Author's response to reviews

**Title:** Th17-related cytokines: new players in the control of chronic intestinal inflammation

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**Author's response to reviews:** see over
Dear Robin,

We would like to thank you for your letter dated September 6th, 2011, and for giving us the opportunity to improve and resubmit our paper. We also thank the reviewers for their helpful comments and suggestions.

As indicated in the point-by-point reply to the reviewers’ comments below we have revised the manuscript taking into account all the issues raised by the two reviewers as well as your suggestions. Since we hope these changes successfully address the reviewer’s comments, we would like to resubmit the paper for publication.

Changes are underlined in the revised version of the manuscript.

Yours Sincerely

Giovanni
Reviewer 1

We would like to thank the reviewer for his/her positive evaluation and for the helpful suggestions.

Major points:

We have specified the cell types that make Th17 cytokines in the gut. The reviewer asked to make a distinction between cells that synthesize anti-inflammatory IL-17A and those that produce the pro-inflammatory cytokine. We have indicated which cells produce IL-17A in IBD tissue and cited a recent paper showing that Th17-producing innate lymphoid cells contribute to the pathogenesis of colitis in mice. Nonetheless it is not yet known whether cells producing anti-inflammatory IL-17A in the normal gut (e.g. CD4+ T cells, NK cells, NKT cells) play also a role during colitis. So, at this stage, it is extremely difficult to fully address the issue raised by the reviewer.

Minor points
1. We did not change the sentence on page 5, because the paper refers to the role of both IL-17A and IL-17F in the control of gut inflammation.
2. We have modified the references 13 and 14
3. page 8: the sentence has been modified.
4. page 9: references 22 and 24 have been added
Reviewer 2

We would like to thank the reviewer for his/her helpful suggestions.

Major comments:
1. We have added a sentence about the association between polymorphisms of Th17 genes and IBD (page 4, revised manuscript) and cited the relative papers.
2. We have made clear that variants of the IL-23R gene can influence IL-22 secretion (page 5, revised manuscript) and cited the relative paper.
3. The role of IL-22 to control epithelial cell growth, goblet cell restitution and mucus and antimicrobial production has been specified at page 6, and the relative papers have been cited.
4. We have specified that CCL20, a chemoattractant for CCR6+ Th17 cells, is over-produced in IBD mucosa, and that IL-21 positively regulates such a production (page 4). The relative papers have been cited.
5. We have added a final paragraph in which results of trials of anti-IL-23/p40 and anti-IL-17A in IBD have been cited.

Minor comments:
1. page 4, we have made the requested changes.
2. Figure 1. We have improved the figure by adding CD11b+CX3CR1 DC and made clear that macrophage-derived IL-12 and IL-23 regulate the shift of Th17 cells to Th1 cells.