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Gene Section
Review

RUNX1 (runt-related transcription factor 1 (acute myeloid leukemia 1; aml1 oncogene))

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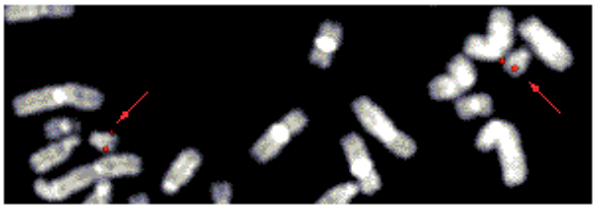
This article is an update of : AML1 (acute myeloid leukemia 1). RUNX1 (runt-related transcription factor 1 (acute myeloid leukemia 1; aml1 oncogene)). Atlas Genet Cytogenet Oncol Haematol.1997;1(2):59-61.

Identity

Other names: AML1 (acute myeloid leukemia 1); CBFA2 (core binding factor A2); PEBPaB (polyomavirus enhancer binding protein aB)

HGNC (Hugo): RUNX1

Location: 21q22.3



AML1 (21q22.3) in normal cells: clone dJ1107L6 - Courtesy Mariano Rocchi, Resources for Molecular Cytogenetics.

DNA/RNA

Description

the gene spans a region of more than 120 kb.

DNA Diagram.

Transcription

transcription is from telomere to centromere --> the fusion gene is located on the 'other' chromosome (eg 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

Description

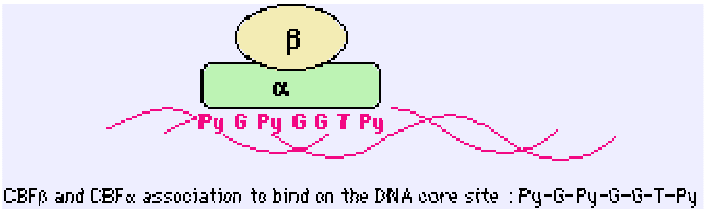
250, 453 amino acids and other forms; forms heterodimers with CBFB.

Expression

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

Localisation

Nuclear.



Protein Diagram.

Function

Transcription factor (activator) for various hematopoietic-specific genes: binds to the core site 5' PyGPyGGTPy 3' of a number of promotors 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); AML3: (also called: CBFA1, CBFa1, PEBPaA) in 6p21;
3- cbfa family (mouse).

Implicated in

Familial platelet disorder with predisposition to acute non lymphocytic leukemia

t(1;21)(p36;q22) treatment related acute non lymphocytic leukemia (ANLL) --> ?/ AML1

t(2;21)(p11;q22) ANLL --> ?/ AML1

t(3;21)(q26;q22)/ myelodysplastic syndrome (MDS) or ANLL --> -EVI1 or EAP/ MDS1 - AML1

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.

t(4;21)(q31;q22) T-cell acute lymphoblastic leukemia (T-ALL) --> ?/ AML1

t(5;21)(q13;q22) myelodysplastic syndrome (MDS) and ANLL --> ?/ AML1

t(8;21)(q22;q22)/ANLL. --> ETO - AML1

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 anomalies are frequent: 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 agrement with the fact that both genes are transcribed from telomere to centromere.

Hybrid/Mutated gene
5' AML - 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 concensus 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(8;21)(q23;q22) MDS --> FOG2 / AML1

t(8;21)(q24;q22) ALL and ANLL --> TRPS1 / AML1

t(12;21)(p13;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' AML1on 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(12;21)(q24;q22) ANLL --> ?/ AML1

t(16;21)(q24;q22) ANLL --> MTG16-AML1

Disease
ANLL and therapy related ANLL; mainly with preceeding MDS

Prognosis
Very poor.

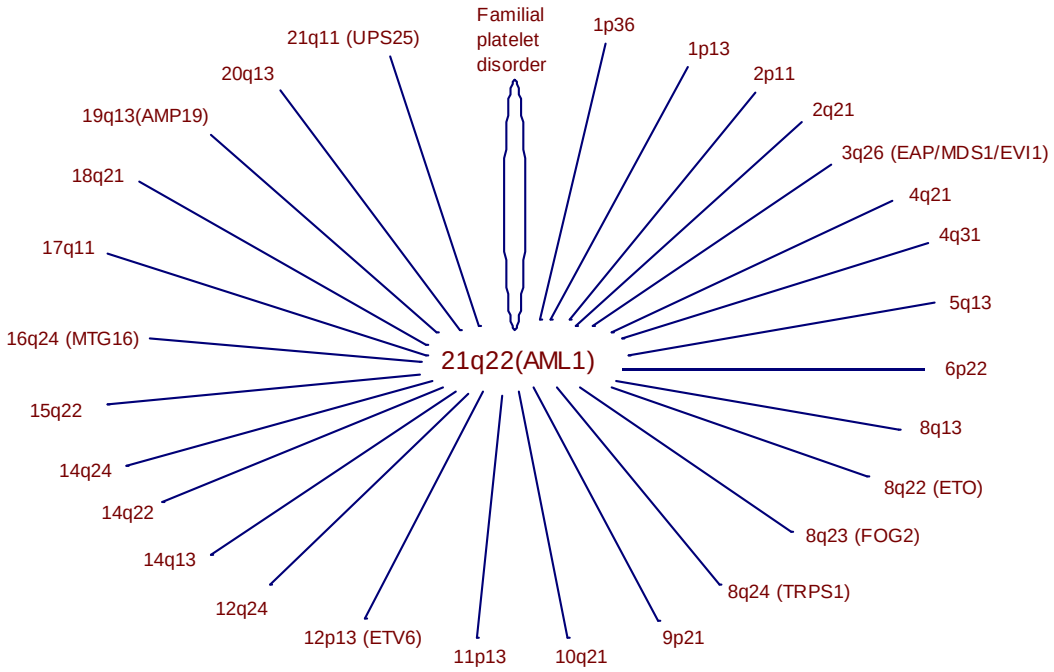
t(17;21)(q11;q22) ANLL

t(19;21)(q13;q22) treatment related ANLL --> AMP19 / AML1

t(20;21)(q1;3q22) treatment related ANL --> ? / AML1

t(21;21)(q11;q22) MDS --> UPS25 / AML1

Breakpoints



AML1 and partners - recurrent translocations. Editor 02/2003; updated 08/2003.
Note: cases of AML1 translocations with either 4q21, 4q27, 8q24 (not the TRPS1 one), 11q24,14q11, 16p13 have been proved to be cryptic t(12;21) with ETV6/AML1 involvement, and we have therefore to be cautious with breakpoints without a partner described.

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