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LETTER TO THE EDITOR

Analysis of Promoter Mutation in Long Non-coding RNA NEAT1 in Acute Leukemias

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To the Editor,

Long non-coding RNAs (lncRNAs) are transcripts longer than 200 nucleotides that do not encode proteins. Recently, lncRNAs have emerged as an important modulator for cancer development [1]. *Nuclear paraspeckle assembly transcript 1* (*NEAT1*), an lncRNA, plays a role in gene regulation by nuclear retention of both protein and RNA in nuclear paraspeckle [2]. NEAT1 is overexpressed in majority of solid tumors and is considered an oncogene. In hematologic tumors, however, it is considered a tumor suppressor gene, suggesting its diverse roles in tumorigenesis [2]. Recently, Rheinbay et al. [3] analyzed non-coding sequences of genes in breast cancers and found somatic promoter mutations in several genes, including *NEAT1*. The *NEAT1* promoter mutations decrease NEAT1 expression, suggesting the loss-of-function activities. Because NEAT1 expression is down-regulated in leukemias and multiple myelomas [2], it is possible that such down-expression of NEAT1 could be related to *NEAT1* promoter mutation. In this study, we analyzed hotspot *NEAT1* promoter mutations in various hematologic tumors.

For this, we analyzed *NEAT1* promoter sequences in hematologic neoplasia using genomic DNA from in bone marrow aspirates of 714 hematologic tumors (acute myelogenous leukemias (AML), acute lymphoblastic leukemias (ALL), multiple myelomas and myelodysplastic syndromes) (Table 1) by polymerase chain reaction (PCR) and single-strand conformation polymorphism (SSCP) assay [4]. All institutional and national guidelines for the care were followed. Informed consent was obtained from all patients for being included in the study except for cases whose informed consents were waived for this study. Because NEAT1 promoter mutations have been focused in a narrow region (chromosome 11: 65190228–31) [3], we amplified this region with a primer pair by PCR (forward: 5-ATACACTGGGGTCC TTGCGT-3, reverse: 5-TCCCTCCCTGTCGCTAACTC-3) and subsequently analyzed by SSCP. After PCR and subsequent SSCP, we did not detect any aberrantly migrating bands in the 714 hematologic neoplasia analyzed (Table 1). By contrast, we detected *NEAT1* promoter mutations in colon cancers with the same procedure (unpublished data), indicating that the absence of *NEAT1* promoter mutations in the hematologic neoplasia may be true negative data.

One of the main concerns in cancer genomics is to address whether any mutation found in a cancer is common in other cancers. Although *NEAT1* promoter mutation is frequently found in some solid cancers including breast cancers [3], its mutation status in hematologic malignancies remains undetermined. Our study detected no *NEAT1* promoter mutation in AML, ALL, myelodysplastic syndrome and multiple myeloma, indicating *NEAT1* promoter mutation is rare in hematologic neoplasia. Previous observations identified down-expression of *NEAT1* in hematologic tumors associated with multidrug resistance, interference with p53-dependent DNA damage response machinery and impaired myeloid differentiation [1–3]. Together, these data indicate that functional loss of *NEAT1* expression in hematologic tumors may not be caused by *NEAT1* promoter mutation and suggest other mechanisms for *NEAT1* alteration in hematologic tumors.

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Table 1 *NEAT1* promoter mutation analyzed in 714 hematologic tumor patients

Type of tumors	Number of tumors	*NEAT1* promoter		
		Wild type	Mutation	Mutation (%)
Adulthood AML	201	201	0	0
Adulthood ALL	152	152	0	0
Childhood AML	20	20	0	0
Childhood ALL	200	200	0	0
Multiple myeloma	75	75	0	0
Myelodysplasia	66	66	0	0
Total	714	714	0	0

AML acute myelogenous leukemia, *ALL* acute lymphoblastic leukemia

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Compliance with Ethical Standards

Conflicts of Interest None to declare.

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