Reviewer's report

Title: Down-regulation of SFRP1 as a putative tumor suppressor gene can contribute to human hepatocellular carcinoma

Version: 1 Date: 20 February 2007

Reviewer: Toshikazu Ushijima

Reviewer's report:

In this manuscript, Huang et al. showed that SFRP1 was down-regulated in 58 of 120 primary hepatocellular carcinomas (HCCs), that introduction of SFRP1 into HCC cell lines suppressed their growth, that LOH of the SFRP1 locus was present in 3-6 of 46 HCCs, and that the SFRP1 promoter CpG island was methylated in four HCC cell lines and in two of three primary HCCs. Although there is one previous report describing methylation of SFRP1 in HCCs (ref #22), the confirmatory value of this study is not small. However, the authors are trying to say that SFRP1 inactivation is involved in hepatocarcinogenesis, and this reviewer finds the following weakness for this conclusion.

1. The authors introduced SFRP1 into HCC cell lines. However, they did not compare the expression level of the introduced SFRP1 with that of normal liver. It is well-known that extreme overexpression of various genes could artificially induce growth suppression. The fact that knock-down of SFRP1 in HCC cell lines MHCC-L and SK-hep-1 did not induce their increased growth (page 16) supports this concern. The meaning of knock-down in a clone (SMMC-7721Z) that overexpress SFRP1 is unclear (page 17). It is requested that the authors compare the expression levels of the exogenously introduced SFRP1 with that of normal liver.

2. In the methylation analysis, the authors observed that all of the eight DNA molecules were methylated in 210C (Fig. 6B). Since a DNA sample from a cancer usually contains DNA derived from contaminating normal cells, it is atypical to observe that all the DNA molecules were methylated. The authors should examine the faction of cancer cells in samples 210C and 230C.

3. There are many grammatical errors, and the authors should ask for professional editing of English language.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests.