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The chromosome 4q21 gene (AF-4/FEL) is widely expressed in normal tissues and shows breakpoint diversity in t(4;11)(q21;q23) acute leukemia

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Abstract

The chromosomal translocation, t(4;11)(q21;q23), is the most common type of 11q23 chromosomal abnormality, being highly prevalent in infant acute leukemias and associated with a poor prognosis. The t(4;11) results in the fusion of an 11q23 gene (MLL, HRX, Htrx-1, or ALL-1) and a 4q21 gene (AF-4 or FEL). To further evaluate the 4q21 gene and its role in t(4;11) acute leukemia, we have cloned a 38-kb genomic region and mapped exons of the AF-4 gene. The 4q21 breakpoints in 19 cases of t(4;11) acute leukemia were analyzed by Southern analysis and pulsed-field gels. Seventeen of the 19 cases had breakpoints on chromosome 4q21 that were scattered in this 38 kb region. Expression of the AF-4 gene was studied in a total of 28 various nonhematopoietic, hematopoietic, and t(4;11) leukemic cell lines. The AF-4 gene was expressed in all cell lines as a major and a minor transcript. In addition to the normal transcripts, two fusion transcripts from the derivative 11 and derivative 4 chromosomes were identified in all t(4;11) cell lines except B1, which had only the der(11) transcript. These findings suggest that the breakpoints on 4q21 cluster over a broader area than do the breakpoints in the 11q23 gene, and that der(11) encodes the fusion RNA found consistently in leukemia cells.

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