Atlas of Genetics and Cytogenetics in Oncology and Haematology

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Gene Section

Mini Review

MLL (myeloid/lymphoid or mixed lineage leukemia)

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Identity

Other names: ALL1; HRX; Htrx (human trithorax); TRX1

HGNC (Hugo): MLL

Location: 11q23

Local order: Telomeric to PLZF, centromeric from RCK.

DNA/RNA

Description

37 exons, spanning over 100 kb.

Transcription

In a centromeric to telomeric direction; 13 and 15 kb; coding sequence: 11.9 kb.

Protein

Description

3969 amino acids; 431 kDa; contains two DNA binding motifs: a AT hook homologous to high mobility group proteins HMGI-(Y) and HMGI(C) that binds to the minor groove of DNA, and zinc fingers, a DNA methyl transferase motif, a bromodomain, and segments of homology with trithorax, in particular in the C-terminal SET domain.

Expression

Wide; especially in: brain, kidney, thyroid; expressed in Taned B lymphocytes and myeloid cells.

Localisation

Nuclear, in punctate spots.

Function

Transcriptional regulatory factor, involved in maintenance of Hox gene expression.

Homology

Trithorax (Drosophila), ALR (human), MLL2 (human).

Mutations

Note

MLL is implicated in at least 10 % of acute leukemias (AL) of various types: acute lymphoblastic leukemias (ALL), acute non lymphocytic leukemias (ANLL), biphenotypic ALs, treatment related leukemias, infant leukemias; the prognosis is poor.

Implicated in

t(4;11)(q21;q23)/acute leukaemias --> MLL/AF4

Disease

Typically CD19+ CD10-precursor B-ALL, biphenotypic AL, at times ANLL (M4/M5); common in

infants may be congenital; treatment related leukaemia (secondary to epipodophyllotoxins).

Prognosis
Median survival < 1 year.

Cytogenetics
Additional chromosome anomalies are found in 1/4 of cases, one of which is the i(7q).

Hybrid/Mutated gene
5' MLL - 3' AF4; 12 kb.

Abnormal protein
240 kDa protein with about 1400 amino acids from NH2 MLL and 850 from COOH AF4 (variable breakpoints); the reciprocal may or may not be expressed.

t(6;11)(q27;q23)/ANLL --> MLL/AF6

Disease
M5/M4 de novo and therapy related ANLL, T-cell ALL.

Prognosis
Poor.

t(9;11)(p22;q23)/ANLL --> MLL/AF9

Disease
M5/M4 de novo and therapy related ANLL.

Prognosis
The prognosis may not be as poor as in other 11q23 leukaemias in de novo cases; very poor prognosis in secondary ANLL cases.

Cytogenetics
May be overlooked; often as a sole anomaly.

Hybrid/Mutated gene
Variable breakpoints on both genes.

Abnormal protein
N-term -- AT hook and DNA methyltransferase from MLL fused to the 192 C-term amino acids from AF9 (as breakpoints are variable, this is only an example).

t(10;11)(p12;q23)/ANLL --> MLL/AF10

Disease
M4 or M5 ANLL; ALL at times; therapy related ANLL.

Prognosis
Poor.

t(11;19)(q23;p13.1)/ANLL --> MLL/ELL

Disease
Mainly M4/M5; treatment related leukemia; all ages.

Prognosis
Very poor.

Cytogenetics
Detected with R banding.

Hybrid/Mutated gene
5' MLL - 3' ELL

Abnormal protein
AT hook and DNA methyltransferase from MLL fused to most of ELL.

Oncogenesis
Potential transcription factor.

t(11;19)(q23;p13.3)/acute leukaemias --> MLL/ENL

Disease
ALL (CD19+), biphenotypic AL, ANLL (M4/M5); mainly congenital; treatment-related leukaemia.

Prognosis
Very poor, except in rare T-cell cases.

Cytogenetics
Detected with G banding.

Hybrid/Mutated gene
5' MLL - 3' ENL

Abnormal protein
AT hook and DNA methyltransferase from MLL fused to, most often, the nearly entire ENL.

trisomy 11/ANLL --> MLL tandem duplication

t(X;11)(q13;q23)/ANLL, T-ALL --> MLL/AFX1

t(X;11)(q22;q23)/ANLL --> MLL/Septin2

t(1;11)(p32;q23)/ALL --> MLL/AF1p

t(1;11)(q21;q23)/ANLL --> MLL/AF1q

t(2;11)(q11;q23)/MDS --> MLL/LAF4

t(3;11)(p21;q23)/t-ANLL --> MLL/AF3p21

t(3;11)(q25;q23)/t-ANLL --> MLL/GMPS

ins(5;11)(q31;q13q23)/ALL --> MLL/AF5q31

t(5;11)(q31;q23)/ANLL --> MLL/GRAF

t(6;11)(q21;q23)/ANLL --> MLL/AF6q21

t(9;11)(q34;q23)/ALL --> MLL/AF9q34

t(11;14)(q23;q24)/ANLL --> MLL/h-gephyrin

t(11;15)(q23;q14)/ANLL --> MLL/AF15q14

t(11;16)(q23;p13)/t-ANLL --> MLL/CBP

t(11;17)(q23;p13)/t-ANLL --> MLL/GAS7

t(11;17)(q23;q12)/ANLL --> MLL/RARa

t(11;17)(q23;q21)/ANLL --> MLL/AF17

t(11;17)(q23;q25)/ANLL --> MLL/MSF/AF17q25

t(11;19)(q23;p13)/ANLL --> MLL/EEN

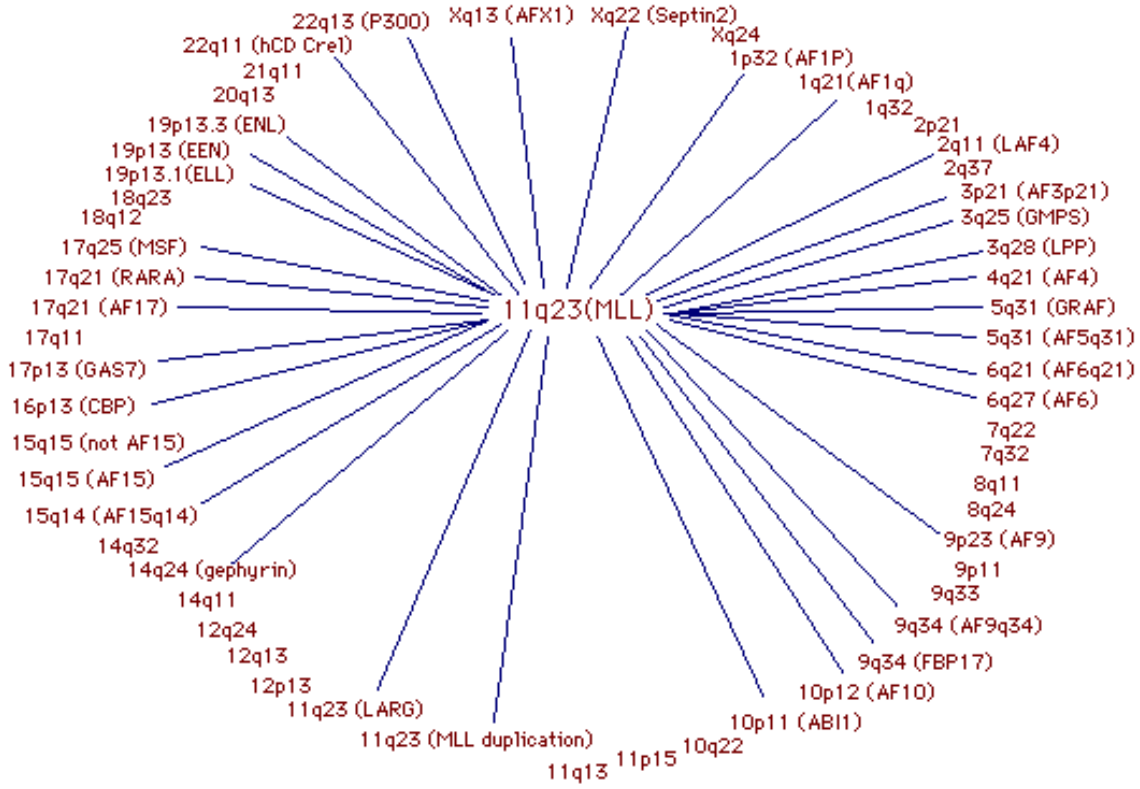
t(11;22)(q23;q11.2)/ANLL --> MLL/hCDCRel

t(11;22)(q23;q13)/ANLL --> MLL/P300

Breakpoints

Note

Spanning a 8 kb genomic region; between exons 5 to 11; highly variable on the partner, ranging from close to the NH2-term in ENL, to near the COOH-term in AF9.



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