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Somatic mutations in long-non-coding RNA *RMRP* in acute leukemias

To the Editor

Long non-coding RNAs (lncRNAs) do not encode proteins, but have been found to play an important role in the modulation for cancer development [1]. RNA component of mitochondrial RNA (*RMRP*), an lncRNA, regulates mitochondrial and ribosomal RNA processing and plays an important role in several genetic disorders including cartilage-hair dysplasia [2]. *RMRP* is overexpressed in many solid tumors and is considered a candidate oncogene [3]. In hematologic malignancies, its elevated expression in multiple myeloma (MM) and oncogenic activities (promoting cell proliferation and inhibiting apoptosis) were recently reported [4], but its alterations remain unknown in other leukemias. Recently, Rheinbay et al [5]. analyzed genome-wide non-coding sequences in breast cancers and found several promoter mutations including somatic *RMRP* mutations. The *RMRP* promoter mutations increased its expression and its protein binding [5], suggesting its enhanced recruitment of transcriptional activator and possible gain-of-function activities.

To see whether *RMRP* promoter mutation is common in leukemias as well, we analyzed *RMRP* promoter sequences in hematologic neoplasia using genomic DNA from in bone marrow aspirates of 710 hematologic tumors (acute myelogenous leukemias (AML), acute lymphoblastic leukemias (ALL), multiple myelomas (MM) and myelodysplastic syndromes) (Table 1) by polymerase chain reaction (PCR) and single-strand conformation polymorphism (SSCP) assay [6]. All institutional and national guidelines for the care were followed. Because *RMRP* promoter mutations have been focused on two regions (chromosome 9: 35658025-63 and 35658224) [5], we amplified them with two primer pairs by PCR-SSCP and subsequently analyzed by DNA sequencing.

Table 1
RMRP promoter mutation analyzed in 710 hematologic tumor patients.

Type of tumors	Number of tumors	*RMRP* promoter		
		Wild type	Mutation	Mutation (%)
Adulthood AML	200	199	1	0.5
Adulthood ALL	150	149	1	0.7
Childhood AML	20	20	0	0
Childhood ALL	200	199	1	0.5
Multiple myeloma	75	74	1	0
Myelodysplasia	65	65	0	1.3
Total	710	706	4	0.6

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

We detected four *RMRP* somatic promoter mutations in the 710 hematologic neoplasia analyzed (0.6%, Table 1). Each one of the mutations was identified in adulthood AML, adulthood ALL, childhood AML and MM (Table 2). All of the mutations were duplication mutations (13–21 bps). To confirm the mutation data, we repeated the DNA sequencing twice and found them to be consistent. There were no significant clinicopathologic parameters associated with the mutations including demographic, karyotypic and prognostic data.

One of the main concerns in cancer genomics is to address the tissue specificity. Although *RMRP* promoter mutation has been found in some solid cancers including breast cancers [5], its mutation in hematologic malignancies remains undetermined. Our study detected *RMRP* promoter mutations in AML, ALL and MM, indicating *RMRP* promoter mutation might be present widely in hematologic neoplasia. However, low prevalence (0.6%) may indicate that *RMRP* promoter mutation is not a generalized driver for leukemogenesis. Low prevalence of *RMRP* promoter mutation was found in breast cancer as well (2.5%), suggesting that such low prevalence could be a feature of both solid and hematologic malignancies. Of note, the duplication type mutations were quite contrast to those previously found in breast cancers (point mutation) [5]. Functional and clinical implication of the duplications in tumorigenesis instead of point mutations should be further analyzed in future studies.

Declaration of Competing Interest

None to declare.

Table 2
Summary of RMRP promoter mutations.

case	diagnosis	Age/sex	Mutation
AML111	AML with multilineage dysplasia	59/M	g.35,658,020_35,658,039 dup CCTCAGCTTCACAGAGTAGT (20 bp duplication)
ALL656	B-ALL	28/F	g.35,658,017_35,658,037 dup CGTCCTCAGCTTCACAGAGTA (21 bp duplication)
ALL158	B-ALL	13/F	g.35,658,029_35,658,041 dupCACAGAGTAGTAT (13 bp duplication)
MM218	Multiple myeloma	46/M	g.35,658,015_35,658,031 dup CACGTCCTCAGCTTCAC (17 bp duplication)

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