

ANSWERING REVIEWERS



October 1, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 13625-review.doc).

Title: Clinical utility of complex mutations in the core promoter and proximal precore regions of the hepatitis B virus genome

Author: Young Min Park

Name of Journal: *World Journal of Hepatology*

ESPS Manuscript NO: 13625

The manuscript has been improved according to the reviewers' suggestions as follows.

1. The format has been updated.

2. Revisions have been made according to the reviewers' suggestions.

- (1) Reviewer-**02860618**: The review by Park YM deals with a very interesting topics byt it is badly written and needs an extensive revision by a native English speaker.

[ANSWER]

A native English speaker has corrected the English language of the manuscript (English language editing company: American Journal Experts, <http://www.aje.com>).

- (2) Reviewer-**01407353**: Here Young Min Park reviews the issue of the possible clinical utility of mutations in the core promoter and proximal precore regions of the HBV genome. In particular, he analyzes the possibility that the number/type of mutations in these regions may predict the development of liver cancer. Overall, the paper is comprehensive and interesting. A review can be inspired by personal investigations and also centered on own results. However, they should be always cited to sustain a discussion rather than presented as the topic of the paper. Note for example at page 7th, first line: "For this article, we analyzed clinical...". This type of expression is not adequate for a review work. Moreover, I suggest a careful revision of the text with the aid of an English native speaker.

[ANSWER]

<1> A native English speaker has corrected the English language of the manuscript (English language editing company: American Journal Experts, <http://www.aje.com>).

<2> "For this article, ...": No studies were available regarding this topic. This part of the description was revised as follows: "Because the literature regarding the clinical features of wild type HBV genotype C2 is lacking, we analyzed this genotype in comparison with three mutation types using our published raw data (N=442)".

- (3) Reviewer- **02456377**: The present study by Young Min Park is investigated the combined effect of number and pattern of mutations in the core promoter and proximal precore regions, and their utility to predict the HCC risk. The results showed that mutation number over six is the most important viral factor to predict the risk of HCC in the group of chronic HBV carriers infected by the BCP mutant type. In general, the work was interesting, except several issues to be addressed

to increase the quality of the present work. 1. The authors should supplement the correlation analysis between the number of mutations and the rate of HCC. Figure 1. (A) 2. The authors should supplement the correlation analysis between the number of mutations of PABC clinical staging and the rate of HCC, respectively. Figure 1. (B) 3. I think that the author should change Figure 1. (C) and Figure 1. (D) to tables, and supplement statistical methods achieving p values in all tables.

[ANSWER]

<1> Figure 1 (A): Figure 1(A) was changed to Figure 1 with supplementary data.

<2> Figure 1 (B): Figure 1(B) was changed to Figure 2 with supplementary data.

<3> Figure 1 (C) and (D) to table: Figures 1(C) and 1(D) were changed to Tables 1 and 2, respectively. In addition, supplementary statistical methods and p-values were included in two tables.

3 References and typesetting were corrected

[ANSWER]

The references were corrected.

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

Sincerely yours,



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