Aug 14, 2015

**Jing Yu**, Science Editor, Editorial Office
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Dear Editor Yu,

**Name of journal: World Journal of Gastroenterology**

**Manuscript NO.: 20235**

**Column: Topic Highlights**

**Title: Metabolic alterations and hepatitis C: from bench to bedside**

Dear Editor Yu,

Thank you very much for your letter of July 27, 2015. We greatly appreciate the comments/suggestions offered by you and the reviewers and the opportunity to improve our manuscript.

We have revised the manuscript accordingly, as described in the following point-by-point responses. All changes in the revision are marked in red:

To Reviewer 1

Reviewer 1.

Some little corrections are needed:

*1. Page 4, line 17: glycprotein 1 needs to be corrected to glycoprotein 1*

**Response:** *Glycprotein 1 has been corrected to glycoprotein 1*

*2. Page 19, line 2: "…. is not associated ?? therapeutic response.*

**Response:** The sentence has been corrected as "..... is not associated with therapeutic response".

*3. Page 50: Figure Legends. In the opinion of this reviewer more informations are needed for figure 2,3 and 4. Or, at least, the authors have to mention "see the text for*

*explanation".*

**Response:** Thank you very much for the valuable comment. We had added "see the text for a detailed explanation" to most of the figure legends and more information had been provided in Figure 1 and 2 legends.

*4. However, in the legend of figures 3 and 4 "altetrations" needs to be corrected. In Figure 2, page 52, Fushion is perhaps Fusion?*

**Response:** Thanks for your comments. As suggested, "altetrations" has been corrected as "alterations", and "Fushion" has been corrected as "Fusion".

Reviewer 2.

*Major points:*
*1.First of all, liver dysfunction such as cirrhosis induced by HCV, HBV or NASH, could evoke diabetes, etc by the deterioration of functional reserve of the liver itself. At least HBV could also induce the similar metabolic change. Author should comment the difference of the etiological specificities.*

**Response:** Thank you for the comment. We have commented on the difference in the etiological specificities (eg. HBV) of metabolic alterations in the introduction.

*2. As the author described in the last part of the paper, lots of the metabolic disorder could be evoked by HCV infection but not only interferon but DAA could eradicate HCV these days. Most of the preliminary data and in vitro research would be re-evaluated after SVR was achieved. At least one table which documents the metabolic disorder and whther recovery after SVR or not should be added. Otherwise clinician could not believe HCV could induced so many metabolic event by infection itself.*

**Response:** Your valuable comment is deeply appreciated. We added a table (Table 1) listing HCV-associated cardiometabolic diseases and the recoverability after SVR.

Minor

*1. The last part of 1-(3) documented direct viral invasion of cardiac vascular tissues cannot be acceptable because HCV tropism specifically to hepatocytes and macrophage etc. No citations were described.*

**Response:** The citation has been added.

*2. Figures should be explained precisely. In the figure 3, virus like particle was not explained at all. Is it LVP? Moreover how does Glut influence HCV in the figure 3? There are several subtypes of Glut. The text clearly documented Glut 2. The figure should describes as Glut 2. In the figure 2, what is LD?*

**Response:** Thank you for the comments. Statements of "see the text for a detailed explanation" have been added to most of the figure legends. We also added more descriptions to all of the figures. LVP means lipoviral particle, and LD means lipid droplet (had been described in the legends already). Both Glut 2 and Glut 4 (please see Section 2.1, Glucose metabolism: Altered pathways) are involved in HCV, so we did not attempt to label Glut 2.

Thank you again for your kind attention.

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