LETTER TO THE EDITOR

CTNNB1 mutations in papillary thyroid carcinoma with prominent myofibroblastic stromal component

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To the Editor: We read with great interest the article by Suster *et al*. titled "Papillary thyroid carcinoma with prominent myofibroblastic stromal component: clinicopathologic, immunohistochemical and next-generation sequencing study of seven cases", in which they report *BRAF* mutations in the follicular cell component and *CTNNB1* mutations in the stromal component [1].

The desmoid-type fibromatosis variant of papillary thyroid carcinoma (DTF-PTC) is a very rare variant of PTC. It is essentially a dual tumor with a component of classical PTC with malignant epithelial proliferation and another component of mesenchymal (stromal) proliferation. In two studies on non-thyroidal DTF cancers, accumulation of β-catenin due to an activating mutation in *CTNNB1* was found in 89% and 92% of the total cases [2,3]. *CTNNB1* encodes β-catenin, a downstream effector of the Wnt signaling pathway that is generally responsible for regulation of cell growth and survival [4] [5]. Several studies have also detected *CTNNB1* mutations in the desmoid-type fibromatosis tissue in DTF-PTC [4,6,7].

In the text of the article by Suster *et al*., it is mentioned that "three cases showed a *CTNNB1* c.121A>G (p.Thr41Ala) mutation" [1]. However, Figure 4 of the paper actually indicates two cases with a CTNNB1 c.121A>G (p.Thr41Ala) mutation and a third case with a CTNNB1 c.124A>G (p.Thr41Ala) mutation [1] (**Figure 1**). Because nucleotides 121 and 124 belong to different codons, they cannot both affect the same amino acid residue (Thr41). Unfortunately, because threonines are present at both positions 41 and 42 of the CTNNB1 protein (**Figure 2**), it cannot be concluded from the information available in the article by Suster *et al*. [1] where the error lies, and which of the two contradictory affirmations is accurate. We suggest that the authors examine this issue and correct their article accordingly.

FIGURE LEGENDS

Figure 1. Phenotypic and genotypic descriptions of the 7 cases of analyzed by Suster *et al*. [1]. Compare the *CTNNB1* genotype of cases 1 and 6 [c.121A>G (p.Thr41Ala)] to that of case 3 [c.124A>G (p.Thr41Ala)]. From Suster *et al*. [1].

Figure 2. Partial cDNA and protein sequence of CTNNB1. Note that nucleotides 121 and 124 belong to different codons (41 and 42, respectively), which code for consecutive threonines. The nucleotide sequences of the codons corresponding to the threonines at positions 40-42 are shown; the numbering corresponds to the underlined adenines. Sequences from National Center for Biotechnology Information Reference Sequence NM_001904.4 (https://www.ncbi.nlm.nih.gov/nuccore/NM_001904.4).

CONFLICT OF INTEREST STATEMENT: The authors declare that there are no competing financial interests in relation to the work described.

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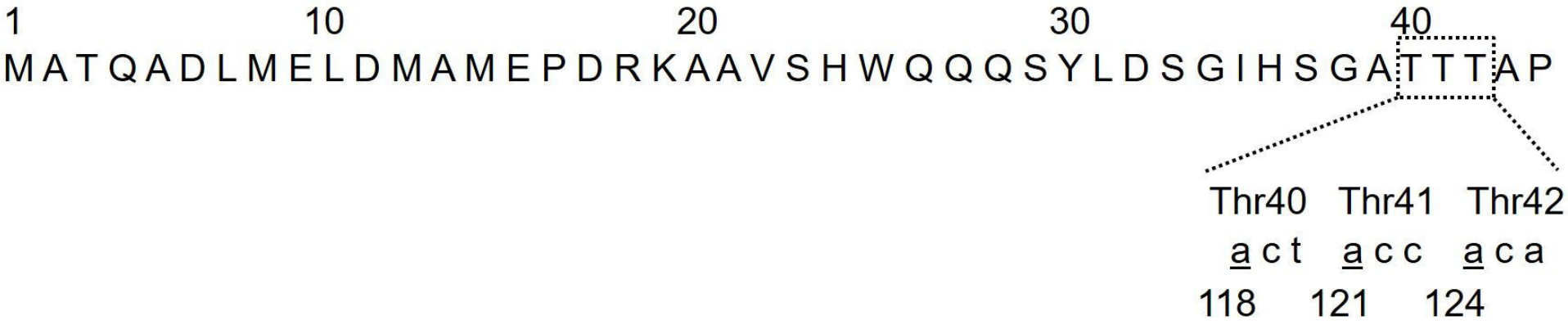
Case Number
1
2
3
4
5
6
7
Epithelial Component
Stromal Component
CTNNB1 c.121A>G (p.Thr41Ala)
CTNNB1 c.124A>G (p.Thr41Ala)
CTNNB1 c.133T>C (p.Ser45Pro)
CTNNB1 c.134T>C (p.Ser45Phe)
BRAF c.1799T>A (p.Val600Glu)
NRAS c.175G>A (p.Ala59Thr)
Legend
Conventional Papillary Thyroid Carcinoma
Conventional Papillary Thyroid Carcinoma but insufficient epithelial component for NGS
Follicular Variant Papillary Thyroid Carcinoma
Desmoid - Type Fibromatosis - like stroma
Nodular Fasciitis-like stroma
Pathogenic Variant Present
Pathogenic Variant Present (Previously reported)


1
10
20
30
40
M A T Q A D L M E L D M A M E P D R K A A V S H W Q Q Q S Y L D S G I H S G A T T T A P
Thr40 Thr41 Thr42
a c t a c c a c a
118 121 124