

Reviewer's report

Title:The High Frequency Aberrantly methylated Targets in Pancreatic Adenocarcinoma Revealed by A Global DNA Methylation Analysis Using MethylCap-seq

Version:1**Date:**20 August 2014

Reviewer number:2

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Comments to the authors

Change in DNA methylation pattern is an important feature of pancreatic cancer (PC). The authors aimed to characterize the genome methylation patterns in various genomic contexts in PC using MethylCap-seq, and mapped the differentially methylated regions (DMRs) in pooled samples from PC tissues and adjacent non-tumor tissues (PN). They have identified large numbers of hypermethylated DMRs and hypomethylated DMRs, and suggest that aberrant hypermethylation in PC typically occurs in regions around the transcription start site (TSS). The data are interesting but I have several comments that need to be addressed in order to improve this manuscript.

Major comments

1. In Figs. 1A-G, all data should be shown for both PC and PN to see if there is a clear difference in the methylation pattern.
2. In Fig. 2A, it is difficult to see which part of the gene locus is methylated or not. The authors should modify this figure.
3. As shown in table S15, change in methylation pattern is seen in only a subset of PC. Therefore, the authors should analyze whether the change in the methylation pattern is related to clinical profiles of PC.
4. The authors state that 'the methylation status of DLX4, ELAVL2, IRX1, PITX2, SIM2, TBX5, and TFAP2C was subsequently validated in tissue samples'. However, the data is not shown and the authors should show the data.
5. In table 2, the authors listed gene ontology enriched in differentially methylated genes in PC. Although it is interesting, it does not show whether genes involved in regulation of tumorigenesis are identified or not. The authors should also make a list of genes that may be involved in tumor suppression or promotion.
6. In Fig. 3C, Orphan7-1 data is not clear. The authors should modify this picture.

Minor comments

There are numbers of typos (for example, p. 6 line 37, 'Four candidate DMR genes which included...', the number should be 'six'). The authors should carefully check and correct them.

Level of interest:An article of importance in its field

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.