Reviewer's report

Title: Characterization of human gastric carcinoma-related methylation of 9 miR CpG islands and repression of their expressions in vitro and in vivo

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Reviewer: Paivi Peltomaki

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This study aimed to examine the role of methylation as a regulator of expression of CpG-island associated miRNAs. Among all such miRNAs, 9 disease-related (5 extragenic, 4 intragenic) were chosen for a detailed investigation. The observed patterns suggested that methylation was tumor-specific (miR-9-1, miR-137), suggestive of a field defect (miR-9-3, miR-34b, miR-210, miR-200b), or suggestive of host adaptation (miR-203, miR-375, miR-193b). Methylation correlated with the expression of mature miRNAs for a majority of miRNAs investigated. For some miRNAs (notably, miR-9-1) important clinicopathological correlations were observed.

The paper adds to the existing knowledge of the expressional regulation of the 9 miRNAs in question and their role in gastric tumorigenesis.

Suggestions for improvement (all are minor essential):

1) By which criteria were the particular regions chosen for methylation analysis within the entire CpG islands?

2) The diagrams depicting the CpG islands associated with each miRNA (Fig. 1, Supplementary Fig. 1) are useful and would become even more informative if a numerical scale would be included to indicate the overall extent of the region studied in base pairs (which would also make it possible to estimate the distances of particular CpG sites to the mature miRNAs).

3) Numerical inconsistencies or errors:

a) Abstract (p. 2) states that 6 % of normal/gastritis samples (2/48) showed methylation at miR-9-1. Two out of 48 makes 4% and not 6%.

b) Results, paragraph entitled “Inverse relationship between miR methylation of CpG islands and their corresponding expression levels” (p. 9) refers to Fig. 2 at several points whereas Fig. 3 would appear to be the correct reference.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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

No competing interests