

Dear Editors and Reviewers:

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "Mucosal bacterial dysbiosis in patients with nodular lymphoid hyperplasia in the terminal ileum" (NO.: 71286). 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 correction which we hope meet the requirements for final acceptance and publication. Revised portion are marked in red in the paper. The main corrections in the paper and the responds to the reviewer's comments are as flowing:

Responds to the reviewer's comments:

Reviewer #1:

1. Response to comment: In the method segment why you are taken variable test group like 11 male and 4 female, you should take same male and female in test group, and also your sample size is too less for any significant result.

Response: It is true as Reviewer proposed that a variable test group were taken in this study due to the nature of terminal ileal NLH, which is thought to be significantly more common in men than women. Although the incidence of terminal ileal NLH in both men and women has not been investigated through a large-scale study, Lin et al observed that males outnumbered females by approximately four to one in a small-scale study (reference 3); their results support, to a certain degree, the suggestion that there is a higher frequency of terminal ileal NLH in males than females. We also performed a correlation analysis to compare the intestinal flora with gender using the Multivariable Association with Linear Models², and we found that there was no correlation between the intestinal floras and gender at the phylum, genus, or OTU levels. Therefore, an unequal gender ratio in test groups did not bring impacts on experiment results. To obtain more rigorous results, we will perform a large-scale study and ensure that there is an equal gender ratio

among groups. We have added the content in the last paragraph of discussion and the reference marked in red in revised paper.

We are very sorry for the relatively small sample size in our study, which was one of limitations being raised in the discussion of the paper. It was only a preliminary correlation analysis between the intestinal flora and terminal ileal NHL. When we found the mucosal bacterial dysbiosis in terminal ileal NLH, we were eager to share with colleagues at the first time. Studies with larger sample sizes covering different regions and populations are necessary to confirm the findings in future.

Special thanks to you for your good comments.

Reviewer #2

1. Response to comment : Abstract should be written in a more understandable way, summarizing the points of interest. Especially the result is too long.

Response: As Reviewer suggested that Abstract should be written in a more understandable way, we have re-written this part especially on the result marked in red in revised paper. All the changes will not influence the content and framework of the paper.

2. Response to comment: Figure 2B and Figure 4A are not shown in the text

Response: We are very sorry for our negligence of description about Figure 2B, We have added the content marked in red in revised paper. In addition, we have readjusted the sentence about Figure 4A and Figure 4B marked in red.

3. Response to comment: At the end of the conclusion, "can effectively improve" is an overstatement.

Response: We have re-written this sentence according to the Reviewer's suggestion marked in red in revised paper.

Special thanks to you for your good comments.

Other changes:

1. The title of Supportive foundations "The Science and Technology Projects of Shanghai Jiangqiao Hospital" was corrected as "the Science and Technology Project of Jiading Hospital, Shanghai General Hospital".

2. According to basic rules on abbreviation, we have make some changes in text and Figures as follows.

(1) The abbreviation of helicobacter pylori "HP" was corrected as "*H.pylori*".

(2) The title of Figure1,"NLH" was corrected as "nodular lymphoid hyperplasia".

(3) The title of Figure5 "Prediction of functional alteration of gut microbiomes in patients with terminal ileal NLH using PICRUSTs" was corrected as "Predictions of the functional alteration to the gut microbiomes in patients with nodular lymphoid hyperplasia in the terminal ileum".

(4) Legend text of Figure1B was corrected as "Endoscopic image of nodular lymphoid hyperplasia(NLH) in terminal ileum of a patients".

(5) The title of Figure2, "OTU" was corrected as "Operational Taxonomic Units".

(6) Legend text of Figure2A,"OTUs" was corrected as "Operational Taxonomic Units(OTUs)".

(7) The title of Figure3, "OTU" was corrected as "Operational Taxonomic Units".

(8) Legend text of Figure3A, "PCoA" was corrected as "Principal coordinates analysis(PCoA)"; Legend text of Figure3B, "NMDS" was corrected as "Nonmetric multidimensional scaling (NMDS)".

(9) Legend text of Figure4E, "LEfSe" was corrected as "Linear discriminant analysis effect size".

(10) The title of Figure5 was corrected as "Predictions of the functional alteration to the gut microbiomes in patients with nodular lymphoid hyperplasia in the terminal ileum".

Additionally, The Image file were upload consist of previous Figures and also decomposable Figures, as I am not sure if it meet the requirements for Figures. Finally, we performed further language polishing. All changes will not influence the content and framework of the paper. We appreciate for Editors/Reviewers' warm work earnestly, and hope that the correction will meet the requirements.

Once again, thank you very much for your comments and suggestions. I look forward to hearing from you.

Sincerely,

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