

Responses to the Reviewer Comments (Manuscript NO.: 75406, Letter to the Editor)

The authors would like to thank the reviewers for their time and efforts, especially these excellent comments. We have revised our letter according to the reviewer's comments. Here are our responses to the reviewer's comments point to point. The comments are shown first, which are followed by our responses in italics. The revised places in the letter are highlighted in yellow.

A. Reviewer #1

Specific Comments to Authors: The authors should be congratulated for the comments sent as a letter to the editor. Some corrections involve shortening the second paragraph that does not contribute to the development of the reader's reasoning "IBD comprising of Crohn's disease (CD) and ulcerative colitis (UC)" . The withdrawal of the statement "these clinical data suggested interestingly that U-II could be involved in the pathophysiology of IBD, especially in the inflammatory responses and disease outcomes." would be welcome as it is not possible to state by the original design of the analyzed study. The counterpoints are pertinent and can enrich the authors' perspective on advancing in the field of research.

Responses: We thank the reviewer for the suggestion. We have shortened the second paragraph. In addition, we have revised the statement in the fourth paragraph indicated by the reviewer. The revised sentence should help to enrich the author's perspective. Please see the highlighted yellow parts.

B. Reviewer #2

Specific Comments to Authors: the Urotensin II (U-II) levels in inflammatory bowel disease (IBD) patients are significantly higher than that in healthy control subjects. To provide future guidance for the management of cardiovascular risks in IBD patients, additional studies with more clinical samples to compare U-II levels in IBD patients and control subjects are worth to be done. This will clarify the possible roles of inflammation factors and related signaling pathways (like EPK1/2, NF- κ B and Rho/ROCK) in the pathophysiology of IBD. Perhaps this is a meaningful study, but further research is needed to confirm it, requiring a large sample and multi-center study.

Response: We agree with the reviewer comments. Therefore, we added one sentence in the abstract to emphasize this. A similar statement is also added to the last paragraph. Please see the revised manuscript for the changes.