Reviewer's report

**Title:** Leptin as a critical regulator of hepatocellular carcinoma development and progression through modulation of human telomerase reverse transcriptase

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**Reviewer:** Young Nyun Park

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The authors examined the biological actions regulated by leptin and its receptors in HCC and the correlation between leptin and human telomerase reverse transcriptase (hTERT). And it was suggested that leptin is a critical regulator of hepatocellular carcinoma (HCC) development and progression through modulation of hTERT. This is an interesting study about the role of leptin during hepatocarcinogenesis. However, this reviewer has several comments to make this paper more attractive.

1) Non-alcoholic fatty liver disease (NAFLD)/ non-alcoholic steatohepatitis (NASH), which can be induced by obesity is considered to be a soil for HCC. To study the role of leptin in HCC development, the pathological information about the background liver whether NAFLD/NASH is present or not is important. However, there is no data about the presence of NAFLD/NASH in both HCC group and control group of this study. In addition, the study for the leptin expression in non-neoplastic liver of HCC patients is required.

2) More detailed data about the patients' BMI and metabolic syndrome including diabetes mellitus are required.

3) The etiologies of HCCs in this study are hepatitis B virus and hepatitis C virus. Is there any difference of leptin expression in HCC according to the different etiologies?

4) In this study, that leptin suppressed MMP-1 expression and triggered MMP-9 and MMP-13 expression in HepG2 cells. Please explain how decreased MMP-1 could contribute to a more favorable environment for invasion and metastasis of HCC in the cirrhotic liver.

5) There are several typing errors