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LETTER TO THE EDITOR

Absence of Promoter Mutation in *TBC1D12* Gene in Solid and Hematologic Neoplasia

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To the Editor:

TBC1 domain family member 12 (*TBC1D12*) gene encodes a recycling endosome-resident protein that binds with Rab11 [1]. Neither cancer-related functions nor biologic functions of TBC1D12 are largely unknown currently. Recently, Rheinbay et al. analyzed genome-wide somatic mutations in promoters in breast cancers and identified the promoter mutations in several genes [2]. One of the top-ranked genes with the promoter mutations was *TBC1D12* (3.9% of breast cancers), the mutations of which decreased TBC1D12 expression, suggesting their loss-of-function activities [2]. Of note, the promoter mutations of *TBC1D12* were found recurrently at two hotspot sites (chr10: 96162368 and 96,162,370). Promoter alterations such as somatic mutation and aberrant methylation in tumor suppressor genes, oncogenes, transcription factors and drug response genes are known to play a role in the cancer pathogenesis [3]. Together, these data suggest a possibility that promoter mutation of *TBC1D12* gene might be present not only in breast cancer but also in other cancers and play a role in cancer development.

For this, tumor tissues from 2018 Korean patients, including hematologic, epithelial and mesenchymal tumor from various origins, were analyzed in this study (Table 1). For solid tumors, malignant and normal cells were selectively procured from by microdissection [4]. Because *TBC1D12* promoter mutations have been focused in a narrow region (chromosome 10: 96162368–6,162,370) [2], we amplified this region with a primer pair by polymerase chain reaction (PCR) (forward: 5-CAGCACCCAGAGCTGTTCTC-3, reverse: 5-GCCCGGATTACCTTCCTGTC-3) and subsequently analyzed by single-strand conformation polymorphism (SSCP) and DNA sequencing. Other procedures of the PCR-SSCP were described in our previous studies [4].

On the SSCP, all of the PCR products for the *TBC1D12* promoter area were clearly seen. However, none of the SSCP from the cancers displayed aberrantly migrating bands compared to wild-type bands from the normal tissues, indicating there was no evidence of *TBC1D12* promoter mutations in the tumors. To confirm the SSCP data, we repeated the experiments twice to ensure specificity of the results, and found that the data were consistent.

An interesting point in cancer genetics is to identify whether any mutation found in a specific tumor type is common to other types. The present study, however, detected no somatic mutations at the *TBC1D12* promoter in 2018 tumors from 16 tumor types. Our data indicate that the *TBC1D12* promoter mutation might be specific to breast cancer or might be very rare in other tumors, if any. Discovery of the recurrent *TBC1D12* promoter mutations might possibly provide an opportunity for developing therapeutic and diagnostic tools for targeting the recurrent mutations. Our data, however, suggest that such approaches should be limited to breast cancers.

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Table 1 Analysis of *TBC1D12* promoter mutation in 2018 tumors

Type of tumors	Number of tumors	*TBC1D12* promoter		
		Wild type	Mutation	Mutation (%)
Adulthood AML	217	217	0	0
Adulthood ALL	146	146	0	0
Childhood AML	21	21	0	0
Childhood ALL	398	398	0	0
Multiple myeloma	75	75	0	0
Myelodysplasia	67	67	0	0
Gastric carcinoma	163	163	0	0
Colorectal carcinoma	372	372	0	0
Prostate carcinoma	261	261	0	0
Ovarian tumors	48	48	0	0
Hepatocellular carcinomas	43	43	0	0
Squamous cell carcinomas, lung	67	67	0	0
Adenocarcinomas, lung	72	72	0	0
Squamous cell carcinomas, esophagus	31	31	0	0
Squamous cell carcinomas, larynx	13	13	0	0
Sarcomas	24	24	0	0
Total	2018	2018	0	0

AML Acute myelogenous leukemia, *ALL* Acute lymphoblastic leukemia

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