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Shui Qiu,

Science Editor, Editorial Office

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Re: World Journal of Hepatology M22855

Dec. 3, 2015

Dear Sir or Madam,

Please find, attached, a manuscript entitled "**HCV inhibitor synergism suggests multistep interactions between HSP90 and HCV replication** (title has been altered)".

I thank the reviewers for evaluation of our paper and for valuable comments to improve our manuscript. Please find revised version of our manuscript M22855 and the following response to the reviewers' comments and additional points that alter according to the Guidelines and Requirements for Manuscript Revision-Basic Study: All changes made in terms of this revision were recorded as corrections in the manuscript Word file.

Reviewer 502973 (comments are indicated by italicized blue characters)

1) *In general, the English language in this manuscript is poor and should be polished by a native English speaker.*

This manuscript was reedited by NPG English language editing service (Certificate 4D39-4D74-7D69-66D6-86FA).

2) *1. It is unusual to cite references in abstract. I would suggest not use the 2 references in the Abstract. 2.*

The two citation in the abstract were removed and the references were renumbered appropriately.

3) *2. In the legend of Figure 2, it wrote "The levels of HCV RNA and core present in the JFH1-infected Huh-7 cells (open squares) and the culture medium (filled squares) were examined as described in the text." However, I cannot find the HCV RNA data in Figure 2B and 2C. 3. Also in the legend of Figure 2, it wrote "The concentrations of 17-AAG and 17-DMAG (0-300 nM) are shown under the histograms." However, it seems that Figure 2D showed the ratio of JFH1 core protein in medium to that in the cells. It was not the JFH1 core protein concentrations after 17-AAG and 17-DMAG treatment.*

I amended appropriately as followed:

For the legend to Figure 2D: “**D.** The ratios of HCV RNA in the medium to the total HCV RNA (the sum of HCV RNA in the medium and in the cells) are shown.” In addition, “**E.** The ratios of the core in the medium to the total core (the sum of the core in the medium and in the cells) are shown.” was added in the legend to Figure 1 to improve readability.

In addition, the legend to figures are rechecked, and we made correction in Figure 6C “**C.** The CI of each ED₅₀, ED₇₅ and ED₉₀ by the combined CsA and radicicol treatment at molar ratios of 3:1, 5:1 and 10:1, respectively.”

Reviewer 5258

This reviewer indicated no comments and the decision was “accept”

In addition, we added the following modifications as appropriate.

A) Upon reviewing the statistical methods, I noticed that the ratios used in Figs 1E, 1D, 2D, 4C and 5C should be ratios of molecules in the medium to that of the total molecules, rather than that in the medium to that in the cells. I recalculated and corrected. Because the level in the RNA/core level in the medium were much lower than that in the cells, these data are basically unaltered and the statistical differences and significances are not altered. The corresponding figures and legends were modified as described above.

B) According to the Guidelines and Requirements for Manuscript Revision-Basic Study, we made alteration as followed:

1. Title has been changed to” HCV inhibitor synergism suggests multistep interactions between HSP90 and HCV replication”
2. Running title was added “Effect of HSP90 inhibitor on HCV replication”
3. We removed the following sentence from the Institutional review board statement, because I aware that we used no recombinant DNA technology for this specific study: “This study was reviewed and approved by the Tohoku University Gene Recombination Experiment Safety Committee and the Tohoku Pharmaceutical University Gene Recombination Experiment Safety Committee”
4. We arranged the followings to fit the Guidelines and Requirements.
 - 1) Length of “Conclusion” in the abstract was shortened.
 - 2) Core Tip was rearranged and the audio Core Tip was prepared.
 - 3) Acknowledgement was replaced to Supportive information.
 - 4) “The statistical methods of this study were reviewed by Prof. Kotaro Tanahashi from Mathematics, Tohoku Pharmaceutical University” was included in MATERIALS AND METHODS.
 - 5) COMMENTS section was included.
 - 6) The format of list of References was altered.
 - 7) P values are included in the text.

We would be most grateful if you would proceed for publication in "World Journal of Hepatology" and we look forward to hearing from you at your earliest convenience.

Sincerely yours

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