

ANSWERING REVIEWERS



January 26, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 15977-review.doc).

Title: Induction of ER-derived oxidative stress by an occult infection related HBsAg variant

Author: In-Kyung Lee, Seoung-Ae Lee, Hong Kim, Yu-Sup Won and Bum-Joon Kim

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 15977

I. Review's comments

[Reviewer #1]

Congratulations for the quality of Yours Work. 1) I criticized the lack of comparative analysis with classical tests used in the window period and in inexplical negative results os HBsAg in the course of hepatitis. All the best-liberatocaboclo

Answer #1-1) The KD mutant used in this study was from Korean occult subjects of HBsAg negative serostatus not showing clinical symptom, not from chronic patients as described previously (PLoS One. 2013;8(1):e54486. doi: 10.1371/journal.pone.0054486. Epub 2013 Jan 18). So, since there is no window period of HBsAg in subject of this variant, we could not do HBsAg ELISA in the window period.

[Reviewer #2]

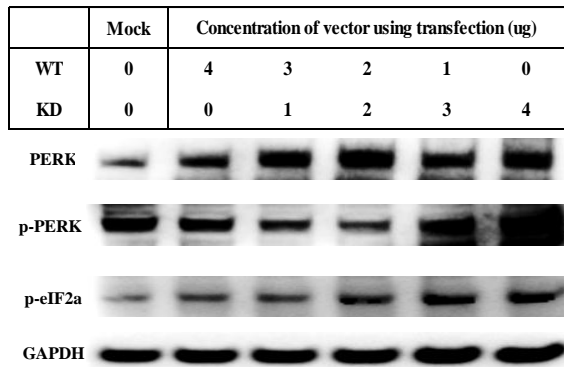
1) There are a number of English spelling and grammar errors, which should be polished and checked by a native English speaker. 2) The KD HBsAg mutant should be described in more detail in the Material section. There is no information concerning the course of liver disease of the CHB patient harboring the KD variant. Did this patient develop severe liver disease such as LC or HCC? 3) The authors have presented convincing data with regard to the induction of ER stress and apoptosis. However, key experiments showing that the effect of the KD variant on ER stress and apoptosis could be competed by wt HBV constructs are missing and would enhance the impact of the results dramatically. 4) Fig. 7a showed induction of p-JNK by the KD variant. Is there any explanation for the double band in this experiment?

Answer #2-1) According to reviewer's comment, revision version was edited by English editing company recommended by WJG (American Journal Experts).

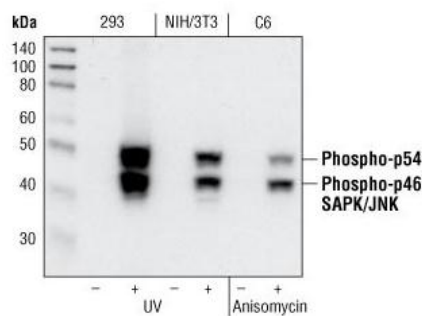
Answer #2-2) The KD mutant used in this study was from Korean occult subjects of HBsAg negative serostatus not showing clinical symptom, not from chronic patients as described previously (PLoS One. 2013;8(1):e54486. doi: 10.1371/journal.pone.0054486. Epub 2013 Jan 18). To clarify it, we added the following sentence in the revised version "The serum for the Hepatitis B surface antigen (HBsAg) variant (KD) related to occult infection and the control HBsAg (wild type or NOR) were acquired from

one a 54 year-old Korean occult subject showing HBsAg seronegative (Kim H et al. Occult infection related hepatitis B surface antigen variants showing lowered secretion capacity. World Journal of Gastroenterology. In press) and a Korean chronic patient, respectively. (line 138-140)

Answer #2-3) According to reviewer's comment, we have checked the KD induction effect on ER stress were inhibited by wild type construct addition.



Answer #2-4) The p-JNK antibody used in this study known as the phospho-SAPK/JNK pathway antibody from Cell-Signaling cooperation was described as double band (phospho-p46 & p54) in western blot assay according to manufacturer's comments.



II. Edit manuscript

Answer 1) We have deleted the section, "Statistical analyses" in Materials and Methods because our data have been based on experimental statics, not medical patients' information. Instead, we have explained the bio-statistical methods from our experimental data in the Figure legend.

Answer 2) The section of "Conflict-of-interest" and "Data sharing" has been inserted to the manuscript.

Answer 3) The lists of PMID and DOI have been edited and rearranged. We have provided the first page of paper which has not PMID or DOI in the Reference.

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

Sincerely yours,

Bum-Joon Kim, PhD

Department of Microbiology and Immunology, Liver Research Institute and Cancer Research Institute, College of Medicine, Seoul National University.

28 Yongon-dong, Chongno-gu, Seoul 110-799, Korea
E-mail : kbumjoon@snu.ac.kr. Tel: (82) 2-740-8316.
Fax : (82) 2-743-0881