Leukaemia Section
Mini Review

\( t(7;19)(q34;p13) \)

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Identity

Note
Non random translocations involving the short arm of chromosome 19 are observed in acute leukemia. The 19p13 genes E2A and LYL1 (see below) lie at two different translocation breakpoints in acute lymphoblastic leukemia. For instance the E2A gene is involved in the \( t(1;19)(q23;p13) \) in acute pre-B leukemia (B-ALL) and the LYL1 gene is structurally altered in the \( t(7;19)(q34;p13) \) in T cell leukemia (T-ALL).

Disease

Specifically associated with T-cell Acute lymphoblastic leukemia (T-ALL).

Phenotype/cell stem origin

Recents works, using oligonucleotide microarrays, show that several gene expression signatures are indicative of leukemic arrest at specific stages of normal thymocyte development:
LYL1 signature: pro-T (CD34+ CD3- CD4- CD8- CD1a-).
HOX11: early cortical thymocyte and TAL1 late cortical thymocyte.
LYL1 positivity is related to higher expression levels of the MYCN, LMO2 and PLZF proto-oncogenes as well as the antiapoptotic gene BCL2.
These findings have clinical importance (see Prognosis).

Epidemiology

Rare: < 1% among T-ALL. The \( t(7;9)(q34;q32) \) is present in one case of a serie of 5 patients with 7q34 involvement.

Prognosis

HOX11 activation is significantly associated with a favorable prognosis, while expression of TAL1, LYL1 and surprisingly HOX11L2 confers a much worse response to treatment.
The upregulation of BCL2 may explain their relative resistance to chemotherapy.

Cytogenetics

Cytogenetics morphological

19p13 is a partner of 7q34. The other partners are 1p34, 1p32, 9q34,9q32,10q24,11p13, 15q22.

Genes involved and proteins

TCRB (T-cell receptor beta-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.

Protein
T cell receptor beta chains.

LYL1

Location
19p13.2-p13.1

Note
The LYL1 gene is assigned to 19p13.2-p13.1 by fluorescence in situ hybridization.
DNA/RNA

An RNA of about 1.5 kb is transcribed from this gene in a wide variety of lymphoid cell lines with the notable exception of thymocytes and T cells.

Protein

LYL1 encodes a basic helix-loop-helix (bHLH) phosphoprotein (size 108 amino acids) that is highly related to TAL1. TAL1 and LYL1 HLH proteins show an 87% level of aminoacid identity.

Result of the chromosomal anomaly

Hybrid gene

Description

The LYL1 gene is structurally altered following the t(7;19) translocation, resulting in its head-to-head juxtaposition with the T cell receptor beta gene. In the human T cell line SUP-T7 established from an acute lymphoblastic leukemia, nucleotide sequence analysis showed that the point of crossover on chromosome 7 occurred immediately adjacent to joining segment beta 1.1 within the TCR beta gene, suggesting that this translocation resulted from an error in TCR gene rearrangement.

The t(7;19) resulted in truncation of the LYL1 gene and production of abnormal-sized RNAs suggesting a role for LYL1 in the pathogenesis of T Leukemia.

Fusion protein

Oncogenesis

Several helix-loop-helix (HLH) proteins are proposed to function as transcriptional regulatory factors based on their ability to bind in vitro the E-box motif of transcription enhancers. The enhancer binding HLH proteins include E47 and E12, two distinct but related polypeptides encoded by E2A gene that are able to form heterologous complexes with other HLH proteins like TAL1 and LYL1 polypeptides.

Thus LYL1 may function as a dominant-negative mutant preventing the activation of E2A responsive genes. It is plausible that the inactivation of E2A target genes is an essential and common step toward the development of a number of T-cell malignancies. LYL1 interacts also with p105 the precursor of NF-KappaB1 p50. Biochemical studies indicate that this interaction is mediated by the HLH motif of LYL1 and the ankyrin-like motifs of p105.

Ectopic expression of LYL1 cause a significant decrease in NF-KappaB- dependant transcription associated with a reduced level of NF-KappaB-dependant proteins.

References


This article should be referenced as such: