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Analysis of promoter mutation in *CTNNB1* gene in solid and hematologic neoplasia

To the Editor:

CTNNB1 gene encodes the β-catenin that is involved in regulation and coordination of both cell adhesion and gene transcription [1]. Mutations and overexpression of *β-catenin* are associated with many cancers, including hepatocellular, colorectal and breast carcinomas [1]. Cytoplasmic accumulation of β-catenin allows itself to translocate to the nucleus to form complexes with transcription factors of Tcf-Lef family that transactivates target genes, which may in turn stimulate cell proliferation or inhibit apoptosis [1]. Rheinbay et al. recently analyzed gene promoters genome-widely in breast cancers and identified somatic promoter mutations in several genes [2]. One of them was *CTNNB1* (1.4% of the breast cancers) [2]. Of note, the *CTNNB1* promoter mutations were recurrent at hotspot sites (chr3: 41240913, 41240914 and 41240920). 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]. Discovery of the *CTNNB1* promoter mutation was a novel finding, since most of the genetic alterations of *CTNNB1* have been identified in the coding region [1]. However, since the prevalence of *CTNNB1* promoter mutation in breast cancer is not high (1.4%), it is necessary to test a possibility that promoter mutation of *CTNNB1* 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 1791 Korean patients, including hematologic and epithelial tumors from various origins, were analyzed in this study (Table 1). For the solid tumors, malignant and normal cells were selectively procured from by microdissection [4]. The *CTNNB1* promoter mutations have been focused in a narrow region (chromosome 3: 41240913-41240920) [2] and we amplified this region with one primer pair by polymerase chain reaction (PCR) (forward: 5-CGC GGGGACTACTTTCCAC-3, reverse: 5- ACCGAGAGGCTTAAAATGGC-3) with subsequent single-strand conformation polymorphism (SSCP) and DNA sequencing analyses. Other procedures of the PCR-SSCP were described in our previous studies [4].

On the SSCP, all of the PCR products for the *CTNNB1* 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 *CTNNB1* promoter mutations in this region. To confirm the SSCP data, we repeated the experiments twice to ensure specificity of the results, and found that the data were consistent.

Although *CTNNB1* promoter mutations were identified in breast cancers [2], our study detected no somatic mutations at the *CTNNB1* promoter in 1791 solid and hematologic tumors from 12 types (Table 1). Our data suggest that the *CTNNB1* promoter mutation might be specific to breast cancer or might be very rare in other tumors, if any. Discovery of the *CTNNB1* promoter mutations provide an opportunity for developing strategies for targeting altered *CTNNB1*. However, the present study suggests that they should be limited to breast cancer.

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Table 1
CTNNB1 promoter mutation in 1791 tumors.

Type of tumors	Number of tumors	*CTNNB1* promoter		
		Wild type	Mutation	Mutation (%)
Adulthood AML	207	207	0	0
Adulthood ALL	112	112	0	0
Childhood AML	21	21	0	0
Childhood ALL	417	417	0	0
Multiple myeloma	75	75	0	0
Myelodysplasia	67	67	0	0
Gastric carcinoma	181	181	0	0
Colorectal carcinoma	387	387	0	0
Prostate carcinoma	198	198	0	0
Hepatocellular carcinomas	40	40	0	0
Squamous cell carcinomas, lung	47	47	0	0
Adenocarcinomas, lung	39	39	0	0
Total	1791	1791	0	0

AML: acute myelogenous leukemia, ALL: acute lymphoblastic leukemia.

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