

ANSWERING REVIEWERS



March 12, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 16663 -review.doc).

Title: Demethylation of Tumor Necrosis Factor- α Converting Enzyme Promoter Associated with high HBeAg level in HBeAg positive chronic hepatitis B

Author: Zhen-Li Wang, Shuai Gao, Xin-You Li, Feng-Kai Sun, Feng Li, Yu-Chen Fan and Kai Wang

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 16663

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

1 Format has been updated

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

(1) Reviewer 1:

Some minor concerns occur

1) In the discussion section, page 11, authors mentioned as "TACE demethylation might participate in the progression of HBV infection and induced liver damage", it should be as "methylation". Check and correct it.

Response: Thank you very much for your kind suggestion. According to your comment, we have checked this sentence and changed "demethylation" to "methylation" in the revised manuscript.

2) Abbreviations in tables should be annotated in the table descriptions.

Response: Thank you very much for your constructive comment. According to your comment, all the abbreviations in the tables have been annotated in the table descriptions in the revised manuscript.

(2) Reviewer 2:

Dear authors:

Thanks for submitting your manuscript titled "Demethylation of Tumor Necrosis Factor- α Converting Enzyme Promoter Associated with high HBeAg level in HBeAg positive chronic hepatitis B" to WJG. Your manuscript presented some useful data that showed aberrant demethylation of TACE promoter existed in HBeAg positive CHB and associated with high HBeAg level. This might potentially serve as a biomarker for HBeAg seroconversion. The research design, and the data analysis and statistics are reasonable. The research protocol was approved by institutional ethic committee and signed informed consent was obtained from participants. However, there are number of writing and concept concerns for in this manuscript

Response: We greatly appreciate your constructive comments and suggestions for our manuscript. According to your comments, we have made corresponding modifications in the revised version and all the changes were highlighted using red color for your checking. We believe that the revised manuscript is of great merit and suitable for publication in *World Journal of Gastroenterology*.

1) The meanings of "methylation" and "demethylation" are easy to induce confusion. According to your statement of "DNA methylation is one of the most important epigenetic mechanisms", as if DNA methylation is related to the occurrence of some diseases. However, the result showed that methylation in normal people is higher than that in patients with HBeAg positive CHB. This should indicate certain DNA methylation is a health biomarker, and demethylation is a biomarker for HBeAg positive CHB. If so, please explain the mechanism of demethylation in

the text.

Response: Thank you for your constructive comments. As you mentioned, the description in our manuscript is truly confusing. As a matter of fact, certain DNA methylation are health biomarkers and aberrant demethylation in promoter regions usually results in long-term overexpression of genes and is associated with many diseases. Previous studies also demonstrate that gene promoter demethylation is stable and suitable to be used as biomarkers for disease detection or prognosis prediction. We have described this issue in more detail and explained the mechanism of demethylation in the revised manuscript. All the changes have been highlighted using red color for your checking.

2) All numbers at the start of sentence are better to used English rather than Arabic, or you can avoid putting numbers at the beginning of a sentence.

Response: Thank you for your kind suggestion. According to your comment, we have changed all the numbers at the beginning of sentences to English writings in the revised manuscript.

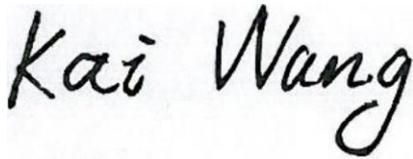
3) Writings in whole manuscript need to be checked and improved. For example: before all of [], there should be a space.

Response: Thank you for your constructive comments. We have checked and improved the writings in the whole revised manuscript.

3 References and typesetting were corrected

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

Sincerely yours,

A handwritten signature in black ink that reads "Kai Wang". The signature is written in a cursive, slightly slanted style.

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