Five years survival of lung cancer is 16%, significantly lower than in prostate (99.9%), breast (88.5%) and colon (64.1%) carcinomas. When diagnosed in the surgical stage it increases to 50% but this group only comprises 14-16% of the cases. DNA methylation has emerged as a potential cancer-specific biomarker. Hypermethylation of CpG islands located in the promoter regions of tumour suppressor genes is now firmly established as an important mechanism for gene inactivation. This retrospective study included 40 squamous cell carcinomas and 40 adenocarcinomas in various surgical TNM stages to define methylation profile and possible silencing of DNA repair genes - MLH1 and MSH2 -- using Methylation-Specific PCR and protein expression by immunohistochemistry in tumoural tissue, preneoplastic lesions and respiratory epithelium with normal histological features. The protein expression of MLH1 and MSH2 genes, in the available preneoplastic lesions and in normal cylindrical respiratory epithelium appeared reduced. The frequency of promoter hypermethylation found on these DNA repair genes was elevated, with a higher prevalence of methylation of MLH1 gene in 72% of squamous cell carcinoma. The differences are not so obvious for MSH2 promoter hypermethylation. No correlation was found among the status of methylation, the protein expression and the clinicopathological characteristics. With a larger study, a better characterization of the hypermethylation status of neoplastic and preneoplastic lesions in small biopsies would be achieved, inherent to tumour histology, heterogeneity and preservation, and finally differences in the study population to elucidate other possible mechanisms of altered expression of the hMLH1 and hMSH.

**Abstract**

**Keywords**

Adenocarcinoma, Squamous cell carcinoma, Lung, Hypermethylation, MLH1, MSH2