ABERRANT HYPERMETHYLATION AND DECREASED EXPRESSION OF THE FOXE1 GENE IN PAPILLARY THYROID CANCER

Zhang, Ling[1]; JI, Qing-hai[1]; Zhu, Yong-xue[1]; Wang, Yu[2]; Sun, Guo-hua[1]
[1]Fudan University Cancer Center/Dept of Head & Neck Surg, Shanghai, China; [2]Fudan University Cancer Center, Shanghai, China

Background/Purpose: Forkhead box E1 (FOXE1) plays an important role in tumorigenesis that is characterized by increased expression in papillary thyroid cancer (PTC). Our study aimed to analyze the methylation status of the promoter region of FOXE1 in thyroid tumor patients and cell lines and to find the relationship between DNA methylation and gene expression, clinical characteristics and a single-nucleotide polymorphism in the proto-oncogene BRAF T1796A.
Methods: The methylation status of FOXE1 was analyzed by bisulfite-sequencing PCR (BSP) in W3, TPC1, IHH-4 and Nthy-ori 3-1 cell lines. In total, 111 paired clinical thyroid tumors (79 PTC and 32 benign thyroid tumors) and adjacent normal thyroid samples were analyzed by methylation-specific PCR (MSP). FOXE1 mRNA expression levels were analyzed by real-time polymerase chain reaction (qRT-PCR). The genotype of BRAF V600E was detected in PTC samples by direct sequencing.
Results: We noted a significant difference in the methylation level of FOXE1 in PTC (5.06%) and benign thyroid tumors compared with paired adjacent normal thyroid tissues (16.46%) ($p=0.040$, t-test). Hypomethylation in the promoter region of FOXE1 was significantly associated with its increased expression in PTC, linear regression). In addition, the methylation status of FOXE1 was significantly associated with Hashimoto's thyroiditis (HT) ($p=0.003$), the T stage of patients ($p<0.001$) and the capsular invasion (CI) of PTC ($p<0.001$). No statistically significant association was identified between the BRAF V600E mutation and the DNA methylation pattern in FOXE1.
Discussion & Conclusion: Epigenetic inactivation of the FOXE1 gene plays a potentially important role in PTC, and it might be a prospective biomarker for the diagnosis of PTC.