

Aug 7th, 2015
Fang-Fang Ji
Science Editor
World Journal of Hepatology

Re; Revised manuscript to World Journal of Hepatology as a Review Article (Number ID: 00009426)

Dear Editor:

Thank you for your email and for the reviewers' comments concerning our manuscript with the title "**Roles of lipoprotein receptor in the entry of hepatitis C virus**" (Number ID: 00009426) by **Jingya Lyu, Hitomi Imachi, Kensaku Fukunaga, Takuo Yoshimoto, Huanxiang Zhang, Koji Murao**. Those comments are all valuable and very helpful for revising and improving our paper. We have studied comments carefully and have made correction which we hope meet with approval. Revised parts are made in red in the manuscript. The main corrections and the answer to the reviewers' comments are as following:

1. reviewer 00012216

- 1) The last part is difficult to understand in the review, since the title is about the role of lipoproteins in HCV entry, but in the last item authors review immunological aspects that could be suitable for a different manuscript.

Answer: We have already deleted the last section in revised manuscript.

- 2) Comment about CLDN1, OCLN, EGFR, EphA2, Tfr1 or NPC1L1.

Answer: As your suggested, we added a section named "Roles of tight junction proteins in the later phase of HCV entry" in the last third paragraph and changed the last second section "Other factors on cell surface involved in HCV entry" to talk about the function of these factors in the HCV entry. We also added some references to support them.

- 3) The current standard of care for HCV is IFN+RBV, but nowadays the standard treatment consists of direct acting antivirals.

Answer: We are sorry for this mistake and revised it as comments: "current therapy for HCV infection is based on direct-acting antivirals (DAAs) with or without peginterferon plus ribavirin". We also added two references to support it as following:

3. Kanda, T., F. Imazeki, and O. Yokosuka, New antiviral therapies

for chronic hepatitis C. *Hepatol Int*, 2010. 4(3): p. 548-61.
10.1007/s12072-010-9193-3

4. Kanda, T., O. Yokosuka, and M. Omata, Treatment of hepatitis C virus infection in the future. *Clin Transl Med*, 2013. 2(1): p. 9.
10.1186/2001-1326-2-9

2. reviewer 00012386

- 1) In Core Tip, Make a correction from “hepatocarcinoma” to “hepatocellular carcinoma”.

Answer: We corrected it in Abstract and Core Tip.

- 2) In Introduction section, Authors described that “Different from hepatitis A virus and hepatitis B virus, there is no available vaccine against HCV until now, and current therapy for HCV infection is based on a combination of interferon-alpha and ribavirin[3].” Now, standard of care for HCV is DAAs with or without peginterferon plus ribavirin.

Answer: Thank you very much for your comment and we learned a lot by reading the two references. We corrected it in the article as following: “current therapy for HCV infection is based on direct-acting antivirals (DAAs) with or without peginterferon plus ribavirin”. We also added two references as following:

3. Kanda, T., F. Imazeki, and O. Yokosuka, New antiviral therapies for chronic hepatitis C. *Hepatol Int*, 2010. 4(3): p. 548-61.
10.1007/s12072-010-9193-3

4. Kanda, T., O. Yokosuka, and M. Omata, Treatment of hepatitis C virus infection in the future. *Clin Transl Med*, 2013. 2(1): p. 9.
10.1186/2001-1326-2-9

- 3) About Ref.[5], authors should also add the original references as follows:...

Answer: Thank you for the kind advise. We added the two references as your suggested.

- 4) Authors described LDLR, SRBI and CD81 as HCV receptors. How was Claudin-1, occluding or other?

Answer: As your suggested, we added a section named “Roles of tight junction proteins in the later phase of HCV entry” in the last third paragraph and changed the last second section “Other factors on cell surface involved in HCV entry” to talk about the function of these factors in the HCV entry. We also added some references to support them.

All authors have read the manuscript and approve its submission with their agreements.

All authors declare that they have no conflict of interest.

Since we don't have the crosscheck software in our university, we are sorry that we can not supply the result of crosscheck.

We have already checked and revised our language by a professional company in Japan before we submitted this article firstly. However, we can not ask for a language certificate now.

Thank you for your invitation and consideration.

Sincerely yours,

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