Reviewer's report

Title: Hepatitis B virus X protein suppresses caveolin-1 expression in hepatocellular carcinoma through regulating DNA methylation

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The manuscript “Hepatitis B virus X protein suppresses caveolin-1 expression in hepatocellular carcinoma through regulating DNA methylation” by Yan and colleagues explored the role of HBx on the hypermethylation of caveolin-1 in HBV related HCC. This work is of importance to further the understanding of the molecular mechanism underlying the oncogenicity of HBx. I have some suggestions/comments:

1. Ethic issue. Has an informed consent been obtained from each of participants?

2. The authors suggested that HBx can induce caveolin-1 gene CpG island methylation, based on their in vitro study using a SMMC-7721 cell line. They also found that 28/33 HCC samples were positive for caveolin-1 gene CpG island methylation. How about the adjacent non-tumor tissues? Since HBx may commonly expressed in the non-tumor tissue, has they seen any caveolin-1 CpG island methylation in specimen derived from the HBV positive non-tumor tissues? Also, it is of informative to compare the methylation statues of caveolin-1 gene CpG island between HBV-positive and HBV-negative HCC tissues.

3. Neither in the method nor the figure legends provides enough information about at what time point post adenovirus infection the cells were harvested for caveolin-1 expression level determination by RT-PCR and western blot. This is information of importance and the author should provide. Also, the method is not detailed enough for others to repeat the experiments.

4. Only one cell line was used. Could same observation be made using different HCC cell lines?

5. The author claimed in the last paragraph of result part that “We found transfected HBx could significantly down-regulate activity from the caveolin-1 promoter”, Dose the observation was made using HBx stably expressed or transiently infected SMMC-7721 cells? Need authors provide detailed information.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests