CpG island methylation and expression of tumour-associated genes in lung carcinoma.

In this study, microarray analysis was used to identify tumour-related genes that were down regulated in lung carcinoma. The promoter sequences of the identified genes were analysed for methylation patterns. In lung cancer cell lines, CpG island methylation was frequently detected for TIMP4 (64%), SOX18 (73%), EGF-like domain 7 (56%), CD105 (71%), SEMA2 (55%), RASSF1A (71%), p16 (56%) SLIT2 (100%) and TIMP3 (29%). Methylation was however rarely observed in cell lines for SLIT3 (18%) and DLC1 (18%). In primary lung tumours, methylation of TIMP4 (94%), SOX18 (100%), EGF-like domain 7 (100%), CD105 (69%), SEMA2 (93%), DLC1 (61%), RASSF1A (44%), p16 (47%), SLIT2 (100%) and TIMP3 (13%) was also detected. Methylation of several CpG islands was frequently found in normal lung tissue of cancer patients and this may have been attributed to epigenetic field defect and/or infiltrating tumour cells. Interestingly, inactivation of RASSF1A and p16 correlated well with an extended smoking habit (P=0.02), and exposure to asbestos (P=0.017) or squamous cell carcinoma (P=0.011), respectively. These results have identified genes whose aberrant promoter methylation could play a crucial role in the malignancy of lung carcinoma.