Comments to the Authors,

This manuscript reported the DNA methylome and transcriptome of purified fibrotic human intestinal fibroblasts from the colons of patients with fibrostenotic CD. The study was performed rigorously and the findings sound interesting. What’s more, it would be an exciting example to elucidate mechanisms of intestine fibrosis of Crohn’s disease. However, I have several concerns to make the manuscript more solid.

**Major Compulsory Revisions**

1, In the DNA methylome analysis, the authors only choose the CpG sites which in the regions of promoters or CpG island/shore/shelf, but discarding the CpG sites in intergenic regions. However, according to the ENCODE project, many of the distal CpG sites which lie in the intergenic regions but functional elements (enhancers for example), may also play a key role in the regulation of the genes. And this notion has been implemented in the newly designed Illumina HumanMethylation 850K Array. As a result, it is preferable to check if any of the intergenic CpG sites lies in the functional elements.

2, In Page 11 Line 11-24, the authors quoted the paper(Reference 64) to show that the mean age difference in the cases and controls will not affect the methylome greatly. However, the sample size of reference 64 is slightly few and reference 64 used the Methylation 27k Array which only detected about 27,000 CpG sites. There is now plenty of HumanMethylation 450K data from the GEO and other datasets. As a result, it is preferable to combining the other datasets to check if the age difference has any impact on the targeted regions in this paper.

3, The tissues used in the methylome measurement were the cultured specimens from the patients. Why not use the tissues dissected directly? Would the DNA methylome be different before and after culturing?

**Minor Revisions**

1, PTGDS was regarded as the differentially expressed gene, however, I can’t find the RNA-seq expression data of PTGDS in Supplementary Table 2.