

December 19, 2013

Dear Editor,

We are thankful to the reviewers and to the editor for their comments and suggestions, which have been thoroughly taken into account. We believe that these comments have been highly constructive and useful, and certainly improve the quality of our manuscript.

Please find enclosed the edited manuscript in Word format (file name: **5674-edited-revised.doc**):

Title: "Immunogenetic biomarkers in inflammatory bowel disease: Role of the IBD3 region"

A review of the literature

Author: Manuel Muro, Ruth López-Hernández and Anna Mrowiec

Name of Journal: *World Journal of Gastroenterology*.

ESPS Manuscript NO: 5674

The manuscript has been improved according to the suggestions of reviewers:

1. Format has been updated
2. Revision has been made according to the suggestions of the reviewers

(Reviewer 1)

- "a) - page 4, line 2: "now" should probably be replaced by "from now on"
- page 4, line 3: "... are defective only in CD; the autophagy genes ATG16L1 and IRGM." It seems that a word is missing.
- page 5, 2nd last line: "... while positive association of CD pathology was associated with..." should be replaced by "... while positive association of CD pathology was found with..."
- page 6, line 10: "... was not associated in our study." should be replaced by "... was not associated to CD in our study."
- page 12, line 5: "... activating NK cells with promoted NKG2D and IFN- γ production" should be replaced by "... activating NK cells with enhanced NKG2D and IFN- γ production"
- page 14, line 9: "...genetics..." should be replaced by "...genetic..."
- page 14, line 13 and others: the symbol after TNF was not clear. Could it possibly be a formatting problem?
- page 15, line 4: "...(-308G/A SNP)..." should be replaced by "...(-308G/A SNP)..."
- page 15, line 11: "... inhibited..." should possibly be replaced by "...inhibitory..."
- page 15, line 27: "... polymorphism..." should be replaced by "...polymorphisms..."
- page 17, line 3: "... anti-TNF- α agents' mechanisms of action ..." should be replaced by "...the mechanisms of action of anti-TNF α agents..."
- page 17, line 25: "... immunogenetics" should be replaced by "...immunogenetic..."

We are thankful to the reviewer for pointing out these mistakes, which we regret. We have rephrased the sentences and corrected the mistakes according to the reviewer's comments.

"b)- page 7, paragraph 4: This paragraph is almost an exact copy from abstract of reference 18. Besides, the 14bp deletion polymorphism should be referred to as Del- or Del+, not Del1 or Del2

- page 8, paragraph 2: " These contradictory data..." which data are contradictory? In my opinion, the following observations are possible explanations for the importance of HLA region for IBD susceptibility and do not explain contradictory data. This paragraph is almost an exact copy of reference 1, page 3629.

- page 13, paragraph 1: This paragraph is almost an exact copy from abstract of reference 54"

We have rewritten these paragraphs and corrected the mistakes, as suggested by the reviewer.

"c) - page 7, paragraph 2: I believe that references are reversed. Where is "(43)" should be "(44)", and also the opposite. Besides, the studies cited are contradictory, not confirmatory. The Chinese study (44) found a positive association with CD but the Japanese study found a negative association. Can the authors give a possible explanation for this?

- page 12, paragraph 5, lines 1-4: There seems to be a redundancy. The authors should refer that it was already stated above.

- page 13, paragraph 2, lines 1-3: "Likewise, we have recently found a higher frequency of MICA-129met/met and a lower frequency of MICA-129val/met genotypes in IBD...". These findings seem contradictory to what Zhao described (ref. 54)... Not likewise?"

References no 43 and 44 have been corrected in the reference list. We regret this error.

We agree with the reviewer that the suggested paragraphs contained inconsistent, unclear observations, which have now been re-phrased in order to correct the conceptual mistakes and to maintain the logic of the manuscript.

(Reviewer 2)

"... I have only minor comments: - remove s from immunogenetics in the title - same for the running title I would use the plural for inflammatory bowel diseases in the title and in the introduction (Inflammatory bowel diseases (IBD) are....)"

We appreciate the reviewer's suggestions. We have made the changes according to the reviewer's comments.

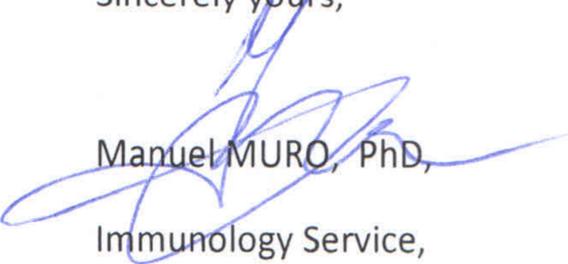
3. References and typesetting were corrected

We also revised the nomenclature of genes and proteins according to WHO nomenclature as kindly suggested by the editor.

We hope that these changes fulfill the requirements to make the manuscript suitable for publication in World Journal of Gastroenterology.

Thank you again for publishing our manuscript in the World Journal of Gastroenterology.

Sincerely yours,


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