

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: This letter to editors entitled "Intestinal inflammation and the microbiota: beyond diversity" mainly focuses on the concept that the presence of the toxin-producing bacteria might play a more important role in the development of inflammatory disorders than alterations in the microbiota composition. The microbiota is an ecosystem in constant regulation. The researches about the intestinal microbiome of patients might be affected by many factors. Further investigations are needed, not only the composition, or the production of toxins by commensal bacteria, but also more deep mechanisms.

REPLY: Thank you very much for your review.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: This "letter to the editor" supplemented the ongoing discussion on intestinal inflammation and the microbiota. Authors mainly make comments about investigations should focus on identify alterations not only on the diversity of the microbiota but the presence of the toxin-producing bacteria. The comments in this letter are objective and serious. But for a letter, there are too many references, please simplify them.

REPLY: Thank you very much for the suggestion. We removed 24 references.

Reviewer #3:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: Dear Author, your letter is very interesting and well written and explained. Congratulations

REPLY: Thank you very much for your review.

Reviewer #4:

Scientific Quality: Grade C (Good)

Language Quality: Grade A (Priority publishing)

Conclusion: Major revision

Specific Comments to Authors: As the authors mentioned, I also think it is important to analyze the pathobiont the role of several resident bacteria for ulcerative colitis. But intestinal flora is too complex to investigate the relation between UC and all type of bacteria. Does the author suggest that we need to focus on Clostridium

perfringens, Bacteroides fragili, Escherichia coli in relation to UC? Please mention the reason why we need to investigate the relation between UC and these bacteria. E.coli and Clostridium is already known to relate to UC. Few study reported that an increase in Escherichia-Shigella in patients with UC in comparison to patients without UC. So I think He's report is worth it.

REPLY: Thank you very much for the suggestion. We agree that He's report is extremely important, we aimed in this letter to put into perspective the complex interaction between the microbiota and host, that goes beyond diversity. We proposed other tree bacteria that are known to influence the development of inflammatory disorders in the gastrointestinal system by the secretion of toxins to highlight our point of view, which is complementary to He et al.

Reviewer #5:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: Medical research often involves qualitative and quantitative issues. Just as He et al performed an investigation on the microbiota composition on the fecal and mucosa samples from patients with ulcerative colitis. This manuscript puts forward the importance of bacterial virulence research and quantification on the basis of He's research, and makes meaningful explanations. There are two deficiencies. First, there is no stratification of the elements involved in the proposal. Just like the "driver- passenger" model cited by the author, who maybe the possible passengers and drivers? Second, there are no specific methodological suggestions on how to carry out such research.

REPLY: Thank you very much for the comment. The main focus of the letter is to highlight that toxins and the interaction between the microbiota may be an important and overlooked factor in investigations on inflammatory disorders and the microbiota. We cited 3 bacteria (Clostridium perfringens, Bacteroides fragili, Escherichia coli) which could affect the intestinal microbiota homeostasis via toxins or interaction with other bacteria. We added a few methodological suggestions.