

## Leukemia Section Review

### t(17;19)(q22;p13)

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Published in Atlas Database: May 1999

Online updated version : <http://AtlasGeneticsOncology.org/Anomalies/t1719ID1078.html>  
DOI: 10.4267/2042/37516

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#### Clinics and pathology

##### Disease

Acute lymphoblastic leukemia (ALL)

##### Phenotype/cell stem origin

Precursor-B cell immunophenotype; characteristic expression of surface markers CD10, CD19, TdT, HLA-DR.

##### Epidemiology

Less than 1% of ALL cases; 1% of childhood B-ALL ; sex ratio 1M/1F; more frequent in children.

##### Clinics

Frequent disseminated intravascular coagulation at diagnosis (not observed in ALL with other translocations).

##### Cytology

Pro-B lymphocytes.

##### Prognosis

Poor; no response to intensive chemotherapy and short survival.

#### Cytogenetics

##### Cytogenetics morphological

Presents usually as a balanced translocation t(17;19)(q22;p13); in some cases, only the der(19)t(17;19) is observed, but not the der(17); the same unbalanced form occurs in the closely related t(1;19).

##### Additional anomalies

Found in approximately 50% of cases.

##### Variants

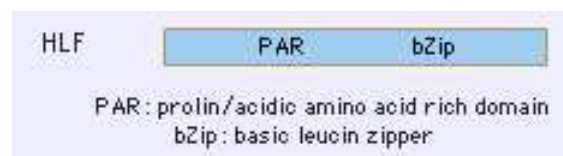
The translocation t(1;19)(q23;p13) and the t(17;19)(q22;p13) can be considered as variants of each other.

#### Genes involved and proteins

##### HLF (Hepatic leukemia factor)

###### Location

17q22



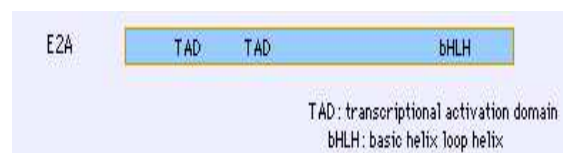
##### Protein

Basic leucine zipper (bZIP) transcription factor; normally expressed in hepatocytes and, at lower level, in lung and renal cells but not in hematopoietic cells.

##### E2A

###### Location

19p13



**Protein**

E2A encodes the basic helix loop helix (bHLH) transcription factors E12 and E47; expressed in most cell types.

## Result of the chromosomal anomaly

**Hybrid gene****Description**

Fusion gene E2A-HLF on der(19); two types of genomic rearrangements: type 1 results from a crossover between E2A intron 13 and HLF intron 3, type 2 from a crossover between E2A intron 12 and HLF intron 3

- t(17;19) type I: 5' E2A exons 1 to 13 <-> cryptic exon formed by E2A intron/HLF intron sequences to reestablish a reading frame <-> HLF exon 4 in 3'

- t(17;19) type II: 5' E2A exons 1 to 12 <-> HLF exon 4 in 3'.

**Transcript**

Expression of two mRNAs of 4.4 and 4.8 kb with the same coding sequence.

**Detection**

RT-PCR.

**Fusion protein****Description**

The fusion results in linking the amino-terminal transactivation domains 1 and 2 of E2A to the carboxy-terminal leucine zipper and basic domain of HLF; the minor structural difference induced in both types of proteins does not appear to have any functional consequence.

**Oncogenesis**

The fusion gene encodes a chimeric transcription factor E2A-HLF with altered DNA binding affinity compared with native HLF; it functions as an antiapoptotic transcription factor in leukemic cell transformation; when E2A-HLF protein was introduced into murine pro-B lymphocytes, it reverted both interleukin-3-dependent and p53-mediated apoptosis; E2A-HLF could act by regulating expression of downstream target genes: possible activation of target genes normally repressed in B-cell precursors by another bZIP protein gene, E4BP4 (dominant negative effect by heterodimerization with endogenous proteins?).

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*This article should be referenced as such:*

Viguié F. t(17;19)(q22;p13). *Atlas Genet Cytogenet Oncol Haematol*. 1999; 3(2):93-94.