Dear *Clinical Epigenetics* Editorial Board,

Please find enclosed the manuscript, The High Frequency Aberrantly methylated Targets in Pancreatic Adenocarcinoma Revealed by A Global DNA Methylation Analysis Using MethylCap-seq, by Jian Yu, et al., which we submit as an Original Research Article to *Clinical Epigenetics* for consideration for publication. Informed consent was obtained for this study. All the co-authors have seen and agree with the contents of the manuscript. We certify that the submission is an original work and is not under review elsewhere.

Our present study aimed to characterize the genome methylation patterns in various genomic contexts in pancreatic carcinoma (PC).MethylCap-seq was performed on pooled libraries from 10 PC samples and from 10 adjacent non-tumor tissue (PN)samples as a control. The library methylation information was obtained as differentially methylated regions (DMRs) in the genome and was validated by MSP, BSP and MSRE-qPCR. The bioinformatic analysis revealed hyper-DMRs and hypo-DMRs in PC vs. PN, and these DMRs were spread across the entire genome in various genomic contexts, such as inclusion (regular CGIs,orphan CGIs, CGI shores and promoters without a CGI). These results suggested that aberrant hypermethylation in PC typically occurs in regions around the TSS. The BSP, MSP, MSRE-qPCR, and RT-qPCR results demonstrated that the aberrant DNA methylation in PC tissue and in PC cell lineswas associated with gene (or related EST) expression. Our results indicated that PC DMRs were scattered among various genetic regions and that they influenced known genes and unknown EST transcripts, leading to numerous disturbances in the biological functions of pancreatic cells and resulting in carcinogenesis. These aberrantly expressed genes and transcripts might be potential diagnostic markers and/or therapeutic targets for the treatment of PC.

We believe that our findings are of potential interest to the readers of *Clinical Epigenetics* because we provide a novel analysis of DNA methylation in PC and discuss the potential of the identified genes and transcripts in the clinical treatment of this deadly disease.

We hope that the editorial board will agree on the interest of this study.

Sincerely yours,

Jian Yu

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