AML1 (acute myeloid leukemia 1)

Jean-Loup Huret

Genetics, Department of Medical Information, University of Poitiers, CHU Poitiers Hospital, F-86021 Poitiers, France

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Identity

Other names: CBFA2 (core binding factor A2), CBFa2, PEBPaB (polyomavirus enhancer binding protein aB)
Location: 21q22.3

AML1 (21q22.3) in normal cells: clone dJ1107L6 - Courtesy Mariano Rocchi, Resources for Molecular Cytogenetics. Laboratories willing to validate the probes are welcome: contact M Rocchi.

DNA/RNA

Description
The gene spans a region of more than 120 kb.

Transcription
Transcription is from telomere to centromere → the fusion gene is located on the ‘other’ chromosome (e.g. the der(8) of the t(8;21), the der(3) of the t(3;21)...); alternate splicing → transcripts of 2, 3.3, ..., 7.5 and 8 kb.

Protein

AML1

Runt trans.activ.

Description
250, 453 amino acids and other forms; forms heterodimers with CBFB.

Expression
Widely expressed, including hematopoietic cells at various stages of differentiation: role in haematopoiesis.

Localisation
Nuclear.

Function
Transcription factor (activator) for various hematopoietic-specific genes: binds to the core site 5’ PyGPyGTPy 3’ of a number of promoters and enhancers, as in GM-CSF (granulocyte-macrophage colony stimulating factor), CSF1R (colony stimulating factor 1 receptor), TCRb sites (T cell antigen receptors), and myeloid myeloperoxidase.

Homology
1- Runt (drosophila): nuclear DNA binding protein; role in segmentation (embryology);
2- AML2 (also called: CBFA3, CBFa3, PEBPaC), located in 1p35-36, expressed in B lineage (3 and 5 kb RNA);
3- AML3: (also called: CBFA1, CBFa1, PEBPaA) in 6p21;
4- cbfa family (mouse)
**Implicated in**

$t(1;21)(p36;q22)$
$t(3;21)(q26;q22)$

**myelodysplastic syndrome (MDS) or ANLL → EVI1 or EAP-MDS1/AML1**

**Note:** translocation protein includes most of the gene, from the second untranslated exon.

**Disease**

CML-BC of myeloid type; ANLL and MDS, often therapy related (secondary to antitopoisomerase II).

**Hybrid/Mutated Gene**

5’ AML1 - 3’ EAP or MDS1 or EVI1.

**Abnormal Protein**

AML1/EVI1: N-term -- Runt -- zn finger -- zn finger -- acidic -- C-term.

$t(5;21)(q13;q22)$

**myelodysplastic syndrome (MDS)**

$t(8;21)(q24;q22)$

**ALL and ANLL → AML1/ETO**

**Disease**

ANLL; M2 mostly.

**Prognosis**

CR is obtained; median survival (1.5-2 yrs) is the range with other ANLL or relatively better.

**Cytogenetics**

Additional cytogenetics anomalies: loss of Y or X chromosome, del(7q)/-7, +8, del(9q); complex

$t(8;21;Var)$ are known and have revealed that the crucial event lies on der(8); in agreement with the fact that both genes are transcribed from telomere to centromere.

**Hybrid/Mutated Gene**

5’ AML1 - 3’ ETO.

**Abnormal Protein**

N-term AML1 with the Runt domain fused to the nearly entire ETO.

**Oncogenesis**

The fusion protein retain the ability to recognize the AML1 consensus binding site (→ negative dominant competitor with the normal AML1) and to dimerize with the cbtb/CBTB subunit → probable altered transcriptional regulation of normal AML1 target genes.

$t(12;21)(p12;q22)/ALL → ETV6-AML1$

**Disease**

B cell ALL (CD10+).

**Prognosis**

CR in all cases; prognosis seems good.

**Cytogenetics**

Often undetectable without FISH; additional anomalies: frequent del(12)(p12) on the other allele.

**Hybrid/Mutated Gene**

5’ ETV6 - 3’ AML1 on the der(21).

**Abnormal Protein**

Helix loop helix of TEL fused to the nearly entire AML1 protein; the other TEL allele is often deleted.

$t(17;21)(q11;q22)/ANLL$
References


This article should be referenced as such: