Dear editor,

Thank you for the kind suggestions from you and invited reviewers. We will try our best to revise this manuscript under your further guidance.

Editor suggestions

Thank you for your suggestions. Please find any relative changes and answers under your inquires in the article.

Reviewer 1,

In this work, authors investigated the expression pattern of plasma LncRNAs in CD patients by microarray screening and qRT-PCR verification of LncRNAs and mRNAs, followed by hierarchy clustering, GO and KEGG pathway analysis. They identified 1211 upregulated and 777 downregulated LncRNAs and 1020 upregulated and 953 downregulated mRNAs after microarray analysis. In comparing the previous study (Ref #12, Mizra et al.) directly analyzed in the intestine, they investigated the pattern of LncRNA in the plasma of the CD patient which may provide the useful information for the non-invasive diagnosis of CD and a resource for further specific LncRNA-mRNA pathway exploration. Even though preliminary in nature, this is a potentially interesting study that suitable for publication in World Journal of Gastroenterology. There are several minor concerns regarding the data presented in the manuscript:

1. Despite of tissue differences, it would be very curious that comparing the out come of this study to previous publications (Ref #12 &13). As the authors noted in the discussion, even though some remarkable targets were related to the immune response

but some others were involved in the function of intestine by exosome secretion. So it would be interesting and informative to the authors that pursuit the changing of dramatic alteration group of previous study in the current analysis for comparing the intestine and plasma .

A: Thank you for your suggestion! After careful comparison, we did not find DQ986243 (reference 13) in our results. Interestingly, there were no overlap of dysregulated LncRNAs between our results and the top 10 dysregulated LncRNAs we extracted from MirZA AH's paper (reference 12), except one LncRNA-DIO3OS that was up regulated in our but down regulated in their results. One possible explanation might be the secretion of DIO3OS from intestinal tissue to circulation, which needs further investigation. We add this in the second paragraph of Discussion section

2. In addition, they analyzed the data from the 12 CD patients with 9 severe cases. If the biological marker can be applied in diagnosis, its alteration would be reflected the progress of disease. In the similar view, is there any fold difference in the severe and mild groups? If there is any co-relation between fold change and progression of CD, it would be helpful to the reader for further study.

A: Thank you for this suggestion and sorry for the confusion. Actually all 12 CD patients were at the stage of severe degree where "over 9" means the HBI>9 and is the criteria for severe CD patients selection. We now make the associated change in the Method Section.

3. Mis-spelling in page 2, Line 12; upregulated

A: Thank you for your suggestions. We corrected this mistake now.

Reviewer 2,

ESPS Manuscript NO: 24671 Manuscript Title: Plasma LncRNAs profile would provide preliminary data for non-invasive diagnosis of CD and a reservoir for further specific LncRNA-mRNA pathway exploration. The aim of this study was to investigate the expression pattern of plasma LncRNAs in CD patients. The Microarray screening and qRT-PCR verification of LncRNAs and mRNAs were used in CD and control subjects. The investigators found 1211 upregulated and 777 downregulated LncRNAs and 1020 upregulted and 953 downregulated mRNAs after microarray analysis. GUSBP2 and AF113016 had the highest fold change of the up and down regulated LncRNAs, whereas TBC1D17 and CCL3L3 had the highest fold change of the up and down regulated mRNAs. I have some comments:

1. What about the comorbidities of patients with CD?

A: Thank you for your suggestions. Actually, to decrease the bias between CD patients, we chose patients of severe CD with small intestine involvement and related comorbidities (3 aphthous, 3 perianal abscess, 2 anal fistula and 2 arthralgia). We now add this information in the Method section.

2. Did have a chance to measure the IL-6?

A: Thank you for your suggestion. IL-6 is the factor of inflammation and we will try to include its measurement in future larger study when comparing the LncRNAs profile between CD patients of different severity

3. I suggest to include the Harvey-Bradshaw index in table 1

A: Thank you for your suggestion. Because HBI in control was 0, we think there

might be no meaning to compare the average and standard deviation of HBI between CD and control and put the data on Table. However, we still think this suggestion is helpful and now we add the “average HBI of 11.3 in CD patients” in the Method Section to provide informative data.

4. In the discussion section explain the limitations of this study

A: Thank you for your suggestion. Actually, we have discussed the limitation of this study in final segment of Discussion and now we add more sentence on this item as “Finally, it is better if we can compare the LncRNAs of plasma and intestinal tissue, which may helpful for the mechanism exploration of CD.”

5. Abbreviations need to be used in a regular form

A: Thank you for your suggestion. We have carefully checked this article and change some abbreviations into regular forms.