Reviewer's report

Title: Toll-like receptor 4 Asp299Gly, Thr399Ile polymorphisms in Moroccan patients with inflammatory bowel disease

Version: 1 Date: 8 July 2014

Reviewer: Javier Martin

Reviewer's report:

In this manuscript, the authors first analyzed two polymorphisms, Asp299Gly and Thr399Ile at the TLR4 gene, in a Moroccan IBD cohort. They found no association of these SNPs with Crohn's disease (CD) or ulcerative colitis (UC). In a second part, they performed a meta-analysis for the Asp299Gly genetic variant including data from previous studies. This combined analysis evidenced an association of this SNP with CD, but not with UC. Some important points should be considered by the authors.

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.

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.

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.

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.

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.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I have no competing interest