

Leukaemia Section

Mini Review

t(1;7)(p34;q34)

Jacques Boyer

Laboratoire d'Hématologie, CH du MANS, France (JB)

Published in Atlas Database: August 2003

Online updated version: <http://AtlasGeneticsOncology.org/Anomalies/t0107p34q34ID1045.html>

DOI: 10.4267/2042/38022

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Clinics and pathology

Disease

Specifically associated with T-cell Acute Lymphoblastic Leukemia (T-ALL). This translocation is related to LCK dysregulation.

Phenotype/cell stem origin

T lineage.

Epidemiology

Rare: < 1% among T-ALL.

Cytogenetics

Cytogenetics morphological

1p34 is a partner of 7q34. The other partners of 7q34 are 1p32, 9q32, 9q34, 10q24, 11p13, 15q22, 19p13. 22q13 is a novel partner of 1p34 in a precursor T-lymphoblastic leukemia.

Genes involved and proteins

TCRB: T-cell receptor β -chain gene

Location

7q35

DNA/RNA

The TRB locus at 7q35 spans 685 Kb. The locus contains 2 types of coding elements: TCR elements (64-67 variable genes TRBV, 2 clusters of diversity, joining and constant segments) and 8 trypsinogen genes. A portion of the TCRB locus has been duplicated and translocated to the chromosome 9 at 9p21.

Protein

T cell receptor beta chains.

LCK (lymphocyte-specific tyrosine kinase gene)

Location

1p34

DNA/RNA

The LCK gene encodes a lymphocyte-specific member of the Src family of protein kinases. Size and orientation strand are unknown. This gene is assigned to bands 1p34.3 by fluorescence in situ hybridation and its mapping relative to the reference marker pYNZ2 (D1S57).

LCK is normally expressed from two distinct promoters.

A proximal promoter initiates transcripts designated as type I.

A distal promoter, found approximately 30 kb further upstream, initiates transcripts designated as type II.

Human thymocytes and all the leukemic T cell lines express both type I and type II LCK transcripts, albeit at different levels. Peripheral blood mature T cell express mainly type II LCK transcripts.

The two types of human LCK transcripts are distinguished by their 5'-untranslated regions. However, the protein kinase encoded by both transcripts is the same.

Protein

The human lymphocyte specific protein tyrosine kinase is a 57869kDa protein (p56LCK) 508 amino acids, involved in T-cell and IL2-receptor signaling important for antigen-induced T-cell activation.

Result of the chromosomal anomaly

Hybrid gene

Description

The T-cell acute lymphoblastic leukemia cell line HSB-2 has the t(1;7)(p34;q34) translocation. The T-cell acute lymphoblastic leukemia cell line SUP-T12 has the same translocation.

The breakpoint in the HSB-2 cell line at 1p34 occurs between the type I and type II promoters and thus separates the two LCK promoters and the type II promoter is translocated to the der(7) chromosome. The breakpoint in the SUP-T12 at 1p34 occurs 2kb upstream of the type II promoter, leaving an intact LCK gene on the der(1) chromosome.

In HSB-2 the t(1;7) fuses the TCRB constant region and transcriptional enhancer with the type I transcription unit of LCK on the der(1) chromosome. (the type II promoter is translocated to the der(7) chromosome). Thus the TCRB enhancer upregulates the type I transcripts.

An independent t(1;7) in SUP-T12 also resulted in the juxtaposition of LCK to TCRB. The p56LCK protein is elevated approximately 2-fold in comparison with that in normal T-cell lines and total cellular tyrosine phosphorylation is elevated approximately 10-fold.

Fusion protein

Note

No fusion protein.

Oncogenesis

The oncogenic p56LCK in T-cell-leukemia lines

contains an amino acid substitution within the CD4/CD8 binding domain, two substitutions in the kinase domain and an insertion between the SH2 and kinase domains. These mutations of LCK and the overexpression of p56LCK protein may contribute to some human T-cell leukemias.

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This article should be referenced as such:

Boyer J. t(1;7)(p34;q34). *Atlas Genet Cytogenet Oncol Haematol*. 2003; 7(4):264-265.
