Reviewer's report

Title: Combination of hepatocyte specific delivery and transformation dependent expression of shRNA inducing transcriptional gene silencing of c-Myc promoter in hepatocellular carcinoma cells

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Reviewer: Zong Sheng Guo

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The study itself is sound. However, the authors have previously published a paper (Ref# 34; Mehndiratta M et al., 2011) which was very similar to the current manuscript. After reading both the previous paper and the current manuscript, it seems that the major differences are two folds. One is the cancer types: the previous study has used glioma, breast, lung and other cancer cell lines, while the current study has used exclusively liver cancer cell lines. The other is the delivery vehicles: liposome (Lipofectamine 2000) was used previously and now it is Sendai virosomes. Yes it may enhance the specificity of hepatic delivery even though the authors have not gone to any in vivo experiment. Thus, this manuscript mainly deals with the specificity of shRNA delivery.

Overall, it is a very good study.

Major compulsory revisions

(1). The previous study by the authors stated that TGS of c-myc by test siRNA is dependent on DNMT activity, but not on HDAC activity (on page 2306, ref #34). However, in the current manuscript, it is stated that both HDACs and DNMTs are involved (page 10). Please reconcile.

(2). References are sometimes overcited and other times undercited. For example, (A). Ref#11 and 12 are from the same group and about the same topic. My suggestion is to delete the older reference (ref#11). (B). in discussing about the specificity of gene transfer, especially at the level of promoter, it is appropriate to cite one review article very relevant to the topic in Introduction: Guo ZS et al., Gene transfer: the challenge of regulated gene expression. Trends Mol Med. 2008; 14:410-8.

Minor Essential Revisions

(1). There are quite a few typos throughout the manuscript, especially in the reference. For example, (A). Line 642: “23” was repeated twice; (B). line 723: “J Int Cancer” should be deleted.

Level of interest: An article of importance in its field

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