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Appointment Category: House Staff Clin Fellow * Research Fellow

Medical Student Graduate Student (Program:)

Register for: Clinical Research Translational Research Basic Research

Full Poster Title * High-throughput DNA methylation profiling using promoter microarrays

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In Preparation *

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Title: High-throughput DNA methylation profiling using promoter microarrays

Authors: Noriyuki Omura, Seung-Mo Hong, Chung-Pin Li, Kimberly Walters, and Michael Goggins

Background: Pancreatic cancer is a genetic and epigenetic disease characterized by widespread and profound alterations in DNA methylation. Effective high-throughput genome-wide methods for identifying DNA methylation patterns are needed to accelerate the discovery of abnormal DNA methylation patterns. We have developed a novel microarray-based method for detecting differential methylation patterns based on a methylated CpG island amplification (MCA) strategy using SmaI methylation-sensitive restriction enzyme. Sequentially MCA fractions are interrogated on high-resolution promoter microarrays with competitive hybridization.

Methods: Replicate DNA was extracted from the pancreatic cancer cell line, Panc-1 and HPDE, a normal pancreatic epithelial line. Amplicons from Panc-1 and HPDE were hybridized to Agilent human 44K promoter array to profile differential methylation. Candidate methylated genes identified by microarray were further evaluated using conventional bisulfite-modified sequencing (BMS).

Results: After normalization and analysis with CGH analytics 3.4®, we identified 589 probes with a significant higher signal in the pancreatic cancer line relative to the normal line (p-value<0.001 and log2 ratio>1.5). A further 493 probes were hypomethylated in Panc-1 relative to HPDE. Replicate analysis of array data showed high correlation value (R^2=0.92~0.93). Several well-known genes as a cancer-specific hypermethylation were identified, including ppENK and HOXA5. 21 of 22 novel genes predicted to be methylated at the CpG sites by microarray data were methylated by BMS.

Conclusion: Our microarray-based method is an accurate and powerful method for detecting methylated DNA profiles in human samples.