

October 16, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format.

Title: Prevention of Hepatocellular Carcinoma in Chronic Viral Hepatitis B and C Infection.

Author: Tao Lu , Wai-Kay Seto , Ranxu Zhu , Ching-Lung Lai , Man-Fung Yuen.

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 5490

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

Reviewer 1: Prevention of hepatocellular carcinoma in chronic viral hepatitis B and C infection was reviewed in this paper. Increasing advances in the standing of the molecular pathogenesis of HCC would hold promise in preventing this highly lethal carcinoma. If appropriate subheadings are added between some paragraphs, it will be easy to read. In this paper, both of HBV and HCV prevention were presented separately, striking similarities and differences should be listed. The paper was proficient in writing.

Response to reviewer

Thank you for your kind suggestions. Appropriate subheadings have now been added throughout the manuscript. The similarities and differences about the prevention of HBV- and HCV-related HCC are now listed in Table 2 and Table 3.

Reviewer 2: The manuscript by Tao Lu et al. reviews the risk prediction and the risk factors to develop hepatocellular carcinoma (HCC) in subjects that are infected with HBV or HCV. Moreover it describes preventive and therapeutic strategies. The subject is very extensive, and the effort of authors to convey a concise account is of merit. I have a few concerns: - The authors should address briefly the issue of HBV and HCV coinfection in the risk of developing HCC and in therapy. - Tables I and II should be regrouped by risk factors and prediction scores rather than be separated in individual studies. - Tables III and IV lack references - A brief account of signaling pathways involved in chemoprevention or protection, triggered by compounds (e.g. resveratrol) should be provided. Of particular importance I suggest to discuss Sirtuins and PI3K/PTEN/AKT pathways, which have been recently involved in the interplay between viral infection, lipid accumulation and tumorigenesis (Ripoli M, *Virus Res* 2011, Benegiamo et al, *Dig Dis Sci* 2012, Sun LJ, *Hepatol Res* 2013 / Clement S *Hepatology* 2011, Rahman MA, *Int J Cancer* 2002, Kong G, *PLOS ONE* 2011). - Reference 22 contains an error - References 27 and 59 are identical

Response to reviewer

We thank you for your kind comments.

HBV and HCV coinfection in the risk and therapy of developing HCC, and the signaling pathways involved in chemoprevention triggered by compounds (e.g. resveratrol) were added according to the suggestions in the revised manuscript(The underlined parts in page 9 and page 12 respectively).

Tables 1 and 2 were regrouped to be the new Table 1 by risk factors and prediction scores. References for Table 3 are now marked.

Problems in References were corrected.

3 References and typesetting were corrected

Thank you for your kind attention.

Sincerely yours,

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Reviewers' comments: