SPECIFIC COMMENTS TO AUTHORS

Undoubtedly, the topic of the study presented by the authors is relevant due to the increasing prevalence of IBD and the potential effectiveness of FMT. The reviewer has no questions regarding the study's methodology, results, figures, and references. However, it is desirable that the authors expand the discussion. The findings identified by the authors are very interesting, but the interpretation of changes in the microbiota after FMT is ambiguous. For example, a significant part of other studies shows not a decrease, but an increase in the relative abundance of Lactobacillus in IBD, which requires further study of their role in the pathogenesis of intestinal inflammation. Turicibacter has recently been discovered and cannot be considered unambiguously as a pathogen/pathobiont associated with IBD and other intestinal disorders. Recent research indicates an important role for this bacterium in host serotonin metabolism. Turicibacter was significantly less abundant in IBS-D patients. Similarly, the role of Clostridium_sensu_stricto_1 also cannot be interpreted unambiguously. In the title, I would recommend replacing "T lymphocyte activation" with "T-cell modulation". The manuscript may be published after a minor revision expanding and deepening the discussion regarding changes in the microbiota after FMT and its relationship with immune effects that could potentially improve colitis.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 62970

Title: Fecal microbiota transplantation ameliorates experimental colitis via gut microbiota and T-cell modulation

Reviewer's code: 03252330

Position: Editorial Board

Academic degree: MD, MSc

Professional title: Associate Professor

Reviewer's Country/Territory: Italy

Author's Country/Territory: China

Manuscript submission date: 2021-01-23

Reviewer chosen by: Jin-Lei Wang

Reviewer accepted review: 2021-01-25 07:51

Reviewer performed review: 2021-01-28 18:01

Review time: 3 Days and 10 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [ ] Grade B: Minor language polishing [Y] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

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SPECIFIC COMMENTS TO AUTHORS

The submitted paper analyzed the effect of fecal transplantation in a mouse model of ulcerative colitis, i.e. the one using DSS for 7 days. The authors fistly observed the macroscopical aspect of the colon and the histogy, observing significant differences between mice treated with DSS and those that, after the DSS treatment, received fecal transplant. They also compared the microbiota of these animals, detecting differences at the genus level, with a transplant effect that changed the microbiota composition making it more similar to the sham animal. The analysis of the transcriptome revealed differentially expressed genes that the authors correlated with the presence of the bacteria identified as highly present in the DSS-only treated mice, namely Clostridium_sensu_stricto_1, Turicibacter and Ruminococcus. Although the presented data are interesting there are some points that need to be addressed by the authors: 1.

Methods section: it is not clear whether they used the supernatant or the "sediment" for gavage; histological score should be defined; RNA used for sequencing was extracted from "inflammatory colonic tissue". If this is correct which percentage of the colon was regarded as having inflammation in the two groups? Was sequencing performed on all animals? 2.Results: in Figure 3 results should be compared by ANOVA. Is there a significant difference in lactobacillus between control and transplanted mice? The same kind of comparison should be applied to Fig 5. 3. Although the GO and Metascape analysis identify the genes differentially expressed in FMT mice as involved in the regulation of T cells, the data provided are not enough to demonstrate this hypothesis "Furthermore, after FMT treatment, the activation of T lymphocytes was significantly inhibited (Fig. 6)". To make this statement the authors should isolate T lymphocytes and test their activation status. 4. The entire discussion needs to be revised.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 62970

Title: Fecal microbiota transplantation ameliorates experimental colitis via gut microbiota and T-cell modulation

Reviewer's code: 05462152
Position: Peer Reviewer
Academic degree: MPhil

Professional title: Doctor

Reviewer's Country/Territory: United States

Author's Country/Territory: China

Manuscript submission date: 2021-01-23

Reviewer chosen by: AI Technique

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Review time: 7 Days and 14 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

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SPECIFIC COMMENTS TO AUTHORS

This manuscript describes an interesting new assessment of the mechanisms involved in changes that occur after fecal microbiota transplant in mice that have DSS-induced colitis. The level of detail provided for the methods is very helpful for understanding the rigor of the study as well as the analysis goals of the authors. However, in the Materials and Methods section, I was not sure I understood what "with specific pathogen free" referred to in the first paragraph. Could the authors please clarify in the text whether this is referring to the environment in which the mice were reared, the mice themselves, or another meaning? In the Results section, does n=7 refer to the DSS and DSS+FMT groups combined? If n=7 is just for the DSS+FMT group, it would be helpful to have the n= for the DSS group mentioned as well. The level of detail provided in the figures is helpful. However, Figure 4b would be more helpful if either the titles of the individual graphs or the figure legend was more clear about which groups were assessed in each graph shown; I am not sure I understand what the titles for the graphs are indicating about the groups. I really like Figure 6; it is visually appealing and provides a helpful illustration of the concepts. I am not very familiar with the GO terms mentioned in this manuscript; it would be very helpful to have the importance of their use and their meaning for this study explained in the Discussion section. Language in the Discussion section needs to be checked; for example, it is encouraging if the authors are planning to carry out future clinical studies on these concepts, but this does not sound like a limitation in itself for this study. It would be helpful to know what the authors mean by limitations of animal models for understanding the mechanism of FMT; I understand there may be limitations in understanding how humans are affected, as opposed to mice, but it would be helpful to have more detail on what makes the authors concerned about this limitation. Overall, this is an interesting study that I believe has useful information

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to inform methods for future studies. For the most part, this manuscript appears to meet the criteria for review. Some revisions are needed for the language quality of this manuscript, but generally, it seems well-written. I would recommend the authors address the comments I have mentioned, but I believe that once revisions are complete, this manuscript should be accepted for publication.

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RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 62970

Title: Fecal microbiota transplantation ameliorates experimental colitis via gut microbiota and T-cell modulation

Reviewer's code: 05402068
Position: Peer Reviewer
Academic degree: MD, MSc
Professional title: Doctor
Reviewer's Country/Territory: United States
Author's Country/Territory: China

Manuscript submission date: 2021-01-23
Reviewer chosen by: Man Liu
Reviewer accepted review: 2021-03-31 06:48
Reviewer performed review: 2021-03-31 06:49
Review time: 1 Hour

Scientific quality	[Y] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

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This work is suitable for publication.

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RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 62970

Title: Fecal microbiota transplantation ameliorates experimental colitis via gut microbiota and T-cell modulation

Reviewer's code: 04091933

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Associate Professor, Senior Researcher

Reviewer's Country/Territory: Russia

Author's Country/Territory: China

Manuscript submission date: 2021-01-23

Reviewer chosen by: Man Liu

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Reviewer performed review: 2021-04-11 14:29

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Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

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All comments of the reviewer were taken into account. The title of the article was corrected as suggested. The description of the results has become more meaningful. The discussion has become clearer. There are no comments on the revised manuscript. The manuscript can be published.