t(7;12)(q36;p13)

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Clinics and pathology

Phenotype/cell stem origin
Mainly cases of acute myeloid leukemia (AML) of various subtypes: M0, M1, M2, M4, M5, M6, M7, and RAEB-t. Four cases of acute lymphoblastic leukemia (ALL) are reported.

Epidemiology
At least 29 cases known; the translocation may be overlooked, and therefore underestimated; was found in 3% of children cases of ANLL, that was also 15% of infant cases of ANLL under 18 mths; sex ratio 15M/14F, age : 0-24 mths (n= 29), median 7 mth (n=29).

Clinics
WBC range 8-230 x 10^9/L, median 12 x10^9/L; organomegaly, central nervous system involvement in 3 of 6 cases

Prognosis
Probably poor prognosis: median survival is 13 months. Of 6 cases, one case had no remission and died at 7 mths; 4 case had relapse (duration first remission 1-20 mths), 2 cases are still alive (16 mths + and 33 mths +).

Cytogenetics

Cytogenetics morphological
Not always visible by chromosome banding techniques alone; may also be misdiagnosed as del(12)(p13).

Cytogenetics molecular
Detectable by dual colour FISH. A cosmid cocktail or YAC 964c10 shows a split signal on the der(12) and der(7). Also the commercial probe LSI TEL/AML1 (ES) for the detection of the t(12;21) shows a split signal on the der(7) and the der(12) in the t(7;12) cases since the breakpoint in these cases falls within the first three exons, which are contained in this probe. FISH using the PAC clone RP5-1121A15 mapping to 7q36 shows a split signal on the der(7) and der(12).

Probes
Chromosome 7 paint, wcp7 directly labelled with SpectrumGreen.
Chromosome 12 paint, wcp12 directly labelled with SpectrumOrange.
YAC 964c10 (CEPH, Paris).
LSI TAL/AML1 (ES).
PAC H_DJ1121A15.
Left: example of FISH performed on bone marrow metaphase from a patient with t(7;12)(q36;p13). Dual colour FISH using whole chromosome paint specific for chromosome 7 (in green) and chromosome 12 (in red) shows the reciprocal translocation. The arrow indicates the der(7) and the arrowhead indicates the der(12) - Sabrina Tosi; Right: Example of double colour FISH performed on bone marrow metaphase from a patient with t(7;12)(q36;p13). The PAC clone 1121A15 for the breakpoint region at chromosome band 7q36 (in green) and a cosmid cocktail for ETV6 at chromosome band 12p13 (in red) show one green signal for the normal chromosome 7, one red signal for the normal chromosome 12 and two fusion signals at both the derivative chromosomes 7 and 12 - Anne RM von Bergh and H. Berna Beverloo.

### Additional anomalies

+19 in 23 of 29 cases, +8 in 7 of 29 cases (+8,+19 in 6 cases).

### Genes involved and proteins

#### HLXB9

**Location**
7q36

**Note**
HLXB9 mutation is found in patients with Currarino syndrome.

**DNA/RNA**
3 exons, 2061 bp mRNA.

**Protein**
403 AA; Homeobox protein HB9; Highly expressed in CD34+ bone marrow cells; Possibly involved in the regulation of growth and differentiation of progenitor cells.

#### ETV6

**Location**
12p13

**DNA/RNA**
9 exons; alternate splicing

**Protein**
Contains a Helix-Loop-Helix and ETS DNA binding domains; wide expression; nuclear localisation; ETS-related transcription factor.

### Result of the chromosomal anomaly

#### Hybrid gene

**Description**
5’ HLXB9 - 3’ ETV6.

#### Fusion protein

**Note**
The t(7;12) is heterogeneous at the molecular level. The presence of an HLXB9-ETV6 fusion transcript has been described in only 2 out of 29 t(7;12) cases.

**Description**
N-terminal HLXB9, including its polyalanine repeat region, is fused to a large C-terminal part of the ETV6 protein including its HLH domain and ETS domain; the
homeobox domain of HLXB9 is not retained in the fusion protein; the reciprocal transcript is not expressed.

References


This article should be referenced as such: