

Format for ANSWERING REVIEWERS



December 01, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 13429-review.doc).

Title: IL-18 Genetic Polymorphisms Differentially Contribute to the Susceptibility to Crohn's Disease

Author: Su-Jun Gao, Li Zhang, Wei Lu, Lu Wang, Lei Chen, Zhen Zhu, Hai-Hang Zhu

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 13429

The manuscript has been edited based on the reviewer suggestions:

To Reviewer 00035982:

Gao and co-authors present their work comprising a meta-analysis of seven case-controlled studies evaluating polymorphisms in the Interleukin (IL)- 18 gene in the context of Crohn disease (CD). Specific Comments:

1. The wording of the title could be enhanced.

Response: Thank you very much for your suggestion. We have changed the title to emphasize the relationship between IL-18 genetic polymorphisms and Crohn's disease. The title was changed to "IL-18 Genetic Polymorphisms Differentially Contribute to the Susceptibility to Crohn's Disease".

2. Line four on page 3 of the MS details that 400000-600000 people have CD. Is this in China? Worldwide? This seems a very small number for the latter. This needs specific details.

Response: Thank you for your advice. The data for CD prevalence is for North America, and the latter incidence was for the entire western world. Therefore, this sentence was revised to "It is estimated that CD affects 400,000 to 600,000 people with an incidence of 1/1,000 per year in western countries".

3. IL-18 was discovered and delineated more than ten years ago - not recently.

Response: Thank you. We have corrected the error. We deleted the modifier "recently discovered" for this proinflammatory cytokine.

4. In line 4, paragraph 2 of the INTRODUCTION, the word pathway should be amended. This should be elaborated to indicate one specific pathway, or should read pathways.

Response: We intended to convey an overview of IL-18 involvement in cell types, thus no specific pathway was being referenced. We changed the word "pathway" to "pathways". In addition, the subsequent sentences convey brief information about the biological context of IL-18 functions.

5. There are other errors of English that also need correction.

Response: Thank you. We have checked and corrected the English errors.

6. In line 5, para 2 of the INTRODUCTION, the word etc should be deleted.

Response: Thank you. It has been deleted.

7. The abbreviation CD could be used after the term is first explained.

Response: Thank you. After the first instance, the remaining occurrences have now been replaced with "CD".

8. The second-last sentence on page 7 (DISCUSSION) does not make sense and needs to be corrected.
Response: Thank you. We have replaced this sentence with a sentence that describes IL-18 functions to make it more logical and compact. This sentence was based on “van de Veerdonk FL, Netea MG, Dinarello CA, Joosten LA. Inflammasome activation and IL-1beta and IL-18 processing during infection. Trends Immunol 2011; 32: 110-116 [PMID: 21333600 DOI: 10.1016/j.it.2011.01.003]”

9. The last sentence on page 7 (DISCUSSION) repeats statement made a little earlier.
Response: Thank you for your suggestion. The sentence has been changed to flow smoothly.

10. Acknowledgements would not usually include the reviewers.
Response: Thank you. The acknowledgments section was deleted.

11. Figure 2 is quite interesting. However, it doesn't have direct relevance to this meta-analysis and could be excluded (especially if space is limited).
Response: Considering its irrelevance, we deleted it per the reviewer's advice.

12. The term used in Figure six for the name of these plots needs to be corrected. It is listed as Beggs and Beggers.
Response: Thank you. As the Figure 6 was changed into Figure 5. “Beggers” was corrected to the term “Begger's” in the title of Figure 5. However, the terms used in Figure 6 cannot be corrected as the figure was auto-generated by systematic software and cannot be amended manually. We can provide you with the decomposable figures.

13. The Table legends could be more descriptive.
Response: We have revised the legends based on your suggestion, thank you. The title of Table 1 was replaced with “Main characteristics and methodological quality of all eligible studies of the relationship between IL-18 genetic polymorphisms and the risk of developing CD” and the title of Table 2 was changed to “Meta-analysis of subgroups for the relationships between IL-18 genetic polymorphisms and CD risk”.

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

Sincerely yours,

A handwritten signature in black ink, appearing to be 'AR' or similar initials, written in a cursive style.