Reviewer’s report

Title: Promoter methylation of CDKN2A and the lack of p16 expression characterize patients with hepatocellular carcinoma

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Reviewer: Jin-zhang Zeng

Reviewer’s report:

The authors used MethyLight technique to detect the methylative status of CDKN2A, comparing to the detection by methylation-specific PCR (MSP). However, the data in general were poor and not convincing. Specific comments are highlighted as follows.

1. Different methods for detecting CDKN2A methylation revealed inconsistent results. In some tumor tissues (cases, 5, 8, and 33, table 1), although MethyLight detected very strong methylation of CDKN2A, MSP showed negative results. This discrepancy was repeated in nontumor tissue from case 12. In contrast, CDKN2A methylation demonstrated by MSP in tumors of cases, 2, 3, 7, and 27, were undetectable in MethyLight analysis. Although methylation is crucial for regulation of p16 expression, both methods in this study did not show an association of CDKN2A methylation with p16 expression (immunostaining). The authors interpreted these discrepancies as due to different sensitivities and specificities of the two methods. This is unconceivable. They should also provide data concerning p16 expression in term of mRNA (RT-PCR) and protein (Western blot).

2. The MS was poorly organized.

Level of interest: An article of insufficient interest to warrant publication in a scientific/medical journal

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.