

Dear Editor,

In response to the reviewers comments and after introducing in the manuscript (# 11826) the required modifications, we are resubmitting the corrected one along with replies to each reviewer's inquiries.

1. Reviewer # 1 - 11826

This reviewer divided his comments into 2 categories: Major and minor

1.1 Major comments:

In response to the many points raised by the reviewer to cover in the manuscript the multiple factors involved in colon tumor genesis (genetic alteration, inflammation, nutrients, hormones, metabolic disorders and molecular mechanisms), the authors wrote two new sections:

- Etiological link of dysbiosis to IBD and CRC (pp 6-10)
- Dysbiosis and diet (pp 10-11)

With these 2 sections the core tips would be adequately covered.

1.2 Minor comments:

- There should be no references in the abstract section.
 - References were removed from the abstract section
- What is the meaning of the following sentence? "It is now established a close interaction between the luminal bacterial flora and intestinal immune system are responsible for the onset and development of several diseases besides IBD's (line 5-7, page 4)
- The corrected sentence would read as follows:
 - "It is now well established that close interactions exist between the luminal bacterial flora and the intestinal immune cells and tissues. Such interactions are involved in the onset and progression of several diseases including IBD and CRC".
- "Did the figures prepared by authors"?
 - Yes, the figures were prepared by the authors.
 - There is no need for permission from any previous author.

1. Reviewer # 2 – 11826

1. Differentiate dysbiosis from dismicrobism
 - The terms dysbiosis and dismicrobism can be used inter-changeably, however, dismicrobism is sometimes more used in reference to the condition evolving from the administration of antibiotics.
Such a statement was inserted (in the introduction page 5, lines 11 to 13).
2. How can we diagnose dysbiosis in the clinical practice? Are there any methods to obtain a quantitative and qualitative composition of normal microbiota?
 - There is a relatively wide spectrum of diagnostic tests used. They cover all four patterns of dysbiosis: putrefaction, fermentation, deficiency and sensitization. Laboratory analysis of both stool and urine has been investigated for markers of dysbiosis. Reference laboratories. A whole new section was written on diagnosis of dysbiosis p - 6.
3. Factors affecting dysbiosis of the luminal or mucosal microbiota and could be modified: Role of diet and other factors. A whole section was newly written on dysbiosis and diet pp 10-11.

2. Reviewer # 3- 11826:

Thank you for the good and encouraging comments, the minor adjustments and revision of English were done on the whole manuscript.