Identification of a Recurrent STRN/ALK Fusion in Thyroid Carcinomas

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Auteur Pérot, Gaëlle [1], Soubeyran, Isabelle [2], Ribeiro, Agnès [3], Bonhomme, Benjamin [4], Savagner, Frédérique [5], Boutet-Bouzamondo, Nathalie [6], Hostein, Isabelle [7], Bonichon, Françoise [8], Godbert, Yann [9], Chibon, Frédéric [10]

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Résumé en anglais Thyroid carcinoma is the most common endocrine malignant tumor and accounts for 1% of all new malignant diseases. Among all types and subtypes of thyroid cancers that have been described so far, papillary thyroid carcinoma is the most frequent. The standard management treatment of these tumors consists of surgery, followed by radioiodine treatment in case of high risk of relapse. The most aggressive forms are commonly treated by chemotherapy, radiotherapy or experimental drug testing. We recently reported the case of a patient presenting an anaplastic thyroid carcinoma with lung metastases. Fluorescence in situ hybridization analysis allowed us to detect a rearrangement of the anaplastic lymphoma kinase (ALK) gene in both tumors. The patient was treated with crizotinib and presented an excellent drug response. We present here the subsequent investigations carried out to further characterize this genetic alteration and to assess the prevalence of ALK rearrangements in thyroid lesions. High resolution array-comparative genomic hybridization data complemented by RT-PCR and sequencing analyses, allowed us to demonstrate the presence of a STRN/ALK fusion. The STRN/ALK transcript consisted of the fusion between exon 3 of STRN and exon 20 of ALK. Subsequent screening of 75 various thyroid tumors by RT-PCR revealed that 2 out of 29 papillary thyroid carcinomas exhibited the same fusion transcript. None was detected in other types of malignant or benign thyroid lesions analyzed. These findings could pave the way for the development of new targeted therapeutic strategies in the treatment of papillary thyroid carcinomas and point to ALK inhibitors as promising agents that merit rapid evaluation.

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