

ANSWERING REVIEWERS



April 23, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 9908-edited.doc).

Title: Effect of Liver Regeneration on Malignant Hepatic Tumors

Author: Ji-Hua Shi, P å-Dag Line

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 9908

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) The statistical data about Hepatocellular Carcinoma has been updated^[1]. The changed part is underlined at line 3, page 3 in the revised version.
- (2) Many reviews discuss the effect proliferating adult hepatocytes might have on tumor growth, and the concept is well established. The layout of Figure 1 is based on the paper in *Anticancer Research*, 2010, 30: 2161-2170^[2]. Thus, we have modified the figure legend and cited the article.
- (3) The relationship between liver stem cells (LSCs) and hepatic progenitor cells
There is no definite conclusion or distinct criteria allowing a strict division between liver stem cells (LSCs) and hepatic progenitor cells. The terms are in many previous publications used synonymously when dealing with stem-like sells of hepatic origin^[3-5].

Some investigators emphasize that liver stem cells may arise from hematopoietic stem cells and hematopoietic stem cells may also differentiate into progenitor cells^[6]. Besides, there is another division about the definition of liver stem cell. The liver stem cells include both mature hepatocytes and hepatic progenitor cell, which may contribute to the liver repair^[7].

- (4) A new manuscript in Microsoft Word (doc format) was submitted to the editor.
- (5) The figures are submitted separately. The format is in Smartdraw (sdr) and bitmap (bmp), hence hey can be edited easily by graphic software packages.
- (6) Policy for manuscripts submitted by non-native speakers of English: We believe the standard of English in the manuscript satisfy the quality requirements indicated in the policy for non-native speakers of English.

3 References were added according to the suggestions made by the reviewers.

Thank you again for considering our manuscript for the *World Journal of Gastroenterology*.

Sincerely yours,

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Reference:

- 1 Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer* 2010; **127**(12): 2893-2917 [PMID: 21351269 DOI: 10.1002/ijc.25516]
- 2 Paschos KA, Bird NC. Liver regeneration and its impact on post-hepatectomy metastatic tumour recurrence. *Anticancer Res* 2010; **30**(6): 2161-2170 [PMID: 20651365 DOI: 30/6/2161 [pii]]
- 3 Kitisin K, Shetty K, Mishra L, Johnson L. Hepatocellular stem cells. *Cancer Biomarkers* 2007; **3**(4): 251-262
- 4 Tanaka M, Itoh T, Tanimizu N, Miyajima A. Liver stem/progenitor cells: their characteristics and regulatory mechanisms. *Journal of biochemistry* 2011; **149**(3): 231-239
- 5 Tanimizu N, Mitaka T. Re-evaluation of liver stem/progenitor cells. *Organogenesis* 2014; **10**(2): 0--1
- 6 Fausto N. Liver regeneration and repair: hepatocytes, progenitor cells, and stem cells. *Hepatology* 2004; **39**(6): 1477-1487
- 7 Greenbaum LE, Wells RG. The role of stem cells in liver repair and fibrosis. *The international journal of biochemistry & cell biology* 2011; **43**(2): 222-229