11q23 rearrangements in leukaemia

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Clinics and pathology

**Disease**

De novo and therapy related leukaemias; acute non lymphocytic leukaemia (ANLL) and acute lymphocytic leukaemia (ALL) grossly represent half cases each; myelodysplasia (MDS) in the remaining 5%; biphenotypic leukaemia at times (likely to be more frequent with more investigations); 11q23 rearrangements in treatment related leukaemias (5-10% of 11q23 cases) are found mainly following a treatment with anti-topoisomerase II, or an intercalating topoisomerase II inhibitor, but also after alkylating agents treatment and/or radiotherapy; the prior cancer is variable.

**Phenotype / cell stem origin**

ANLL: M5a in half cases, M4 (20%), M1 or M5b (10% each), M2 (5%); ALL: B-cell mostly, L1 or L2, CD19+ in 60% of B-ALL cases, CD10+ 35%; T-ALL in rare cases (<1%); MDS: most often RA or RAEB±T.

**Epidemiology**

25% are infant (<1 yr) cases; children and adults each represent 50% of cases; M/F = 0.9 (NS).

**Clinics**

Organomegaly; frequent CNS involvement (5%); high WBC (> 50 X 10⁹/l in 40%).

**Prognosis**

Very poor in general; variable according to the translocation, the phenotype, the age, and whether the leukaemia is de novo or secondary.

**Cytogenetics**

**Cytogenetics, morphological**

- +11: 1% of ANLL and MDS as well; M1, M2, and M4 ANLL; therapy related ANLL; MDS evolving towards ANLL; partial tandem duplication (in situ) of MLL; visible dup(11q) also occur.
- inv(11)(p15q23): rare; ANLL and MDS.
- t(X;11)(q13;q23): rare; ANLL; the gene involved in Xq13 is AFX1, a transcription regulator.
- t(1;11)(p32;q23): rare; ALL and ANLL; the gene involved in 1p32 is AF1P.
- t(1;11)(q21;q23): rare; mostly M4 ANLL; the gene involved in 1q21 is AF1q.
- t(2;11)(p21;q23): rare; ANLL and MDS; may be found associated with del(5q).
- t(3;11)(p21;q23): very rare; involve AF3p21.
- t(4;11)(q21;q23): represent 1/3 of cases; found mainly (95%) in B-ALL (CD19+ in 75%, CD10+ in 15%); treatment related ALL in 5%; unbalanced sex ratio < 4 yrs (1M/2F); children represent half cases (infants <1 yr) accounting for 1/3 of all cases); children aged 2-9 yrs appear to have a much better prognosis; the gene involved in 4q21 is AF4, a transcription activator.
- t(6;11)(q27;q23): 5% of cases; mostly; children and young adults; male predominance; the gene involved in 6q27 is AF6; role in signal transduction.
- t(9;11)(p23;q23): represent 1/4 of cases; found in ANLL mainly in M5a (70%), or M4 (10%); in ALL in 10%; de novo and therapy related AL; children represent half cases (infants <1 yr) accounting for 15% of all cases); the gene involved in 9q22 is AF9, a transcription activator.
- t(10;11)(p12;q23): 5% of cases; M4 or M5 ANLL; ALL at times; from infants and children to (rare) adult cases; the gene involved in 10p12 is AF10, a transcription activator.
- t(11;16)(q23;p13): rare; treatment related ANLL/MDS; most cases are children cases; the gene involved in 16p13 is CBP, a transcriptional adaptor/coactivator.
- t(11;17)(q23;q21): rare; ANLL; the gene involved in 17q21 is AF17; not to be confused with the t(11;17)(q23;q21) in M3 ANLL variant, with...
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involvement of PLZF in 11q23 and RARα in 17q21.
- t(11;17)(q23;q25): rare; ANLL and MDS.
- t(11;19)(q23;p13.1): 5% of cases; M4 or M5 ANLL most often; de novo and therapy related AL; adults mainly; the gene involved in 19p13.1 is ELL, a transcription activator.
- t(11;19)(q23;p13.3): 5% of cases; ALL, biphonotypic AL and ANLL (M4/M5 mainly); therapy related AL; T-cell ALL at times, these T-cell cases are the only cases of t(11;19) with an excellent prognosis, a rather rare feature in this page!!!; mostly found in infants (half cases), and other children (altogether: 70%), or young adults (cases 40 yrs are 4%); 23 unpublished cases and review of 90 cases); the gene involved in 19p13.3 is ENL, a transcription activator.

Various other poorly known 11q23 rearrangements have been described:
- t(5;11)(q31;q23),
- t(6;11)(q21;q23): ANLL; the gene involved in 6q21 is AF6q21, a transcription regulator,
- t(10;11)(q22;q23),
- t(11;11)(q13;q13),
- t(11;12)(q23;q13),
- t(11;15)(q23;q15),
- t(11;17)(q23;p13),
- t(11;18)(q23;q23),
- t(11;21)(q21;q11),
- t(11;22)(q23;q13): ANLL; the gene involved in 22q13 is P300.
Various other breakpoints with 11q23 are: Xq22, 1q32, 2q37, 8q11, 9p11, 9q33, 12p13, 14q11, 14q32, 17q11, 18q12, 20q13, …

Additional anomalies
+X and i(7q) in the t(4;11); +8, +19, +21 in the t(6;11); +8 and +19 in the t(9;11); inv(11) in the t(10;11); +X, +6 and +8 in the 19p13.3; +8 in the 19p13.1.

Genes involved and Proteins

MLL

Location: in 11q23
DNA / RNA
21 exons, spanning over 100 kb; 13-15 kb mRNA; coding sequence: 11.9 kb.

Protein
431 kDa; contains two DNA binding motifs (a AT hook, and Zinc fingers), a DNA methyl transferase motif, a bromodomain; transcriptional regulatory factor; nuclear localisation; wide expression; homology with trithorax (drosophila).

Variable gene, from a variable chromosome partner (see above)

DNA / RNA
These genes appear to have, in most cases, no apparent homology to each other; for DNA and protein description of each, refer to their gene entry.

Results of the chromosomal anomaly

Hybrid gene

Description
5’ MLL - 3’ partner; highly variable breakpoints on the partner.

Fusion protein

Description
N-term AT hook and DNA methyltransferase from MLL fused to (little or most of) the partner C-term part; the reciprocal (partner-MLL) may or may not be expressed.

References


This article should be referenced as such: