

November 25, 2013

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 6839-review.doc).

Title: Molecular basis and therapeutic options of virus-related liver cirrhosis

Author: Ji Lin, Jian-Feng Wu, Qi Zhang, Hong-Wei Zhang, Guang-Wen Cao

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 6839

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated.

2 Revision has been made according to the suggestions of the reviewer

(1) Reviewer #1 (01560858)

The manuscript reviewed the molecular mechanisms of virus-related liver cirrhosis. The manuscript is well written, and informative. However, there are minor concerns. 1. The authors cited reference 74, and stated that macrophages promote the resolution of fibrosis by produced interstitial collagenases like MMP13 (page 16, lines 16-17). However, the report cited as reference 74 showed only an involvement of macrophages, but not interstitial MMP13, in resolution of fibrosis. Therefore, the authors should correct the statement, or cite a proper reference. 2. There are some typing errors. The authors should carefully read again, and correct them

Answer:

Thank you very much for your time spent on this manuscript, the thoughtful comments, and the kind instructions. I am so sorry to cite an improper reference and the reference 74 has been replaced by "Scar-associated macrophages are a major source of hepatic matrix metalloproteinase-13 and facilitate the resolution of murine hepatic fibrosis". We rephrased the antiviral

treatment sections, also corrected references and typing errors as indicated.

(2) Reviewer #3 (00199518)

The article does not address what is written in title. The article is written patchily. The flow is not proper. There is no co-relations shown between pathogenesis described and stem cell therapy.

Answer:

This article mainly describes the process of HBV and HCV caused cirrhosis and the most important treatments nowadays. Our main idea about this complex process is the evolution of viral variation-selection-adaption, which contributes to the continuous liver damage. Because the patients will experience the long chronic infection status, so we think that the evolution of viral occurs under the environment of chronic infection. In other words, the environment of chronic infection contributes to the viral variation, which helps the virus continue to exist and finally results in the persistent liver damage. So the central idea of this article is that the immune response to the HBV and HCV cause the liver damage, which contributes to the evolution of viruses and then the viral selection and adaption also conduct the progression of pathogenesis.

Indeed, stem cell therapy is not related to viral infection, but hepatocyte regeneration. I made the correction in Abstract section. Stem cell therapy can be developed to replace liver transplantation.

(3) Reviewer #4 (00503191)

Dear Authors, with interest I have read your manuscript "Molecular basis and therapeutic options of virus-related liver cirrhosis". My initial recommendations are: -improve language, a review by a native speaker is advised -improve level of evidence, there are interesting studies but pretty few Meta-analyses in the basis of your manuscript -although the part of the molecular basis of the virus induced cirrhosis is

comprehended enough, this cannot be said for the treatments. A detailed pathogenesis requires an equally detailed treatment review

Answer:

Thanks for giving us so many meaningful suggestions for our manuscript. We have revised this manuscript according to your suggestions one by one. We add some Meta-analyses about antiviral treatment of decompensated virus-related cirrhosis. These studies definitely point out the importance of antiviral treatment in patients with decompensated cirrhosis. Stem cell therapy is not related to viral infection, but hepatocyte regeneration. I made the correction in Abstract section. Stem cell therapy can be developed to replace liver transplantation. Thanks you very much for seriously reviewing this manuscript.

We rephrased the antiviral treatment sections, also corrected references and typing errors. Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

A handwritten signature in black ink on a light pink background. The signature is cursive and reads "Guangwen Cao".

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