

Name of Journal: *World Journal of Gastroenterology*

Manuscript NO: 36134

Manuscript Type: ORIGINAL ARTICLE

Article title: Fecal microbiota transplantation induced remission of infantile allergic colitis through microecology re-establishment

Authors list: Sheng-xuan Liu, Yin-hu Li, Wen-kui Dai, Xue-song Li, Chuang-zhao Qiu, Meng-ling Ruan, Biao Zou, Chen Dong, Yan-hong Liu, Jia-yi He, Zhi-hua Huang, Sai-nan Shu

Corresponding Author: Sai-nan Shu, MD, PhD, Associate Professor of pediatrics, Department of Pediatric, Tongji Hospital, Tongji Medical College, Huazhong University of Science & Technology, No. 1095 Jiefang Avenue, Wuhan 430030, Hubei Province, China, snshu@tjh.tjmu.edu.cn

Dear Editor and Reviewers,

Many thanks for your kind comments on the submission, and we really appreciate your suggestions which could make our manuscript published with higher quality. The point-to-point responses are shown as follows, please kindly check it.

Comment 1 (Reviewer's code: 02529197): In my opinion, the manuscript is correctly

written. I have no remarks to this manuscript.

Reply 1: Thank you for your agreement with our research and discoveries, and it's our honor to earn your approval.

Comment 2 (Reviewer's code: 02439990): 1- In a general way, the writing is not clear and English revision is necessary.

Reply 2: A native English speaker was invited to polish the manuscript carefully. Grammar, punctuation and syntax errors have been revised as much as possible, but we will do more revision if there is needed.

Comment 3 (Reviewer's code: 02439990): 2- Abstract section "results": the first sentence is not clear. Please only mention the number of infants with complete follow-up.

Reply 3: The sentence was revised. The number of the infants who complete 15 months' follow-up was mentioned here, and the infants who were lost to follow-up were excluded.

Comment 4 (Reviewer's code: 02439990): 3- page 7, lines 6-7: what do the authors mean by "unique human genetics"?

Reply 4: This language was re-organized, and the words "unique human genetics" was replaced with "aberrant immune system". We hope the sentence could summarize various factors contributed to allergic colitis.

Comment 5 (Reviewer's code: 02439990): 4- Page 10, "FMT procedure": Please define NS (3ml NS/mg stool).

Reply 5: Thank you for your kind remind. "NS" was replaced with "saline" in the manuscript.

Comment 6 (Reviewer's code: 02439990): 5- Page 13, lines 19-21: The sentence should be included in the section "materials and methods" but not in the discussion.

Reply 6: The sentence was moved to the section "MATERIALS AND METHODS" as you suggested.

Comment 7 (Reviewer's code: 02439990): 6- Discussion: different points need to be discussed: -did the three patients with decreased GM diversity after FMT show the same improvement than the patients increased diversity?

Reply 7: Remission of AC symptoms was also observed in 3 patients with decreased GM diversity after FMT treatment, and it was speculated that donors' GM complexity and patients' individual-specific intestinal environments contributed to the results. The assumption was discussed in the section "DISCUSSION".

Comment 8 (Reviewer's code: 02439990): -the reasons why FMT was carried out using both stools from infants and adults. Is there any impact on the clinical results?

Reply 8: According to physical examinations (manuscript-Table2), nine patients' parents were unqualified as fecal donors, so stools from healthy infants were collected for FMT in these patients. And the same efficacy was observed with stools from either infants or adults.

Comment 9 (Reviewer's code: 02439990): -the efficacy of the technique needs to be discussed as FMT has to be repeated up to 5 times in children with AC.

Reply 9: Multi-FMT was executed in the infants with severe AC symptoms to ensure the effect of refiguring the gut microbiota, and it also gave us the ideas to facilitate FMT through changing keystone players in gut microbiota. The related discussion was added and highlighted in the revised manuscript.

Comment 10 (Reviewer's code: 02439990): 7- Conclusion: the authors claimed that this study "extended our understanding of microbiota changes and their roles in immune regulation". This is not true as no mechanism was examined in the manuscript.

Reply 10: The mentioned sentence was removed, and the summary which reflected

microbiota changes before and after FMT was inserted in here.

Comment 11 (Reviewer's code: 02439990): 8- Fig 2: the collection date is not clearly shown so that it is difficult to discriminate between pre- and post FMT data. ID can be removed.

Reply 11: Patients' ID was removed from Figure2 and Figure3. In addition, "pre" or "post" which indicated the data collected before or after FMT was added in the new sample ID. We hope the new sample ID can be easily understood, and please tell us if it needs more revision.

Comment 12 (Reviewer's code: 00503545): However, the authors should address the following point. Allergic colitis shows overlap with classical inflammatory bowel disease (IBD). Thus, it is very important in this study whether the 19 patients were correctly diagnosed as AC. In this context, histological findings of the colonic lesion are key points to distinguish AC from IBD. Thus, the authors should show that the histological findings of the colonic lesions in 19 patients enrolled in this study were compatible with AC.

Reply 12: Thank you for your kind remind. We investigated the histological results of 19 patients, and discovered that all their intestinal mucosa exhibited chronic inflammation with eosinophils infiltration. Combing with the screening criteria of AC pediatric patients mentioned in the section "MAERIALS AND METHODS", these patients can be diagnosed with AC other than IBD. The photographs of histological examination were concluded in "Supplementary File 1", and please kindly check it.

Besides these revisions, we also made corrections to the manuscripts according to the "Guidelines and Requirements for Manuscript Revision-Retrospective Study".

1. The sections of "ORCID number" and "Article Highlights" were added to the revised manuscript.

2. The section of "Clinical Trial Registration Number" was moved to the proper places in the manuscript.

We appreciate for Editor and Reviewers' warm work earnestly, and hope that the correction will meet with approval.

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

Best wishes,

Sainan Shu

Sai-nan Shu, MD, PhD, Associate Professor of Pediatrics

Department of Pediatrics, Tongji Hospital, Tongji Medical College, Huazhong University of Science & Technology

No. 1095 Jiefang Avenue, Wuhan 430030, Hubei Province, China

Email: snshu@tjh.tjmu.edu.cn.

Telephone: +86 027-83662688

Fax: +86 027-83662640