Author's response to reviews

Title: Toll-like receptor 4 Asp299Gly, Thr399Ile polymorphisms: New data and a meta-analysis.

Authors:

Nezha Senhaji (nezha.senhaji@gmail.com)
Brehima Diakité (br.diakitee@yahoo.fr)
Nadia Serbati (nadia.seerbati@yahoo.fr)
Younes Zaid (younnes_zaid@yahoo.ca)
Wafaa Badre (wafabadre@yahoo.fr)
Sellama Nadifi (nadifisell@yahoo.fr)

Version: 2
Date: 20 September 2014

Author's response to reviews: see over
Dear Editor,

We appreciate the time and effort spent by you and the referees in reviewing our manuscript and for 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 BMC Gastroenterology.

Thank you for your consideration.

Nezha SENHAJI, PhD
University Hassan II
Faculty of Medicine and Pharmacy
Laboratory of Medical Genetic and Molecular Pathology
19, rue Tarik Ibnou Ziad, Faculté de Médecine et de Pharmacie, Casablanca, Maroc 20000.
Cell phone: + 212 665896590
Email: nezha.senhaji@gmail.com
A point-to-point reply to the reviewers' comments:

Major

1. There are several studies in the literature analyzing the role of both Asp299Gly and Thr399Ile in the IBD susceptibility. Taking this into account, why the authors did not perform a meta-analysis for the Thr399Ile polymorphism? mainly considering that a meta-analysis evaluating the role of Asp299Gly, but not of Thr399Ile, in IBD has already been published. For the Thr399Ile SNP, a combined analysis of the present data and those from previous studies should be included in the manuscript.

A meta-analysis of the present data and those from previous studies evaluating the association of the Thr399Ile polymorphism and CD, UC and IBD has been performed and was included in the manuscript.

2. Given the low statistical power of the case/control analysis, the most important results of the present study are those derived from the meta-analysis. In my opinion, the discussion should be focused on the results of these pooled analyses. In addition, these results should be included in the abstract of the new version of the manuscript.

The abstract and the discussion sections were modified according to the results drawn from the meta-analysis.

3. It is known that a number of genetic risk factors are shared between CD and UC. Indeed, associations between the Asp299Gly and Thr399Ile genetic variants and both diseases have been found in several studies. From this point of view, it would be interesting to perform a meta-analysis combining CD and UC patients for the two tested SNPs.

Meta-analysis for the overall IBD correlated risk for the two tested SNPs were added to the manuscript.

4. In the last paragraph of the results section authors stated: “Noteworthy, there was a higher percentage of mutated allele coexistence in Crohn’s disease patients compared to ulcerative colitis or healthy controls, suggesting that mutated allele coexistence might increase susceptibility to CD”. Was a haplotype analysis performed? The results of this analysis should be included in the manuscript.

The statement was changed.
Minor

1. TLR4 should be written in italics when referring to the gene

2. Some references about the epidemiology and etiopathogenesis of IBD should be included in the first paragraph of the introduction.

3. The introduction, results, and discussion sections, should be reorganized. Paragraphs relating to the same subject should not be separated by full stop.

4. In Tables 1 and 2, Asp299Gly is mistyped.

5. The abbreviations of Crohn’s disease, CD, and ulcerative colitis, UC, should be indicated when these terms are used for the first time (in the study population section). Then, abbreviations should be used through the manuscript.

All the required minor modifications were done throughout the whole manuscript.

A point-to-point reply to the reviewers' comments:

Major Compulsory Revisions

1. The manuscript needs to be seen by a statistician

As requested by the reviewer 2, the manuscript was revised by a statistician who performed all the statistical study.

Minor Essential Revisions

1- In abstract they gave the study population as 117 patients and 128 healthy unrelated blood donors but in article, they said 114 IBD patients and 112 healthy unrelated blood donors, so they have to correct the numbers.

The above typing mistakes were corrected.

2- Researchers have done a meta-analysis, I think they have to change the article title

The title has been changed to the following one: Toll-like receptor 4 Asp299Gly, Thr399Ile polymorphisms: New data and a meta-analysis.