

ANSWERING REVIEWERS



July 19, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 4125-review.doc).

Title: Overexpression of IGF-I receptor as a pertinent biomarker for hepatocytes malignant transformation

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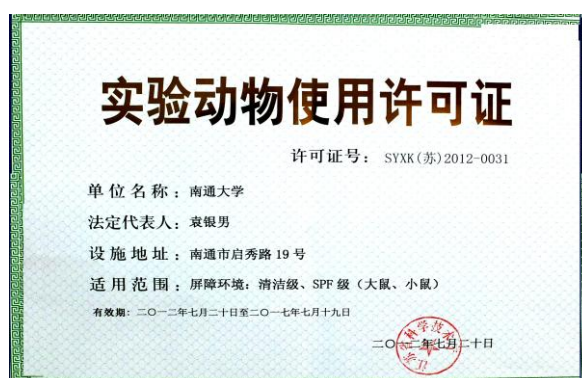
The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated.

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

(1) In the Ethics statement, more detail of the approval number of the reviewed and approved by the Institutional Animal Care and Use Committee is need. Not only has the guideline in the Guide for the Care but also the Use of Laboratory Animals as promulgated by the Institute of Laboratory Animal Resources, National Research Council, USA needed to descript detail.

The MS has been done that all procedures performed on the animals were conducted in accordance with the guidelines for experimental animals approved by the Animal Care and Use Committee of Nantong University, China.



(2) Chemical induced hepatoma in animal model is much difference not only what happens in the human beings but also the complication of the viral induced hepatocellular carcinoma. Therefore, the author needs to mention in the conclusion section.

Authors agree to this suggestion and have done in the conclusion section.

(3) According to the Ref. 13, there was a human HCC xenograft model. (Tovar V, Alsinet C, Villanueva A, Hoshida Y, Chiang DY, Solé M, Thung S, Moyano S, Toffanin S, Múñez B, Cabellos L, Peix J, Schwartz M, Mazzaferro V, Bruix J, Llovet JM. IGF activation in a molecular subclass of hepatocellular carcinoma and pre-clinical efficacy of IGF-1R blockage. *J Hepatol.* 2010; 52: 550- 559. The author described that this study was rat hepatoma models. Please describe more detail over there.

Thanks to Reviewer for your nice suggestion and it has been added.

(4) The process of the control, degeneration, precancerosis and HCC seems to be a progressive alteration in dynamic change in the histopathological picture, total RNA, IGF-IR mRNA and liver IGF-IR, linear regression analysis with error bar parameter description may be easy to understand for the readers.

Thanks to Reviewer, this section without bar figure, because few Tables have showed more information There was a rising tendency of serum or liver IGF-IR along with the morphological changes in rat hepatocarcinogenesis with HCC > precancerous > degeneration > control. Serum IGF-IR level in the precancerous group was significantly higher than that in the control or degeneration group ($P < 0.01$); and the level in the HCC group was significantly higher than in the control or degeneration group ($F = 11.850$, $P < 0.001$); The IGF-IR level in the livers in the HCC group was obviously higher than that in the control, degeneration or precancerous groups ($F = 8.720$, $P < 0.001$). Moreover, there was a positive correlation ($r = 0.91$, $P < 0.001$) found between serum and liver IGF-IR, suggesting that the over-expression of liver IGF-IR release into blood and circulating IGF-IR monitor hepatocyte malignant transformation.

(5) Where the figure 4 was came from? A signature is found in the figure 4 right hand side middle part. It needs to describe carefully.

It has been deleted.

(6) In the figure 4 left hand side, it is a pathway talking about the chronicity mechanism of the chronic hepatitis/cirrhosis/hepatocellular carcinoma. It may not be suitable to use to describe in this animal model.

It has been deleted.

3 References and typesetting were corrected

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

Sincerely yours,

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