Peer Review File

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Reviewer A

1. Professional English-language editing is necessary for this paper.

Reply 1: We thank this respected reviewer for the useful comment. Professional English-language editing helped us to correct a lot of grammatical errors and ambiguous expressions for us. We hope that the revised draft meets the requirements for publication.

Changes in the text: Page 2, line 27, 30; Page 14, line 273, 274; Page 16, line 318, 334; Page 17, line 335, 352; Page 18, line 363, 370, 372, 378; Page 19, line 385, 400; Page 20, line 401, 402, 405-408; Page 21, line 434, 435, 437, 439, 442; Page 22, line 457-459, 461, 463, 466; Page 23, line 467.

2. Line 47-48, it would be helpful to list some specific types of cancer with overexpressed BST-2.

Reply 2: We thank this respected reviewer for the useful comment. We list some BST-2 expression correlational specific cancer types in the revision.

Changes in the text: Page 4, paragraph 2, line 62-70.

3. Introduction. To help understand the clinical significance of this study, I would like to suggest the authors to use on paragraph to briefly review the disease burden of HBV and HCC. In addition, a brief review on other molecular mechanisms underlying HCC is needed. The last paragraph, in fact, are results of and comments on findings from the current study, which should not be placed here. Please briefly introduce the study hypothesis and objectives in this paragraph.

Reply 3: We thank this respected reviewer for the useful comment. We have carefully modified the relevant research background in “Background” part.

Changes in the text: Page 4-7, line 50-129.

4. Because this is an in vitro experimental study, the findings are difficult to generalized to human patients. This should be discussed as a limitation.

Reply 4: We thank this respected reviewer for the useful comment. According to the suggestion of reviewer, we modified some conclusion statement accordingly.

Changes in the text: Page 3, line 43; Page 7, line 128; Page 16, line 328; Page 19, line 392.

Reviewer B

Hepatocellular carcinoma (HCC) is a prevalent malignancy worldwide and one of the difficult cancers to cure completely. The mechanisms for HCC tumorigenesis and progression have been still unclear. The authors clarified the mechanism of HCC tumorigenesis and progression by bone marrow stromal cell antigen 2 (BST-2)

overexpression in patients with hepatitis B virus (HBV). The reviewer is also interested in these results, there are however some questions to clear up more as below:
1. The authors insisted that BST-2 both functioned in HBV-derived HCC tumorigenesis via the nuclear factor-κB (NF-κB) pathways and contributed HCC cell growth. The authors certainly demonstrated that BST-2 was related to "tumor growth" through N-glycosylation in Figure 4, HCC "tumorigenesis" however could not be demonstrated in BST-2 involvement. Could co-transfection with BST-2 and HBV induce HCC tumorigenesis not in HCC cell lines but in normal cells?

Reply 1: Thank the reviewer for the concern, and we agree with the opinion of the reviewer. We constructed wild type and N65/92A mutant of BST-2 expressing L02 (normal hepatic cell) cell lines. The characteristic of cell proliferation, would healing, and colony formation were measured. The result showed that BST-2 and mutant could enhance tumor characteristics of L02 cells.
Changes in the text: The results were submitted as Figure S1. And the corresponding changes are in the following text: Page 17, line 344-348. Page 31, line 709-714.

2. In this study, the authors used a number of HCC clinical samples, survival analyses were not however performed. To demonstrate the clinical importance of BST-2 function, please indicate Kaplan-Meier curve, dividing BST-2 into high and low expression group.

Reply 2: We thank this respected reviewer for the useful comment. We performed the survival analysis by Kaplan-Meier curve. The result demonstrated that high BST-2 expression accelerated the death of the patient.
Changes in the text: The Kaplan-Meier curve was added as Figure 1G in the revision. And the corresponding changes are in the following text: Page 13, 248-252; Page 14, line 284-287. Page 28, line 645-646.

3. Related to #2, the authors displayed patients' characteristics in table 1, there were however too little information. Please add laboratory data (including tumor markers), histological information (tumor size, tumor number, differentiation, vascular invasion), TNM staging.

Reply 3: We thank this respected reviewer for the useful comment. Detailed information including tumor markers, histological information, and TNM staging et al. were added in Table 1 of the revision.
Changes in the text: Detailed information including tumor markers, histological information, and TNM staging et al. were added in Table 1 of the revision. And the corresponding changes are in the following text: Page 14, line 271.

4. In figure 2B, the band of β-tubulin as positive control were not constant. Please change this picture to make better.

Reply 4: We thank this respected reviewer for the useful comment. New picture has

been added to substitute the original one in the revision.
Changes in the text: We have added the new picture in the Figure 2B.