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20739 | Evaluation of RRAS2 and TTP1 promoter mutations in thyroid tumours

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Abstract

Thyroid cancer is the most frequent endocrine neoplasm, being the tenth most prevalent in both genders and it presenting an overall good prognosis [1]. Ras related 2 (R-Ras2), also known as TC21, is a GTP-binding protein that together with R-Ras1 and R-Ras3, is part of the R-Ras GTPase subfamily. Mutations in *RRAS2* gene in the long-tailed hotspot Q72L/H block the hydrolysis of guanosine triphosphate (GTP) in Ras superfamily proteins, generating constitutively active proteins that will preferentially bound to GTP [2]. This gene is composed by five exons encoding a member of the Ras superfamily that participates in the RAS-MAPK pathway [3]. The tripeptidyl peptidase 1 promoter (TPP1p) encodes the telomere-binding protein TPP1 that recruits telomerase to the telomeres. This process plays a key role in the telomere stability and length regulation. Mutations in this promoter were reported to create novel transcription factor binding sites as previously presented for telomerase promoter (TERTp) [4]. Co-expression of these two promoters lead to telomere elongation, indicating that mutations in the *TPP1* and *TERT* promoter cooperate for the immortalisation of cancer cells [5].

Our project aimed to evaluate mutations in the Q72L hotspot of the *RRAS2* gene and in the *TPP1p* in thyroid tumours. Upon genotyping of *RRas2* and *TPP1p*, we conclude that the presence of mutations in the Q72L hotspot may not represent an oncogenic event, as we did not detect them. For *TPP1p*, still under study, although already presented in the literature, at the moment we have not detected them in our series, pointing that they may be a rare event in thyroid tumours.

Keywords: Thyroid cancer; Tumours; *R-Ras2* gene; Q72L hotspot; Telomerase promoter (TERTp); TPP1 promotor (TPP1p).

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