Point by point responses to reviewers.

First, we would like to thank the reviewers and the editor for the positive and constructive comments and suggestions.

Responses to reviewers' comments:

Reviewer 1:

1) There are some grammatical corrections that need to be done.

Response: The manuscript has been edited by an English language editing company.

2) The only methods part that you need to clarify is where the biopsies were taken from and the methodology for obtaining the LM samples.

Response: Thank you very much for your suggestion. Following your comment, we have added on page7, line5 of the revised manuscript. And, Similar to studies in literature we describe the microbiota from faecal samples as luminal microbiota. (Ringel Y, *et al*., High throughput sequencing reveals distinct microbial populations within the mucosal and luminal niches in healthy individuals. Gut Microbes. 2015;6(3):173-81; Carroll IM, *et al*., Molecular analysis of the luminal- and mucosal-associated intestinal microbiota in diarrhea-predominant irritable bowel syndrome. Am J Physiol Gastrointest Liver Physiol. 2011;301(5):G799-807; and Carroll IM, *et al*., Luminal and mucosal-associated intestinal microbiota in patients with diarrhea-predominant irritable bowel syndrome. Gut Pathog),

3) The final question is about the influence of age. We know that the microbiota changes during lifetime, and for example as we get older the diversity diminishes,. The age of the population ranges from 29 to 65 years. Did you take age intoconsideration?

Response: Thank you for raising this important topic. In fact, we have taken age into consideration. The microbiota changes extensively during infancy and therefore there are large differences between infants, adults, and the elderly. During adulthood, the microbiota composition is relatively stable. We enrolled subjects between 18 and 65

years and we have added this to page 6, line 6 of the revised manuscript.

Reviewer 2:

1) I would suggest checking all the abbreviations (mainly in the abstract) and use the full terms when they are used for the first time in the text. Also, please correct some typos in the titles of paragraphs.

Response: Thank you for your suggestions. I have corrected all the errors in the manuscript.

2) I would suggest including some updated references in the discussion (e.g. Nolfo F, *et al*, BMC Surg 2013; Uccello M, *et al*, BMC Surg 2012).

Response: Thank you for your careful reading and reviewing of our manuscript. I have added this publication in the manuscript as reference 20.

Reviewer 3:

1) The manuscript comes across as the start of a study that needs further support and proof of a correlation between immunological factors and certain microbial phylum in disease.

Response: Thank you for your valuable and thoughtful comments. We have designed future studies on this topic and we are performing the study to verify the relationship between certain bacterial strains and TLRs in disease. For example, we study the effects of bacteria supernatant on TLRs *in vivo* and *in vitro* and explore the treatment effect against bacteria in an IBS model animal. Because this is the first time we perform this type of work, we just finished some preliminary experiments.

2) A major problem is the lack of clinical data, other than non-specific "abdominal discomfort", to link to their correlations.

Response: You suggest that clinical data should be included. We did select patients with functional gastrointestinal disorders (FGID), but we left the data out of the manuscript, because it included a number of syndromes, there were some

difficulties making a final diagnosis and our subjects were only part of a few disease in the group of FGID. We really agree with your point of view, so we have added the clinical data in the results.

3) Also, there is no data on protein level to substantiate the correlation between those phylum and immune responses.

Response: Thank you for your instructive suggestion. We apologize for the lack of work on this topic, but this was due to some limitation in the study. Because FGIDs are functional disorders, according to the ethical guidelines, we were only allowed to collect the fewest amount of tissue. Therefore, we took two tissue biopsies by enteroscopy and each one was no more than 70–80 mg. One sample was used for microbiota analysis and the other one was used for TLRs analysis. We tried immunohistochemistry on formalin-fixed paraffin tissues, but the morphology after biopsy by enteroscopy was not good. We tried western blotting, however we did not see the target band on our gels because of the limited amount of sample. We have planned further studies to verify the relationship between certain bacterial strains and TLRs in disease.

4) The discussion could better define the implications and importance of their findings.

Response: Thank you very much for your suggestion. As suggested, we have added this to the discussion. As you mentioned, there are some limitations in the present study, therefore the implications are limited too.

5) There are multiple grammatical and spelling errors throughout the manuscript.

Response: The manuscript has been edited by an English language editing company.