Dear Editor and Reviewers:

Thank you very much for sending us the Reviewers' report on our manuscript (Manuscript ID: 46231), entitled "Interleukin-22 receptor 1 is expressed in multinucleated giant cells: a study on intestinal tuberculosis and Crohn's disease". In particular, we would like to thank you for the valuable comments and criticisms provided. They have been of great help in improving the quality of our manuscript. We have carefully revised our manuscript with coloured text (Red). The following is a detailed list of responses to all comments and criticisms and the changes the authors have made.

Q1: Abstract is particularly extensive and exceeds the limit of 260 words.
A1: We agree with the reviewer's comments and made corresponding changes to make the abstract more concise (Page 3).

Q2: In the Introduction section consider adding a figure about the IL-23/IL-17 axis, which will represent the network of genes and cells that are involved.
A2: Thank you for the reviewer's suggestion. We added Figure 1 to make it easier for the reader to understand the differentiation process of Th17 cells as described in the article.

Q3: In the Methods section there is no information about paraffin processing of tissue. Abbreviations FFPE and EP are not fully described. In immunohistochemistry technique, you could state the nature of the immunohistochemical positive and negative control that was performed and the microtome which was used for cutting sections. Also there is no clear justification for the use of biopsy specimens of colon polyps and colon cancer.
A3: We apologize that the methods were not explained in detail. We have added detailed descriptions of those sections to improve the reader's understanding (Page 9 line 18-28).

Q4: In table 1 abbreviations WBC, Hb, T-SPOT, 5-ASA are not fully described

A4: According to the reviewer's comments, we have revised this section in Table 1.

Q5: In table 2 consider adding the title "Groups" to the column which include the terms HC, ITB, CD.

A5: According to the reviewer's comments, we have revised and added "Groups" in Table 2.

Q6: In the Discussion section there is extensive reference to function and immune pathway of IL22, which could be added in Introduction section. Moreover you should add more information about IL-22/IL-22R1 axis in CD.

A6: Thank you for the reviewer's suggestions. We have modified the Introduction to the manuscript and added a description of the function of IL-22 in intestinal diseases. In addition, in the Discussion section, we provided more information about the IL-22-IL-22R axis in Crohn's disease (Page 6-7 & Page 15-16).

Q7: A more clear and detailed report of how the results of your previous studies in TB (regarding with IL22, IL1β, IL6 and other loci within the IL-23/IL-17 axis) are related to the this study data is needed.

A7: We apologize that we did not describe the previous study. We have supplemented the research content of SNP on the IL-23/IL-17 axis, such as IL22 (Zhang G, et al. Sci Rep 2011), IL6(Zhang G, et al. J Infect Dis 2012) and IL1 (Zhang G, et al. PLoS Pathog 2014) (Page 7 line 11-17).

To make the scientific voice of the manuscript meet the publishing requirements of WJG, we have improved the statistical methods of the research. The statistical review of this study was performed by Lei Wu, Associate professor, Department of Statistics and Epidemiology, School of Public Health, Nanchang University.

1. We tested whether this polymorphism study satisfied Hardy-Weinberg

equilibrium and whether it had sufficient statistical power (Page 10 line 24-27 & Page 11 line 22-27).

2. At the same time, we used unconditional logistic regression models to analyse differences in genotype and allele frequencies between different groups, which increased the credibility of the results (Page 10 line 27-28 & Page 11 line 1-2 & Page 12 line 1-7).

3. According to the relevant literature, a small number of diseases have been shown in a clear genetic model, while in most cases can only be used to quantify what the genetic model the disease may follow. We first used the Cochran–Armitage trend test to analyze the genotype association data between HC - ITB. The analysis process is as follows:

group	genotype			Total
	CC	CT	TT	
Case	n_{11}	n_{12}	n_{13}	N_{1+}
Control	n_{01}	n_{02}	n_{03}	N_{0+}
Total	N_{+1}	N_{+2}	N_{+3}	N
Influence value	x_1	x_2	x_3	

$$\chi^2=\frac{N\left(N\sum_{j=1}^{3}n_{1+}x_j-N_{1+}\sum_{j=1}^{3}N_{+j}x_j\right)^2}{N_{1+}N_{0+}\left[N\sum_{j=1}^{3}N_{+j}x_j^2-\left(\sum_{j=1}^{3}N_{+j}x_j\right)^2\right]}$$

Under the additive model, $x_1=0$, $x_2=1$, $x_3=2$; The standard practice is to test the additive model, and test other models only if the additive model is significant or there is a prior hypothesis to do so, otherwise, the SNP site is considered to be unrelated to the disease. We substitute the numerical value into the above formula and calculate. We have explained the detail information in revised manuscript (Page 11 line 2-8 & Page 12 line 11-19).

The editor's comments on the manuscript format have also been carefully revised. We hope that the revised version of the manuscript is now acceptable for

publication in your journal. We are looking forward to hearing from you soon.

With best wishes,

Jian-yong Chen