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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 85918

Title: Fecal microbiota transplantation alleviates experimental colitis through the Toll-like receptor 4 signaling pathway

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05662946
Position: Peer Reviewer
Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: China

Manuscript submission date: 2023-05-22

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-05-22 14:49

Reviewer performed review: 2023-05-31 01:35

Review time: 8 Days and 10 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[Y] Grade A: Excellent [ ] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[Y] Grade A: Excellent [ ] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No creativity or innovation

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Scientific significance of the conclusion in this manuscript	[Y] Grade A: Excellent [ ] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No scientific significance
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

SPECIFIC COMMENTS TO AUTHORS

This is an interesting study, finding the role of TLR4 in FMT inhibiting colitis. The results are good enough to support this conclusion. However, some issues need to be solved as follows: 1. What is the relationship between AKK and TLR4? 2. Where is the results of the compare of WT groups? There should be 6 groups compared together: WT (Water), KO (Water), WT (DSS+Water), KO (DSS+Water),WT (DSS+FMT), KO (DSS+FMT). 3. What's Aqp4, Clca4a, Dpm3, Fau, Mcrip1, Meis3, Nupr1l, Pank3, Rps13 ? What is the connection between them and TLR4?

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Reviewer's code: 05230210
Position: Editorial Board
Academic degree: MD
Professional title: Associate Professor
Reviewer's Country/Territory: Egypt
Author's Country/Territory: China

Manuscript submission date: 2023-05-22

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-06-09 07:04

Reviewer performed review: 2023-06-16 15:50

Review time: 7 Days and 8 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No creativity or innovation

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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

SPECIFIC COMMENTS TO AUTHORS

I would like to thank the authors for their important work. Comments: Title and abstract: • What "DSS-induced mice" stands for? (is it Dextran sodium sulfate?) • TLR4 is only mentioned as abb in the title > please mention in full Introduction: Good Methods: • It is not clear why the TLR-4 knock-out mice still have colitis, their coltitis might resolve by time from itself due to absent TLR-4? • and if the microbiota of FMT were not affected in this group due to lack of inflammation in the first place, could the authors delineate these two points? • As the authors explained "We further investigated whether the protection against DSS-induced colitis was attributed to TLR4 knockout or microbiota re-composition. We detected the gut microbiota of WT and KO mice in the basal and DSS-treated states.">> but the effect on colitis in the knockout mice may take time , and early state may not be an enough indicator, while the treated state (could be ignored) as it could be resolved by time without treatment, could you elaborate more on this point? Results: Well presented. I suggest adding a figure of the proposed pathway and its link to the specific microbiota re-balance as mentioned in the conclusion. Discussion: Please add this reference to your discussion: Guo, J., Liao, M., & Wang, J.

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(2021). TLR4 signaling in the development of colitis-associated cancer and its possible interplay with microRNA-155. Cell communication and signaling : CCS, 19(1), 90. https://doi.org/10.1186/s12964-021-00771-6 The authors wrote "However, in this study, FMT did not exert effect on colonic inflammation in TLR4-KO mice. It is intriguing to detect that the abundance of Akkermansia, which had dominated in TLR4-KO mice, significantly decreased after FMT.">> could this be due to the reason I mentioned before in the methods section, kindly elaborate? Conclusions: needs modification. References: needs modification.