BRAF$^{V600E}$ mutation and RET/PTC rearrangements in thyroid nodules

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BRAF mutation and RET/PTC rearrangements are the most frequent genetic events in papillary thyroid carcinoma (PTC). The prevalence of these oncogenes in benign and malignant thyroid nodules and their mutual exclusivity are debated issues. The aim of this study was to determine the prevalence of individual and concomitant BRAF$^{V600E}$ mutation and RET/PTC rearrangements in thyroid tumors. Total RNA and DNA were extracted from fine-needle aspirates (FNA) of thyroid nodules with a definitive benign (N=30) and malignant (N=90 of which 72 PTC and 18 follicular thyroid carcinomas, FTC) diagnosis. RET/PTC-1 and RET/PTC-3 rearrangements were searched by Southern blot on RT-PCR, whereas the percentage of mutant BRAF alleles was assessed by pyrosequencing on genomic DNA. BRAF$^{V600E}$ alleles were detected only in PTC (56.9%) in the range of 44.7 to 5.1%. RET/PTC rearrangements were present in benign nodules (13.9%) and in PTC (36%, of which 12% RET/PTC-1, 20% RET/PTC-3 and 4% both rearrangements). Concomitant subclonal BRAF and RET/PTC were demonstrated in 19.4% PTC. These data establish the prevalence of RET/PTC rearrangements and BRAF mutation in benign and malignant thyroid nodules, and demonstrates that these two oncogenes are not mutually exclusive but rather are frequently co-expressed in the same PTC. The data, do not exclude the hypothesis of a coexistence of the two oncogenes in different cells within the tumor.