Reviewer's report

**Title:** Clinical Implication of ZEB-1 and E-cadherin Expression in Hepatocellular carcinoma

**Version:** 1 **Date:** 14 June 2013

**Reviewer:** Jun-Yang Liou

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Major Compulsory Revisions

**COMMENTS FOR THE AUTHORS**

In this manuscript entitled “Clinical implication of Zeb-1 and E-cadherin expression in hepatocellular carcinoma”, the authors described that positive Zeb-1 expression combined with loss of E-cadherin expression are correlated with poor prognosis in a HCC cohort with 108 patients. The authors also concluded that malignancy of positive Zeb-1 tumor associated with EMT. Although the clinical impact of Zeb-1 and E-cadherin has been shown in various tumors, including HCC, the combination of both factors in prognostic analysis has not been reported. Overall, this study is potentially interesting and the experimental design is decent, however, the results with less novelty. Specific comments are listed below:

1. The clinical outcomes of Zeb-1 and E-cadherin expression were reported previously. Thus, Fig. 2a and 2b is not informative in this study. In addition, it's well known that expression of E-cadherin is suppressed by Zeb-1. Can the authors compare the overall survival between groups of Zeb-1 (+)/E-cadherin (-) with Zeb-1 (+)/E-cadherin (+)?

2. The percentage of positive Zeb-1 expression in this study is relative lower than the earlier study (Annals of surgical oncology, 2012). It may due to the different assay methods by Western blot and immunohistochemistry. However, a similar finding of Zeb-1 positive percentage (14/110) in HCC was reported recently (PLoS ONE 2013, 8:e57968). The authors should consider including this finding in the discussion.

3. Does the Zeb-1 or E-cadherin correlated with smad4 expression in HCC which was reported by the authors? Whether smad4 (or other TGF-beta downstream factors) synergizes with Zeb-1 as a more powerful statistical tool in predicting clinical outcomes?

4. Is it reasonable to define “at least 1% of nuclear staining of Zeb-1” as positive expression? How the E-cadherin defined into preserved and reduced expression? The density of staining and percentage of cells were considered?

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