New somatic mutations and WNK1-B4GALNT3 gene fusion in papillary thyroid carcinoma.

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Abstract

Papillary thyroid carcinoma (PTC) is the most frequent thyroid malignant neoplasia. Oncogene activation occurs in more than 70% of the cases. Indeed, about 40% of PTCs harbor mutations in BRAF gene, whereas RET rearrangements (RET/PTC oncogenes) are present in about 20% of cases. Finally, RAS mutations and TRK rearrangements account for about 5% each of these malignancies. We used RNA-Sequencing to identify fusion transcripts and mutations in cancer driver genes in a cohort of 18 PTC patients. Furthermore, we used targeted DNA sequencing to validate identified mutations. We extended the screening to 50 PTC patients and 30 healthy individuals. Using this approach we identified new missense mutations in CBL, NOTCH1, PIK3R4 and SMARCA4 genes. We found somatic mutations in DICER1, MET and VHL genes, previously found mutated in other tumors, but not described in PTC. We identified a new chimeric transcript generated by the fusion of WNK1 and B4GALNT3 genes, correlated with B4GALNT3 overexpression. Our data confirmed PTC genetic heterogeneity, revealing that gene expression correlates more with the mutation pattern than with tumor staging. Overall, this study provides new data about mutational landscape of this neoplasia, suggesting potential pharmacological adjuvant therapies against Notch signaling and chromatin remodeling enzymes.

KEYWORDS:

RNA-sequencing; gene fusions; mutations; papillary carcinomas; thyroid