

ANSWERING REVIEWERS

October 27, 2022

Dear Editor,

Please find enclosed the manuscript in word format(file name: 79311_Auto_Edited).

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 79311

Title: Interleukin-34 Deficiency Aggravates Development of Colitis and Colitis-Associated Cancer in Mice

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

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: Dear Editor, Thanks to the authors for this experimental study. In the study, the authors investigated the function of IL-34 in acute colitis, in a wound healing model and in colitis-associated cancer in IL-34-deficient mice. The manuscript adequately describes the background, present status and significance of the study. The manuscript interprets the findings adequately and appropriately, highlighting the key points concisely, clearly. Also, the latest and important references are cited in the manuscript. Introduction part of the manuscript is too long, it should be shortened. The authors stated that "All animal experiments were approved by the Institutional Ethics Committee of Nantong University", but there is no date/number ? please add the date of Ethical approval?

Response #1: Thanks for your comments. We have shortened the introduction part as you suggested. In the Materials and Methods section of the manuscript, we add the date and number of Ethical approval(Date: 21/12/2015, Number: S20151221-908).

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: The topic of study is very relevant and concerns a little-studied cytokine IL-34 and its role in experimental (ulcerative) colitis and colitis-associated cancer (CAC). The authors showed that IL-34 does not drive the inflammatory response, but protects from inflammatory injury and reduces the risk of CAC. The authors competently conducted the study, illustrated it well, and referred to relevant sources (without self-citation). However, it is highly recommended to include in the discussion new evidence that IL-34 is critical for the suppressive function of CD4⁺ Tregs, and its deficiency leads to increased susceptibility to autoimmunity (Freuchet A, ... Guillonneau C, 2022). This will make the authors' conclusions even more convincing. In addition, a list of references should be arranged in accordance with the requirements of the WJG. The manuscript can be recommended for publication after a minor revision.

Response #2: Thanks for your comments. We have added new evidence in the discussion based on your suggestion that IL-34 is essential for the suppressive function of CD4⁺ treg and that its deficiency leads to increased autoimmune susceptibility (Freuchet A, ... Guillonneau C, 2022). For the list of references, we have adapted the formatting of the references by means of the reference detection program embedded in the editor algorithm.

Thanks again for the reviewer's guidance. I hope our manuscript can be successfully published in *World Journal of Gastroenterology*.

Sincerely yours,

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