Dear Science Editor Ya-Juan Ma and reviewer,

Thank you for your positive comments and detailed instructions for further revision of our
manuscript entitled "Comprehensive Screening for 10 genes in Chinese patients suffered very early onset inflammatory bowel disease" (ESPS Manuscript NO: 25201).
I have done all the revisions as your request and highlighted them in yellow. All the docutements which you required have been enclosed when the manuscript was resubmitted.
Following are the responses for the reviewer.

Responses for the comments of the reviewer 00009417:

1. *"The interesting study is limited by the small number of patients included. In consequence, the data should given with more caution. The high percentage is probably due to the small number of patient in the cohort."*

Reply: Thank you for your opinion. I agree that this is a small sample size study.But as you know, IBD, especially VEO-IBD is a rare disease in children, it is difficult to collect a large samlple. Because our department is one of pediatric IBD centers in China mainland, most of our patients who were reffered by other clinics or centers were very ill (So we revised and added this interpretation in discussion and highlighted it in yellow.). Even so, our results is similar as previous study in Korean.

2. *"Tools of data analysis are essential in the interpretation of NGS results. The clinical correlation should be more critically discussed. "*

Reply: For *IL-10RA*, mutaitons such as R101W, R117H, were pathological because these mutation have been already found in other studies. For Y64C and V100G in *IL-10RA*, and E141K mutation in *IL-10RB*, they are novel mutations.We analyzed these mutaitons by SIFT and Polyphen 2. These tools are use widely in predicting nsSNP function. According to the American College of Medical Genetics and Genomics and the Association for Molecular Pathology, these 2 mutations were defined as pathological supporting.
For patient 4 and 5, we mention that "the 2 patients that did not conform to a Mendelian genetic pattern might also carry abnormal sites on other genes that cause the disease symptoms" and hypothesized "their disease development

may be due to “trans-heterzygous”: the collective effects of a variety of detected mutations”.This phenomenon was also observed in a Korean study.

3. “Do the authors belief that the genetic findings are new/ founder mutations?”

Reply: According to previous report, we belived that the genetic findings are founder mutation.

Responses for the comments marked in the manuscript:

We added language certificate, IRB statement, fund supported certificate, Informed consent statement, Conflict-of-interest statement, Data sharing statement. According documents are attached.

We revised title/runing title, added abstract and keywords, added information of authors, telephone number, Fax. And we revised references according to the WJG format and added comment and core tip.

Audio core tip recorded and attached.

I sincerely hope that you consider our manuscript eligible for publication in World Journal of Gastroenterology.

Kind regards,

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