

**31 January 2024**

**Dear Editor**

**World Journal of Gastroenterology**

We wish to re-submit the manuscript entitled “Interaction between diet and genetics in patients with inflammatory bowel disease.” Manuscript NO: 90150. EDITORIAL.

We would like to thank the reviewers for their thoughtful comments and efforts towards improving our manuscript. Our responses to the Reviewers’ comment are described below in a point-to-point manner. Appropriated changes suggested by the Reviewers have been introduced to the manuscript (highlighted within the document). The manuscript has been rechecked and the necessary changes have been made in accordance with the reviewers/editors’ suggestions. These changes are indicated by highlights with yellow color in the main file.

### **Point-by-point response**

#### **Reviewers Comments**

##### **Reviewer #1:**

The present manuscript describes comparison between two types of dietaries, western versus Mediterranean to the epigenetic modulation during the genesis of inflammatory bowel disease (IBD). A major concern was that the comparison, as well the impact of the dietary is mainly based on statistic data. It would informative the main chemical components in the food consumed as related the molecular aspects of the epigenetic approach is dealt with.

**Answer:** We have included in the text explanations regarding the main chemical components in the food consumed as related the molecular aspects of the epigenetic approach, as shown below: “The UPF components, such as emulsifiers, thickeners, salt, artificial sweeteners, phosphate, and food colorants (titanium dioxide, Azo dyes) can negatively affect the intestinal barrier, inducing dysbiosis, affecting the mucus layer, increasing the permeability of the intestinal epithelium, or directly interacting with the immune system.<sup>18,20</sup>”

##### **Reviewer #2:**

a) Please include in the introduction some information on the implication of circular RNAs (which are a particular class of non codingRNAs) in modulating the inflammatory response in the gut. Authors are encouraged to check and mention <https://www.frontiersin.org/journals/oncology/articles/10.3389/fonc.2021.779706/full>.

Introduction, how DNA methylation can influence the microbiota composition? For instance, the methylation of immune cells? Introduction. Concerning DNA methylation, these two additional references should be included PMID: 27223861 and PMID: 36890579.

**Answer:** We have included in the introduction some information on the implication of circular RNAs in modulating the inflammatory response in the gut. We also added references suggested by the reviewer to the paper. <https://www.frontiersin.org/journals/oncology/articles/10.3389/fonc.2021.779706/full>, and other articles.

Regarding DNA methylation, this subject was extensively discussed in the review article commented by this editorial (Marangoni K, Dorneles G, da Silva DM, Pinto LP, Rossoni C, Fernandes SA. Diet as an epigenetic factor in inflammatory bowel disease. *World J Gastroenterol* 2023; 29(41): 5618-5629 URL: <https://www.wjgnet.com/1007-9327/full/v29/i41/5618.htm> DOI: <https://dx.doi.org/10.3748/wjg.v29.i41.5618>). In this editorial we mention DNA methylation and reference the commented article for further details.

b) More supporting references should be introduced in the DIETARY TIPS FOR PATIENTS WITH IBD section.

**Answer:** In the DIETARY TIPS FOR PATIENTS WITH IBD section, more supporting references were added, including the new published article: Hashash JG, Elkins J, Lewis JD, Binion DG. AGA Clinical Practice Update on Diet and Nutritional Therapies in Patients with Inflammatory Bowel Disease: Expert Review. *Gastroenterology*. 2024 Jan 23:S0016-5085(23)05597-X [PMID: 38276922 DOI: 10.1053/j.gastro.2023.11.303] Epub ahead of print.

c) Please include a couple of conclusive sentences

**Answer:** We have included the “**Conclusions**” section in the text, which is transcribed below: “Diet is thought to play a role in the pathogenesis of IBD and may contribute to triggering IBD flares. In particular, some dietary components may interact with gut microbiota and genetics to trigger or perpetuate intestinal inflammation. Patient with IBD often requests recommendations on what types of foods he/she should avoid or consume since it is not uncommon for the patient associate their diet with symptoms. Briefly, cumulative evidence strongly suggests that higher levels of consumption of ultra-processed foods increase the risk of CD. Conversely, a healthier or Mediterranean-style diet is likely to be protective for CD development. From a therapeutic point of view, the Specific Carbohydrate Diet, CDED or a Mediterranean-style diet may be beneficial for the treatment of patients with CD who have mild to moderate symptoms. In addition, a low FODMAP diet is beneficial for patients with functional gut symptoms in association with quiescent IBD. For patients with IBD in remission the consumption of the Mediterranean diet and dietary fibers as adjunctive therapies may be recommended to reduce the risk of IBD flares, particularly in CD patients. For patients with UC, the increased intake of natural sources of omega-3 fatty acids and follows the same restrictive recommendations aimed

at CD patients, with the possible inclusion of red meats may be useful in reducing UC flare-ups.”

#### **EDITORIAL OFFICE’S COMMENTS**

- a) The revised manuscript was resubmitted to English review. The English Language Certificate issued by a professional English language editing company was provided, after careful professional review of the English language of the paper.
- b) The conflict-of-interest disclosure form was provided.
- c) We provide a new standard three-line table.
- d) We have added the WJG article (Marangoni K, Dorneles G, da Silva DM, Pinto LP, Rossoni C, Fernandes SA. Diet as an epigenetic factor in inflammatory bowel disease. *World J Gastroenterol* 2023; 29(41): 5618-5629 URL: <https://www.wjgnet.com/1007-9327/full/v29/i41/5618.htm> DOI: <https://dx.doi.org/10.3748/wjg.v29.i41.5618>), which this editorial discussed into the main text and references list.

Thank you for your consideration. I look forward to hearing from you.

Yours sincerely,

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