

Casablanca, May 6th, 2017

Name of journal: *World Journal of Gastroenterology*

Manuscript NO.: 34055

Column: Basic Study

Title: Polymorphisms in oxidative pathway related genes and susceptibility to inflammatory bowel disease

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Reviewer code: 02441062, and 00225291

First decision: 2017-04-21

Scientific editor: Ya-Juan Ma

Dear Editorial board,

We appreciate the time and efforts spent by you and the referees in reviewing our manuscript and your helpful comments.

Attached, please find a revised form of our manuscript, in which we have addressed the concerns raised by the reviewers. A point-by-point response to the reviewer's concerns is included, and the changes were applied and highlighted in the revised manuscript.

We hope that our revised and improved manuscript will be acceptable for publication in the *World Journal of Gastroenterology*.

Thank you for your consideration.

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A point-by-point reply to Editor's comments:

We thank the editor for his/her helpful comments. As requested, all the required modifications addressed in the section below were applied.

Please provide language a certificate letter from a professional English language editing company (Classification of the manuscript language quality evaluation is B).

Since we weren't able to provide a language certificate letter, the manuscript was copy-edited by Prof. Adam Ziad from Florida Atlantic University.

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Institutional review board statement:

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Please add these content, which must be provided, otherwise the manuscript will be unaccepted finally.

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We have applied the required modifications.

COMMENTS

Background

To concisely and accurately summarize the related background of the article and to enable the readers to gain some basic knowledge relevant to the article, thus helping them better understand the significance of the article.

Research frontiers

To briefly introduce the hotspots or important areas in the research field related to the article.

Innovations and breakthroughs

To summarize and emphasize the differences, particularly the advances, achievements, innovations and breakthroughs, from the other related or similar articles so as to allow the readers to catch up the major points of the article.

Applications

To summarize the actual application values, the implications for further application and modification, or the perspectives of future application of the article.

Terminology

To concisely and accurately describe, define or explain the specific, unique terms that are not familiar to majority of the readers, but are essential for the readers to understand the article.

Peer-review

To provide the comments from peer reviewers that most represent the characteristics, values and significance of the article, and allow the readers to have an objective point of view toward the article.

[We have inserted these items on the paper.](#)

Please add PubMed citation numbers and DOI citation to the reference list and list all authors. Please revise throughout. The author should provide the first page of the paper without PMID and DOI.

PMID (<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed>)

DOI (<http://www.crossref.org/SimpleTextQuery/>)

[We have added PubMed citation numbers and DOI citation to the reference list and listed all authors.](#)

A point-by-point reply to reviewer#1 comments:

[We thank the reviewer for his/her helpful comments/suggestions. We address the reviewer's comments in the section below.](#)

Reviewer #1: The manuscript is of interest. However, the results shown are somewhat weak. Only CCTTT 7 and 8 repeat show solid conclusions. Thus, a comment must be added commenting on the fact that, contrary to what was initially expected, no differences were found between patients and healthy subjects in the frequency of the polymorphisms analysed, and the implications this may have. This is not necessarily a caveat. Finding no differences may also yield a clue as to the underlying mechanisms in both diseases. And no comments are shown on the difference between CD and UC. Certainly, they are both IBD but they are different in their nature and pathophysiologic mechanisms and differences may then be expected. And if no differences are found in the pathways analysed it should be clearly stated in the manuscript. In addition, some minor corrections are required.

[The concern raised by the reviewer was taken into consideration; please see the manuscript \(Discussion and conclusion sections, pages: 9-10\).](#)

1. INTRODUCTION The sentence stating that “IBD was thought to be a Western disease...” might be changed “IBD was previously found mainly in Western countries....” In addition, when stating that its incidence has increased in developing countries including Morocco, a reference specific for Morocco must be added, if available

As requested, “IBD was thought to be a Western disease...” was replaced by the following “IBD was previously found mainly in Western countries....”. However, there is no specific reference for Morocco.

2. MATERIALS AND METHODS/RESULTS There is a discrepancy in the number of healthy subjects analysed 311 in Materials and Methods and 308 in Results. Why?

This was a mistake. Accordingly, 311 was replaced by 308 in the Materials and Methods section.

3. RESULTS Readers are referred to a previous manuscript (35) when mentioning demographic and clinical data of patients. In addition to keeping the reference provided a brief picture of the population studied would help readers. Moreover, in this section, differences between both IBD, CD and UC, must be emphasized, if present. And if not, the absence commented.

As required by the reviewer, demographic and clinical data of patients were added. (Please see the manuscript, Table 1). In addition, differences between CD and UC patients were pointed out.

4. MINOR GRAMMAR COMMENTS In the RESULTS section the sentence beginning with “Hundred ninety-nine patients...” should be changed to “One hundred ninety-nine patients...” In the DISCUSSION section, the paragraph (prior to the last one) beginning “In the other hand, the present study...” should be changed to “On the other hand, the present study...”

Done.

A point-by-point reply to reviewer#2 comments:

This is an interesting paper, concerning the role of genetic factors related to the oxidative pathway in the susceptibility of inflammatory bowel disease. There are some points that need to be addressed.

We thank the reviewer for his/her helpful comments/suggestions. We address the reviewer's comments in the section below.

1. the number of healthy controls is 308 in the abstract, 311 in Materials and methods, and again 308 in results. This should be corrected.

Corrected.

2. the authors refer for demographic and clinical characteristics to a previous paper. In my opinion, a table with these data should be added.

As requested, demographic and clinical data of patients were added. (Please see the manuscript, Table 1).

3. in the discussion, when considering the paper by Oliver et al (23), demonstrating contrasting results with respect to the present paper, the different results should be commented and discussed.

As requested by the reviewer, the discrepant findings were commented and discussed (Discussion section).