

August 24, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 12769-review.doc).

**Title:** The role of liver stem cells in hepatocarcinogenesis

**Author:** Lei-bo Xu, Chao Liu

**Name of Journal:** *World Journal of Stem Cells*

**ESPS Manuscript NO:** 12769

We thank the reviewers for their helpful and constructive comments. We thoroughly addressed all concerns and issues raised and revised our manuscript accordingly. All changes in the revised version are highlighted yellow. Below you will find our point-by-point responses to the comments of the reviewer(s).

1 Format has been updated

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

(1) **Question:** The topic of this review was covered in similar previous works (Alison MR Stem Cell Rev 2005; Mishra L et al, Hepatology, 2009). The authors need to clearly describe what is new in this review.

**Answer:** The reviewer is correct, but this review highlights many of the most important articles published from February 2009 to May 2014 regarding liver stem cells and cancer stem cells, especially vascular endothelial transdifferentiation of cancer stem cells.

(2) **Question:** Please update all the news included in this review: for instance, PLC accounts for the 2nd leading cancer-related death according to GLOBOCAN data (introduction - line 1).

**Answer:** We accept the reviewer's critical comments and all the news included in this review were updated.

(3) **Question:** A figure and/or a table summarizing the interactions between Wnt, Notch, TGFb, Hedgehog would be useful.

**Answer:** We thank the reviewer for this valuable comment and will continue to improve, but our understanding of the molecular mechanisms underlying malignant transformation of liver stem cells is still in its infancy. We expect that this review may be of interest to some investigators in this field and they could take the studies to the next step.

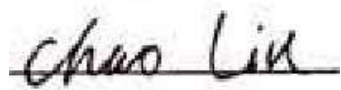
(4) **Question:** English language, grammar and spelling need an extensive revision by a native speaker.

**Answer:** The revised manuscript has now been edited and corrected by an American native speaker of English.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Stem Cells*.

Sincerely yours,

A handwritten signature in black ink, appearing to read 'Chao Liu', written over a horizontal line.

Chao Liu, MD, PhD

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