

February 20, 2014

Dear *WJG* Editor,

Please find enclosed the edited manuscript in Word format (file name: 7477-review.doc).

Title: STAT3 and sphingosine-1-phosphate in Inflammation-associated colorectal cancer.

Authors: Andrew V. Nguyen, Yuan-Yuan Wu and Elaine Y. Lin

Name of the Journal: *World Journal of Gastroenterology*

ESPS Manuscript No.: 7477

We would like to thank all of the reviewers for their valuable suggestions to our manuscript. The manuscript has been improved according to these suggestions.

1. The language has been polished to Grade A level.
2. Revision has been made according to the suggestions made by the reviewers:
 - a) Reviewer 00057684 suggested that the manuscript should include more recent publications. We have revised the manuscript accordingly so that 53 articles published within the last four years including 17 published in 2013-14 are cited.
 - b) Reviewer 00068518 indicated that the manuscript needed to be better organized and present more studies. We have re-organized the entire manuscript to make the points clearer. Several recent studies were added into the cited reference list as per the suggestion made by the reviewer.
 - c) Reviewer 00058563 requested to add more review of IBD-colorectal cancer (CRC) incidence/risk and available prevention therapies. Responding to this request, we revised the introduction section of the manuscript to focus on IBD-CRC incidence/risk. We have also added discussion of the recent development of treatment that targeted inflammation in IBD patients. Such treatment aimed to reduce the risk of CRC induced by inflammation in this population. In addition, the reviewer pointed out that a lack of logical flow with regards to other tumors in our manuscript. We agreed with the reviewer so that the section regarding other tumors in the first section of the manuscript was removed. Finally, we thank the reviewer for the suggestion of adding recent study of JAK-inhibitor, Tofacitinib. We have added it into the section of therapeutic strategies for inflammation-associated CRC.
 - d) Reviewer 00068574 pointed out that our original manuscript consists of multiple English errors and references which were incompletely presented. We have carefully read through our revised manuscript and corrected these errors.
 - e) Reviewer 02567654: we completely agree with the reviewer that the first paragraph of the original manuscript was irrelevant to the main focus of the review. Thus the

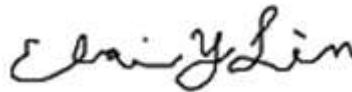
paragraph was replaced by a brief review for the link of IBD and CRC as the reviewer instructed. In addition, the reviewer suggested that we should review more primary studies. In the revised manuscript, we have added discussion for multiple primary studies and now more than 60 primary studies are cited. In addition, the reviewer pointed to that our original manuscript was disorganized with awkward sentences. As discussed above, we have corrected language errors and re-organized paragraphs and sections to better present our ideas. Finally, similar to Reviewer 00058563, this reviewer also suggested adding discussion of Tofacitinib. We have added it to the last section of the manuscript as mentioned above.

- f) Finally we would like thank Reviewer 02530212 for his/her time and effort to review our manuscript. No change was requested by this reviewer.

3. References and typesetting were corrected.

Thank you for considering our manuscript for publication in the *World Journal of Gastroenterology*.

Sincerely yours,



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