Reviewer’s report

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

Version: 1  Date: 25 January 2010

Reviewer: Jing Shen

Reviewer’s report:

Major Compulsory Revisions:
Although epidemiological studies observed that obesity was associated with hepatocellular carcinoma (HCC) risk, it was still unclear on how to properly explain the biological mechanism of obesity in HCC development and progression. Through the current study, the authors investigated the relationship between leptin, leptin receptors and hTERT mRNA expression as well as telomerase activity (TA) in thirty-six liver tissues and HEPG2 cells. Their results suggested that leptin may regulate HCC development and progression through modulation of hTERT. It provided a novel explanation for the potential mechanism of obesity playing a role on HCC development and progression. The hypothesis is novel, and the experiments are well designed. But the rationale for establishing the relationship between obesity and HCC seems weak. DNA methylation occurred at gene promoter region is also an important regulating mechanism on gene expression. Its role need discussed in the text.

If leptin was not expressed in health live tissue, the higher expression of leptin found in HCC tissue may indicate that leptin is caused by cancer cell itself, not due to obesity (leptin) to lead to HCC, i.e. leptin overexpression may be the result of HCC, not the cause. How to exclude this possibility needs more discussions.

How to explain the observation that “blocked leptin’s expression in HepG2 cells …… did not significant decrease hTERT mRNA levels and TA (Figure 2a, 2b)”?

Minor Essential Revisions:
Statistical analysis should be described briefly, not omitted.

Figure 1: it is unclear how to conduct statistical analysis for comparison leptin expression (unexpressed in healthy liver tissue compared with 5.9 in HCC liver tissues).

The role of references [28, 29] cited in the text of “we seeked to determine whether there is an association between leptin and hTERT mRNA expression” are unclear.

Level of interest: An article of importance in its field

Quality of written English: Acceptable
**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests.