Reviewer's report

Title: Comprehensive analyses of imprinted differentially methylated regions reveal epigenetic and genetic characteristics in hepatoblastoma.

Version: 4
Date: 4 November 2013

Reviewer: Ian Morison

Reviewer's report:

Major Compulsory Revisions
Nil

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Abstract: In the following: “Aberrant methylation at imprinted differentially methylated regions (DMRs) in humans 11p15.5” change to human, not humans.

Methods/MALDI-OF MS: correct spelling of “rangde”.

Results: p17. Please provide a reference for hot-stop PCR. “Hot-stop” is not a widely used expression (Uejima H, Lee MP, Cui H and Feinberg AP. (2000). Nat. Genet., 25, 375–376.)

P17/18: Change “We found seven genetic alterations in four tumors resulting in the aberrant methylations:” to “We found seven genetic alterations in four tumors resulting in aberrant methylation:”

P20: Change “In the TxC comparison, both hypermethylation and hypomethylation were observed in tumors in the frequencies of no significant difference.” To “In the TxC comparison, both hypermethylation and hypomethylation were observed in tumors (no significant difference).”

P22: change “However, other CpG sites did not show hypomethylation although bare hypermethylations (less than 2.5%) were found...” to “However, other CpG sites did not show hypomethylation although bare hypermethylation (less than 2.5%) was found...”

Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore)

P22. I recommend deletion of the last sentence of the results section – it is not needed and it suggests more certainty that it should. Line-1 methylation has been used as a surrogate for genome-wide methylation but it is not the same as quantifying total methylation.

Fig 1 Legend: It is useful to be reminded of “Aberrant methylation of a DMR was defined as when more than 60% of total CpG units or CpG sites were aberrantly..."
methylated. Aberrant methylation of a CpG unit or CpG site was defined as occurring when the difference of its methylation indexes in two samples exceeded 0.15.” However, it would be adequate to state “Aberrant methylation is defined in Methods”.

Fig 4 legend: The last sentence of the legend (starting CpG#1) is not needed. The figure is clear.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

No competing interests