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HOXA9 and SOX1 – a promising DNA methylation based diagnostic biomarker for epithelial ovarian cancer

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Abstract

Epigenetic alterations play a major role in cancer. Transcriptional silencing by CpG island hypermethylation is a potential mechanism for the inactivation of tumor related genes. Aberrant DNA methylation patterns might be used as a biomarker for diagnosis and management of cancer patients. Ovarian cancer is characterized by few early symptoms, presentation of the disease at late stage and resulting poor survival. At present, no single epigenetic biomarker is able to accurately detect early ovarian cancer in either tissue or body fluid. Analysis of the methylation status of multiple genes simultaneously in a blood based assay may provide a more sensitive and specific method for the molecular classification and diagnosis of ovarian cancer. To develop a potential, DNA methylation based screening assay for early diagnosis of ovarian cancer, we quantitatively assessed the promoter methylation of HOXA9 and SOX1 gene in 54 ovarian cancer and 18 non neoplastic ovarian specimens by means of a high throughput quantitative, real time PCR based technique (MethyLight). We identified DNA methylation of HOXA9 and SOX1 to be the best discriminator between cancer and non-neoplastic tissue. The gene methylation achieved 93.47% and 78.26% sensitivity for HOXA9 and SOX1, respectively when analyzed in singleplex assay. However the sensitivity increased to 95.92% in the multiplex assay when either or both of the HOXA9 and SOX1 gene promoters showed methylation thereby indicating that these genes appear to have great potential to be evaluated for their methylation level in cell-free DNA or serum DNA as a non-invasive diagnostic marker the early diagnosis of ovarian cancer.