t(1;19)(q23;p13)
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Identity

Note: balanced form: -1, -19, +der(1), +der(19); unbalanced form: -19, +der(19).

Clinics and pathology

Disease
ALL, L1/L2 type; exceptionally found in L3-like ALL, T-ALL, NHL, or ANLL.

Phenotype / cell stem origin
‘Pre B’ (cIg+) ALL; may be cIg- or sIg+.

Epidemiology
5% of ALL, or 20% of pre B ALL; found in children and young adults (1-60 yrs, median: 10 yrs → one of the most frequent ALL in childhood); 3 male/4 female patients.

Clinics
Moderate organomegaly; frequent CNS involvement; blood data: high WBC (median 20 X 10^9/l); high LDH.

Cytology
CD19+, CD10+, and also CD9+.

Prognosis
Chromosome anomaly associated with adverse prognostic features; CR in most cases; median event
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free survival: 2 yrs; no age (?) or blood data prognostic significance; according to some -but not other- authors, the unbalanced form is of better prognosis (5 yr survival = 70%); median survival: 4 yrs in children, 6 mths in adults in one study, > 3yrs in adults in another.

Cytogenetics

Cytogenetics, morphological

Breakpoint is in 19p13.3; two different forms (with different prognoses?): - the balanced t(1;19), one fourth of cases, with a der(1) and a der(19); - the unbalanced form, found in ¾ cases, with 2 normal chromosomes 1, a der(19), and 1 normal chromosome 19: → partial trisomy for 1q23-1qter and monosomy for 19p13.3pter; the 2 forms can be in mosaic; note: 19p13 and 19q13 may be confused (e.g. literature reports).

Additional anomalies

In half cases; partial dup(1q), +6, del(6q), +8, i(9q), +17, i(17q), +21, t(17;19)(q22;p13) is not stricto sensu a variant, but, so far, an equivalent, with HLF (hepatic leukemia factor), on 17q22, involved in the translocation.

Genes involved and Proteins

Note: the following are (most often) involved, except in some cases lacking the clg expression:

PBX1

Location: 1q23
DNA / RNA
Alternate PBX1a and PBX1b.

Protein
Contains a homeodomain to binds to DNA; nuclear localisation; transcription regulation.

E2A

Location: 19p13
DNA / RNA
Alternate splicing → E12 and E47.

Protein
Contains transcriptional activation domains and a basic helix-loop-helix DNA binding site; binds specifically to an immunoglobulin enhancer; nuclear localisation; transcription factor.

Results of the chromosomal anomaly

Hybrid gene

Description
5’ E2A from 19p13 fused to 3’ PBX1; breakpoints are clustered on both genes (between exons 13 and 14 in E2A); the reciprocal 5’ PBX1 - 3’ E2A is not transcribed.

Fusion protein

Description
550 amino acids; 85 kDa; N-term transcriptional activation domains from E2A fused to the Hox cooperative motif and homeodomain of C-term PBX1; potent transcriptional activator.

Expression localisation
Nuclear localisation.

Oncogenesis
Pleiotropic transforming activity.

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