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Abstract: Promotor hypermethylation is a common event in human cancer. O6-Methylguanine-DNA Methyltransferase (MGMT) is a gene involved in DNA repair, which is methylated in a variety of cancer types. In colorectal cancer and lung cancer, hypermethylation of MGMT has been correlated with p53 mutation. In the present study, 132 samples of esophageal adenocarcinoma and 58 samples of normal esophageal tissue were investigated for MGMT hypermethylation status by methylation-specific real-time PCR and results were correlated to clinicopathological parameters, patient's survival, p53 mutation and expression of p53 protein and MGMT protein. In the carcinomas, hypermethylation of MGMT was found in 63.6% of cases and loss of MGMT protein expression in 48.5% of cases. Furthermore, MGMT hypermethylation was found in 5.7% of normal esophageal smooth muscle tissue, in 20.0% of esophageal squamous epithelium and in 61.5% of nonneoplastic Barrett's mucosa. In the carcinomas, hypermethylation of the MGMT gene was correlated with loss MGMT protein expression (p< 0.0001) and with high tumor differentiation (p = 0.0079). In contrast, no correlation between MGMT hypermethylation, Lauren's classification, WHO classification, tumor size, gender, age,
pT category and pN category, and p53 status was found. Neither MGMT hypermethylation nor loss of MGMT protein expression was correlated with patient's survival. In conclusion, MGMT hypermethylation in esophageal adenocarcinoma is a frequent event that is associated with loss of MGMT protein expression but not with patient's outcome.