Point to point response

Reviewer 1:

1) This is an interesting study of important clinically issue. The concept is challenging. The title reflect the main subject/hypothesis of the manuscript, but I suggest changing “initiative factor” to initiating factor. Abstract summarize and reflect the work described in the manuscript, the key words reflect the focus of the manuscript Comments

Response: We would like to thank the reviewer very much for this encouraging comments and critiques and we are pleased to respond to them. The title has been changed and highlighted.

2) While Helicobacter pylori polyclonal antibody was used, a possibility that this antibody reacts with other Helicobacter species, e.g. H. enterohepaticus or other bacteria cannot be excluded, and there is no information regarding this on the ThermoFisher website. Current view is that H. pylori growth and survival is dependent on acid and colon has rather a neutral pH. These issues should be discussed.

Response: Monoclonal antibodies testing for H Pylori Ag in stool was performed for confirmation following detection of the organism in colonic tissue by both Giemsa and Immunohistochemical methods. This has been clarified in the patients and methods section and highlighted. Plus characteristic features of H pylori organism were clear on histopathological examinations of the colonic tissues.

3) It would be very important to provide well labelled figures showing histologic slides and to discuss bacterium localization – cellular or extracellular, its affinity to specific cells etc.

Response: Pathological figures of Giemsa and immunohistochemical staining have been attached.

4) The paper requires correction of some errors and style, e.g. in some areas Geimsa is misspelled

Response: These have been corrected.

5) “Helicobacter pylori was significantly higher in UC than in controls” should be rephrased

Response: This statement has been rephrased and highlighted in the results section.

6) Reference to Streutker CJ et al. in the text (16) should be corrected. In references it is 15.

Response: These have been corrected in the discussion and references sections and highlighted.

7) The authors may consider to use references listed below

Lord AR et al. Protective effects of Helicobacter pylori for IBD are related to the cagA-positive strain.Gut. 2018 Feb;67(2):393-394.

Response: This reference has been used in introduction section and highlighted.

Wu XW1, et al. Helicobacter pylori infection and inflammatory bowel disease in Asians: a meta-analysis. World J Gastroenterol. 2015 Apr 21;21(15):4750-6. doi: 10.3748/wjg.v21.i15.4750.

Response: This reference has been used in introduction section and highlighted.

Shen Z, et al. Helicobacter saguini, a Novel Helicobacter Isolated from Cotton-Top Tamarins with Ulcerative Colitis, Has Proinflammatory Properties and Induces Typhlocolitis and Dysplasia in Gnotobiotic IL-10-/- Mice. Infect Immun. 2016 Jul 21;84(8):2307-2316. doi: 10.1128/IAI.00235-16.

Lertpiriyapong K, et al Pathogenic properties of enterohepatic Helicobacter spp. isolated from rhesus macaques with intestinal adenocarcinoma. J Med Microbiol. 2014 Jul; 63(Pt 7):1004-16.

Reviewer 2:

The authors show that H.pylori may associate with UC. The idea is very interesting. However, there are several major concerns with regards to the investigation. Please see below.

Response: We would like to thank the reviewer very much for this encouraging comments and critiques and we are pleased to respond to them.

Major Points

1) The H.pylori in the colon, which is identified by your institution, should be clearly demonstrated by several Figures, ex. Giemsa, immunohistochemical staining, and electron microscopic Figures if possible.

Response: Figures of Giemsa and immunohistochemical staining have been attached.

2) Usually, it is very difficult to discriminate between chronic nonspecific colitis and early microscopic features of UC by pathological approach. The differences should be clearly demonstrated by your pathological Figures.

Response: Pathological figures have been attached.

3) There is a high possibility that the improving UC inflammation by H.pylori eradication therapy is caused by disinfection of another bacteria. The authors should discuss on this point.

Response: Monoclonal antibodies testing for H Pylori Ag in stool was performed for confirmation following detection of the organism in colonic tissue by both Giemsa and Immunohistochemical methods. This has been clarified in the patients and methods section and highlighted. Plus characteristic features of H pylori organism were clear on histopathological examinations of the colonic tissues.

Minor points

1) Table 6 is unnecessary.

Response: This table has been removed.

2) H.pylori is written in italic.

Response: This was corrected in the manuscript.

3) There are several spelling errors.

Response: These have been corrected.