

First of all, we would like to express our sincere gratitude to the reviewers for their constructive and positive comments.

Replies to Reviewer comments:

Reviewer #1: This interesting, observational study by Xue and colleagues examines the fecal microbiota characteristics in a small group of patients with very early onset IBD, associated with IL10RA mutations, and compares these findings with healthy controls and with Crohn disease patients. The information included in the report is important and informs on early (at <1 year of age) differences in fecal microbial populations characteristic of IBD subjects. Specifically, clear similarities were found in IL10RA and CD (I assume w/o IL10RA mutations) subgroups, suggesting that the immune mediated changes occur very early in the course of disease. The authors should address the following concerns: Patients with IL10RA mutations had early disease onset and exhibited more severe colitis.

1. Conclusions in the abstract should not include the statement, “Patients with IL10RA mutations had early disease onset and exhibited more severe colitis”. The statement should more appropriately read, “In patients with IL10RA mutations and early onset IBD, gut dysbiosis.....”

Response: Thank you for the insightful suggestion. The conclusions subsection of the abstract has been corrected in the revised manuscript, as follows:

"In patients with *IL10RA* mutations and early onset IBD, gut dysbiosis showed a moderate association with disease severity."

2. Page 5, paragraph 2: The authors should state that IBD (in animal models) occurs only in the presence of intestinal microbiota, as germ-free animals do not develop colitis. IL10^{-/-} mice are not “dependent” on microbiota, IBD is.

Response: The sentence has been corrected in the revised manuscript. The revised sentence reads as follows:

"IBD (in animal models) occurs only in the presence of intestinal microbiota, as

germ-free animals do not develop colitis."

3. Page 6, paragraph 1: The authors imply that patients with IL10RA mutations ranged up to 18 years of age. I found this difficult to comprehend, as the mean age of these subjects, as indicated in Table 1, was 1 year. Please clarify.

Response: This was an observational study and we screened all patients who admitted at our hospital during the study reference period. The age of patient ranged up to 18 years at our hospital.

4. Page 6, paragraph 1: Were the CD subjects screened for relevant mutations? This should be addressed.

Response: CD patients who developed the disease at the age of less than 6 years were screened for relevant mutations by Whole Exome Sequencing. The sequencing results were negative for all these patients. This information has been added in the revised manuscript (Methods).

5. Table 1: Approximately 80% of IL10RA mutation subjects were breast fed. Were these infants exclusively breast fed? Were differences in microbiota found between exclusively breast fed infants and others in this study group. As exclusive breast feeding exerts a profound effect on the nature and diversity of the fecal microbiome, this should be addressed.

Response: The percentage (approximately 80%) of breast fed infants mentioned in Table 1 refers to the feeding status before the disease onset. At the time of sample collection, most infants have had diverse diets as per prescription (as listed in Table 1, "Self-reported diets"). We consider that it is not relevant to compare the differences in microbiota between exclusively breast fed infants and others in our study.

6. Overall, the article contains numerous grammar and syntax errors, requiring relatively minor language polishing.

Response: The revised manuscript has been edited and proofread to eliminate all

language-related errors.