"Exclusive" p15^INK4B Gene Deletions in Acute Lymphocytic Leukemia Include the E1β Exon of the p16^INK4 Gene

To the Editor:

The finding of homozygous deletions and intragenic inactivating mutations of the p16^INK4 gene has established the role of this gene as a tumor suppressor in various malignancies, including acute lymphocytic leukemia (ALL). The neighboring p15^INK4B gene is commonly codeleted with p16^INK4. We have previously reported on ALL cases with homozygous deletions of the p15^INK4B gene, sparing p16^INK4 sequences. A similar deletion pattern has been reported in glioma, suggesting that the p15^INK4B gene may also be a tumor suppressor. However, the p15^INK4B gene has never been shown to carry inactivating intragenic mutations in any malignancy; therefore, the role of this gene in malignant transformation is uncertain.

The recent report describing the genomic organization of the p16^INK4 gene with an alternative exon (usually referred to as E1β) situated in close proximity to the coding sequence of the p15^INK4B gene raise the question as to whether the exclusive p15^INK4B gene deletions described are in fact deletions including the 5'-end of p16^INK4. We have used the polymerase chain reaction product of the E1β-exon as a probe in hybridizations with DNA from three ALL patients with previously observed exclusive p15^INK4B gene deletions. All three patients were found to carry homozygous deletions of the E1β-exon of p16^INK4 (Fig 1).

At present, the importance of these deletions is not clear, because the significance of the E1β exon is unknown. It does not seem to code for a translated transcription product. However, the deletions extend into p16^INK4 sequences and may very well disturb regulation of p16^INK4 expression. The findings emphasize the importance of the p16^INK4 gene as a tumor suppressor and add further doubt regarding the role of p15^INK4B as a tumor suppressor gene.

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REFERENCES
Exclusive p15INK4B gene deletions in acute lymphocytic leukemia include the E1 beta exon of the p16INK4 gene [letter]

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