LETTER TO THE EDITOR:

Re: Prognostic significance of a short sequence insertion in the MCL-1 promoter in chronic lymphocytic leukemia.

We read with great interest the recent article by Moshynska et al. (1) in the Journal, which reported short sequence insertions in the MCL-1 promoter of B-cell chronic lymphocytic leukemia (B-CLL) samples. The authors analyzed genomic DNA from B-CLL cells of 58 B-CLL patients and from lymphocytes of 18 healthy control donors. The sequence of the promoter region of the gene MCL-1 gene revealed the presence of a 6- or 18-base pair insertion in approximately 30% of the B-CLL samples. In contrast, and very interestingly, these insertions were completely absent in all healthy control subjects and in the normal soft tissues from two B-CLL patients whose lymphocytes harbored these insertions. These alterations would appear to represent one of the most frequent somatic genomic alterations described so far in B-CLL patients, and these results deserved an editorial in the same issue of the journal (2).

To confirm the presence of these insertions in the B-CLL samples from patients at our hospital, Hospital Universitari de Bellvitge, we obtained the corresponding MCL-1 gene promoter region from genomic DNA of lymphocytes of 26 B-CLL patients. From each genomic DNA sample, the putative presence of the insertions was analyzed in both alleles by polymerase chain reaction amplification and electrophoresis analysis. Each amplified band eluted from the gel, purified, and sequenced. The nucleotide sequences obtained for this region corroborated the three variants observed in the electrophoresis, corresponding to the absence of insertion, the 6-nucleotide insertion, and the 18-nucleotide insertion (Table 1).

Surprisingly, and in contrast to the results described by Moshynska et al (1), when we analyzed genomic DNA from normal lymphocytes from 10 control subjects

we also found that the same insertions were present. Furthermore, genomic DNA from mouth epithelial cells from 10 additional healthy individuals also contained these insertions. Moreover, different allelic combinations for this polymorphism were present in all kinds of samples. In fact, as shown in Table 1, the allelic frequencies were similar in the B-CLL and control samples. Consequently, we conclude that the MCL-1 insertions represent hereditary polymorphisms that likely do not predispose to chronic lymphocytic leukemia. We do not have a clear explanation for the discrepancy between our data and those of Moshynska et al. (1) other than technical problems or some kind of bias in the use of control subjects.

In summary, our data show that these MCL-1 insertions correspond to a polymorphism and their significance in the pathogenesis of B-CLL should be re-evaluated.

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NOTES

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Table 1. Summary of the allelic analysis of insertions in MCL-1 gene promoter

*wt = wild-type allele. 6 = 6-nucleotide insertion; 18 = 18-nucleotide-insertion.

Patterns of allelic combinations	B-CLL (n=26)	Controls		
		Lymphocytes (n=10)	Mouth epithelial cells (n=10)	Total (n=20)
Numbers of each allelic combination				
wt/wt	16	6	4	10
wt/6	2	1	3	4
wt/18	5	2	2	4
6/6	1	0	0	0
6/18	2	1	0	1
18/18	0	0	1	1
Polymorphism frequencies				
wt	39 (75%)	15 (75%)	13 (65%)	28 (70%)
6	6 (11.5%)	2 (10%)	3 (15%)	5 (12.5%)
18	7 (12.5%)	3 (15%)	4 (20%)	7 (17.5%)
% alleles with an insertion	25%	25%	35%	30%