Atlas of Genetics and Cytogenetics in Oncology and Haematology

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Gene Section
Mini Review

MLLT10 (myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, Drosophila); translocated to, 10)

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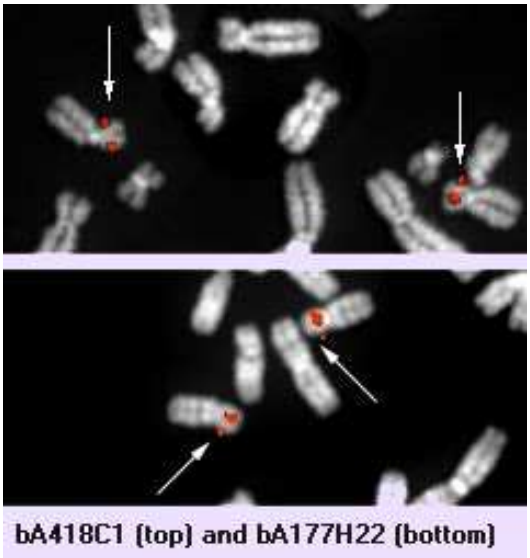
Identity

Hugo: MLLT10
Other names: AF10 (ALL1 fused gene from chromosome 10)
Location: 10p12



AF10 (10p12) - Courtesy Mariano Rocchi, Resources for Molecular Cytogenetics.

DNA/RNA

Transcription

5' telomeric → 3' centromeric direction; 5.5 kb mRNA; coding sequence: 3.1 kb.

Protein

Description

1027 amino acids; 109 KDa; N-term - LAP (leukemia associated protein)/PHD finger - Ext-LAP/PHD (Cys-rich region) - NLS (nuclear localisation signal) - AT-hook - LZ (leucine zipper) - Gln-rich domain - C-term.

Expression

Mainly in the testis.

Localisation

Nuclear.

Function

Transcription factor.

Homology

With AF17 and BR140.

Representation of the AF10 protein modified by Linder B et al. J Mol Biol 2000 and Jones LK et al. Leukemia 2001.

Implicated in

t(10;11)(p12;q23)/ANLL ⟶ MLL-AF10

Disease

Mainly M4/M5 ANLL.

Cytogenetics

Due to the opposite orientation of AF10 and MLL on their respective chromosome arms, MLL-AF10 gene fusion requires complex rearrangements with three or more breakpoints. An inversion of the 5'MLL or 3'AF10 is required in order to allow an in-frame MLL-AF10 fusion.

Hybrid/Mutated Gene

5' MLL - 3' AF10; breakpoints are at variable places along AF10.

Abnormal Protein

The AF10 Ext-LAP/PHD is always deleted, as are the MLL PHD fingers. Both retain the C-term LZ domain necessary for malignant transformation.

inv ins(10;11)(p12;q23q12)/ANLL ⟶ MLL-AF10

Disease

One case of pediatric M5 ANLL.

Hybrid/Mutated Gene

5' MLL - 3' AF10 and 5' AF10 - 3' HEAB, a gene at 11q12.

Abnormal Protein

Only MLL-AF10 is expressed.

t(10;11)(p13;q14-21) ⟶ CALM -AF10 and/or AF10-CALM

Disease

Present both in myeloid and non myeloid acute leukemias: in T-cell ALL specific to TCRgd lineage; in myeloid leukemia described in FAB M0-AML, M1-AML, M5-AML, M7-AML.

Prognosis

Poor.

Cytogenetics

May well be confused with the above t(10;11)(p12;q23).

Hybrid/Mutated Gene

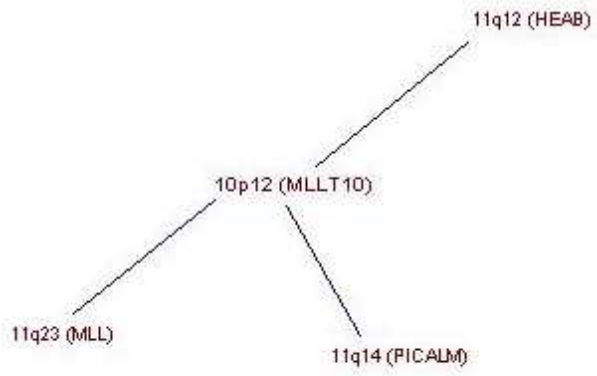
5' CALM - 3' AF10 and 5' AF10 - 3' CALM.
In a 5' breakpoint cluster region (nucleotides 424 and 589), AF10 sequences retained the Ext-LAP/PHD domain. The presence of these kinds of sequences seems to be necessary for maturation toward the TCRgd lineage, whereas their absence leads to maturation arrest at a more immature stage.

Abnormal Protein

Both CALM-AF10 and the reciprocal AF10-CALM are expressed. However, the CALM-AF10 contains most of the functional domains present in each of the two proteins.

Breakpoints

Note: the breakpoint in the t(10;11)(p13;q14-21) is more in 5' of AF10.



MLLT10 and partners. Editor 08/2005.

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