

Promoter Methylation of RASSF1A and MGMT Genes in Head and Neck Squamous Cell Carcinoma

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Abstract : Promoter hypermethylation of tumor-related genes has been associated with prognosis in early-stage head-and-neck cancers, providing strong evidence that these hypermethylated genes are valuable biomarkers for prognostic evaluation. Hence, we selected the MGMT and RASSF1A genes to examine the methylation status in head and neck squamous cell carcinomas (HNSCC) samples matched with non-tumor tissues (tumor-surrounding tissues or peripheral blood samples). DNA methylation analysis was based on Methylation-Sensitive High Resolution Melting, and the methylation status was correlated with clinic-pathological characteristics of the patients. RASSF1A and MGMT promoter methylation was detected in 43.24% (16/37) and in 44.44% (16/36) of the tumors, respectively. RASSF1A and MGMT methylation was significantly more frequent in tumor tissue than non-tumor tissues, as well as, simultaneous methylation of RASSF1A and MGMT also was higher in tumor tissue than non-tumor tissues. In relation to anatomic site, larynx cancer presented significant methylation of MGMT gene compared to tumor-surrounding tissue. The frequency of RASSF1A and MGMT promoter methylated was higher in tumor tissues in relation to peripheral blood from the same patient. No association was found between methylation and the variables analyzed, including gender, age, smoking or alcohol drinking habits. Clinic-pathological characteristics also showed no association in the presence of methylation. The Kaplan-Meier's method showed no association of methylation and both disease-free and overall survival. In conclusion, the presence of epigenetic abnormalities in normal-appearing tissue corroborates the hypothesis of the 'field cancerization', or it can reflect preneoplastic and/or preinvasive. Moreover, MGMT methylation may serve as an important laryngeal cancer biomarker because it showed significant difference between laryngeal cancer and surrounding tumor tissues.

Keywords : head and neck cancer, DNA methylation, MGMT promoter methylation, RASSF1A promoter methylation

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