

August 25, 2012

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 6998-review.doc).

Title: Cigarette Smoking and Innate Immune Responses to Influenza Infection

Author: Wenxin Wu and Jordan P. Metcalf

Name of Journal: *World Journal of Immunology*

ESPS Manuscript NO: 6998

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

1 Format has been updated

Response: The change has been made as requested.

2 Revision has been made according to the suggestions of the reviewer

- (1) This review describes some of the process involved in the innate response to influenza virus infection affected by cigarette smoking. The manuscript is well written, concise and comprehensive. I consider it is necessary to finish the manuscript with a paragraph that summarizes the main molecular remarks involved. It would be useful to include a figure describing the main molecular process of the innate antiviral response affected by smoking.

Response: We appreciate the reviewer's positive comments about this manuscript. This is an excellent suggestion. As the reviewer requested, a figure has been added in the revised manuscript and a paragraph added to summarize the main molecular remarks involved (page 7 in the revised manuscript).

- (2) Major comment: This is a well-written short review. I recommend to prepare 1 schematic figure to describe the relationship between cigarette smoking and influenza infection. In addition, I also recommend to include 1 table which summarize the effects of cigarette smoking on innate immune responses. Minor comments: Page 3: 1918 Flu should be 1918 flu Page 3: phlegm should be sputum Page 5: In Vivo should be In vivo Page 5: Recently Todd et al reported should be Recently, Todd et al have reported Page 8: Yageta ei al examined should be Yageta et al have examined Page 10: Flu should be flu.

Response: The reviewer is correct and a figure will be helpful for readers. As the reviewer requested, a figure has been added in the revised manuscript. Since a table will basically repeat the information from the figure, we decided to add the figure only.

We have corrected all the minor comments from the reviewer.

- (3) This concise review is well written. Appropriate references are cited. Effect of cigarette smoking on innate immune response and oxidative stress related to infection with influenza virus and other respiratory viruses should be interesting for the reader of this journal.

Response: We appreciate the reviewer's positive comments about this manuscript.

- (4) Comprehensive review with a focus on innate immunity and oxidative stress in COPD and enhanced viral infection. A figure demonstrating the pathways how CS inhibits the RIG1 and NLR pathways would be helpful.

Response: We appreciate the reviewer's positive comments about this manuscript. As the reviewer requested, a figure has been added in the revised manuscript.

3 References and typesetting were corrected

Response: Corrected as requested.

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

Sincerely yours,

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