Reviewer's report

Title: IQGAP1 and IQGAP2 are Reciprocally Altered in Hepatocellular Carcinoma

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Reviewer: Yinkun Liu

Reviewer's report:

1. Although the western blot and IHC validation was done, according to the description, a sufficient number of individual independent specimens need to be quantified by analysis. Moreover, expression of IQGAP1 and IQGAP2 on same single sample should be presented, rather than only expression rates.

2. There will be serious remodeling of liver at the cirrhosis stage. Is the cirrhosis compensated? What clinical criteria were used to match the groups? There is no information about such clinical criteria; details have to be provided to exclude the possibility of bias.

3. The reciprocal IQGAP expression pattern may be a characteristic of a more invasive and metastatic HCC phenotype. More evidences should be given by the functional assays on cell adhesion, motility, invasion as well as the colony formation in soft agar. In another point of view, how does this alternation of IQGAPs to be regulated during HCC progression.

4. In the study, a high degree of sensitivity and specificity for IQGAP1 positivity and IQGAP2 negativity in HCC should be supported by more strong evidences, not only positive expression rates. Does it only dependent on the ability of metastasis?

5. Based on pyrosequencing, authors concluded methylation of the Iqgap2 promoter is not the principle mechanism by which IQGAP2 is downregulated in HCC. What be contributed to the paper objective by the result?

Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being published

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