Aberrant methylation of the adenomatous polyposis coli promoter 1A in bronchial aspirates from patients with suspected lung cancer.

Abstract:
Promoter hypermethylation is a major mechanism for gene silencing and offers a promising starting point for developing molecular biomarkers. The purpose of our study was to determine aberrant methylation of the adenomatous polyposis coli (APC) gene promoter 1A with respect to its prevalence and quantitative level in bronchial aspirates from patients with suspected lung cancer. Applying quantitative methylation-specific PCR, 155 bronchial aspirates from patients with non-small cell cancer (NSCLC) and small cell cancer (SCLC) of the lung as well as 67 bronchial aspirates from patients diagnosed for nonneoplastic lung disease were examined in a retrospective case-control study. Aberrant APC promoter 1A methylation was seen in 71% of NSCLCs, 38% of SCLCs and 42% of patients with nonneoplastic lung disease, being therefore not specific for the presence of primary lung cancer. In contrast, quantitative analysis showed a significantly higher methylation level of bronchial aspirates from NSCLC as compared to patients without neoplastic lung disease. Introducing a cutoff point that defined high level of APC hypermethylation NSCLC could be discriminated from cases without neoplastic disease with a specificity of 98.5% and a sensitivity of 39%. The data suggest that quantitative analysis of APC hypermethylation may serve as a biomarker of primary lung cancer.