

Dear Ya-Juan Ma,

We appreciate the review of our manuscript and the opportunity to respond. The reviewer had two comments, which we address below:

1) "**Line343, NCM cells treated with 10ng/ml TNF showed a 60% increase in β -catenin activation. Please add one reference in support of your statement here.**" This comment references Fig 3D. We have now included the raw data in the text to support our statement that there was a 60% increase in β -catenin activation (lines 344-345). Additionally, in the Materials and Methods section (lines 236-237) we have now included the following references, 1) Molenaar et al 1996, in which the TCF/Lef construct used to report β -catenin activation in the TOPFlash assay was first described; 2) Treed et al 2009, in which 10ng/ml TNF is used to treat epithelial cells in vitro; and 3) Kim et al 2007, in which 5mM myo-inositol is used in vitro.

2) "**Line361, This small sample size impaired statistical interpretation; yet, analysis of collected tissue proved valuable. What is the meaning of this sentence which is saying that the 3 patient's tissue can proved. With what and why?**" We agree that this statement was poorly-worded. We have clarified the text to explain that, with only 3 patients, rigorous statistical analysis of the data is not possible. However, the data are still informative and support the hypothesis that myo-inositol reduces the frequency of activated stem cells in patients at high risk for colitis-associated cancer (lines 363-365). We have changed the wording to "*Statistical analysis of this small study size is not possible. However, the results of the staining were used to identify a trend of myo-inositol-induced reductions in the number of crypts with high numbers of $p\beta$ -cat-positive intestinal epithelial cells.*"

If you have any further questions or concerns, please do not hesitate to contact us.

Sincerely,

Emily Bradford, PhD