

Telomerase Reverse Transcriptase (TERT) Mutations Are Common in Advanced Thyroid Cancer

Jerome M. Hershman

Landa I, Ganly I, Chan TA, Mitsutake N, Matsuse M, Ibrahimasic T, Ghossein RA, Fagin JA. Frequent somatic TERT promoter mutations in thyroid cancer: higher prevalence in advanced forms of the disease. *J Clin Endocrinol Metab* 2013;98:E1562-6. Epub July 5, 2013; doi: 10.1210/jc.2013-2383.

SUMMARY

Background

Thyroid cancers contain oncogenic mutations that are considered “driver mutations” because they play a key role in the disordered proliferation and metastasis of the cancer. TERT encodes the reverse transcriptase component of telomerase, which adds telomere repeats to chromosome ends, thereby enabling cell replication. This paper shows that specific mutations in TERT are frequently found in thyroid cancers and may occur concurrently with mutations in the MAP kinase pathway.

Methods

The study included 183 thyroid tumors and 42 human thyroid cancer cell lines. DNA from the samples was tested by PCR for two mutations in the proximal promoter of TERT, C228T and C250T, as well as for

mutations in BRAF and RAS.

Results

TERT mutations were found in 22% of papillary thyroid cancers (PTCs), 51% of advanced thyroid cancers, 23% of widely invasive Hürthle-cell cancers, and 86% of the thyroid cancer cell lines. There was a more frequent co-occurrence of TERT mutations with advanced thyroid tumors harboring BRAF and RAS mutations as compared with those that did not have these mutations. Only one of the two TERT mutations was found in a given tumor.

Conclusions

TERT mutations are highly prevalent in advanced thyroid cancers, especially those with BRAF or RAS mutations.

ANALYSIS AND COMMENTARY

TERT mutations have been found in some melanomas and glioblastomas. Acquisition of the TERT mutation could extend the life span of the tumor cell and thus provide time for other mutations to develop. Concurrently with this paper, the laboratory of M. Xing published a report on TERT mutations in thyroid cancer with similar findings with regard to prevalence (1). The Xing laboratory found that the C228T was much more common than the C250T mutation.

During a presentation at the recent meeting of the ATA, Xing reported that tumors with both BRAF and TERT mutations had a much higher recurrence rate as compared with tumors that had only one of these mutations (2). It is likely that the two TERT mutations will become part of a panel of mutations that are detected in thyroid nodule FNAs by next-generation sequencing, as noted in the previous article in this issue.

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References

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2. Xing M, Liu X, Liu R, Pai S, Zeiger M, Bishop J. TERT Promoter mutation cooperates with BRAF mutation to promote thyroid cancer recurrence. *Thyroid*. October 2013;23(Suppl 1):A-115-A121. doi: 10.1089/thy.2013.2310.sc.


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