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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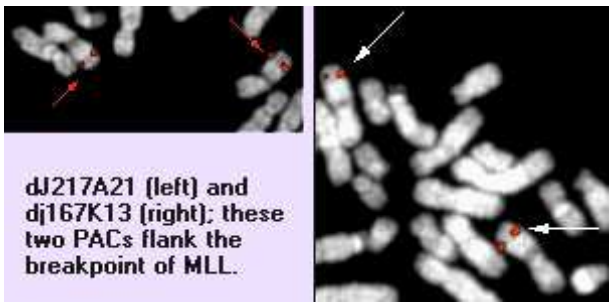
Identity

Other names: ALL1, HRX, Htrx (human trithorax), TRX1
Location: 11q23
Local order: telomeric to PLZF, centromeric from RCK.

DNA/RNA



MLL (11q23) - Courtesy Mariano Rocchi, Resources for Molecular Cytogenetics. Laboratories willing to validate the probes are welcome: contact rocchi@biologia.uniba.it.

Description

21 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 (to bind to the minor grove), and Zinc fingers to bind to the major grove of DNA, a DNA methyl transferase motif, a bromodomain, and segments of homology with trithorax, in particular in the C-term.

Expression

Wide; especially in: brain, kidney, thyroid, lymphoid tissue.

Localisation

Nuclear.

Function

Transcriptional regulatory factor.

Homology

Trithorax (drosophila); G9a (human).

Implicated in

Note: 5 to 10 % of acute leukaemias (ALL, ANLL, biphenotypic AL, treatment related leukemia, infant leukemia) with poor prognosis.

t(1;11)(p32;q23)/ALL → MLL/AF1p
t(1;11)(q21;q23)/ANLL → MLL/AF1q
t(4;11)(q21;q23)/acute leukaemias → MLL/AF4

Disease

Typically CD19+ B-ALL, biphenotypic AL, at times ANLL (M4/M5); may be congenital; treatment related leukaemia (secondary to epipodophyllotoxins).

Prognosis

Median survival < 1 yr.

Cytogenetics

Additional chromosome anomalies are found in ¼ of cases 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

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 exemple).

t(10;11)(p12;q23)/ANLL → MLL/AF10

t(11;17)(q23;q21)/ANLL → MLL/AF17

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

Other 11q23 rearrangements

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.

References

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