

Leukaemia Section

Short Communication

t(9;12)(p24;p13) ETV6/JAK2

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Published in Atlas Database: March 2014

Online updated version : <http://AtlasGeneticsOncology.org/Anomalies/1122t0912.html>
DOI: 10.4267/2042/54139

This article is an update of :

Huret JL. t(9;12)(p24;p13). Atlas Genet Cytogenet Oncol Haematol 1998;2(2):54.

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Abstract

Short communication on t(9;12)(p24;p13) ETV6/JAK2, with data on clinics, and the genes implicated.

Clinics and pathology

Disease

Myeloproliferative disease in transformation, myelodysplastic syndrome (MDS), B-cell acute leukemia (B-ALL), and T-cell acute leukemia (T-ALL).

Phenotype/cell stem origin

One B-ALL was CD10+, the two others were not otherwise specified.

The myeloproliferative disease was an atypical chronic myelogenous leukemia (a-CML).

Epidemiology

Seven patients to date: 5 male and 2 female patients. Median age was 26 years (range 1.5-80), with two children cases (one B-ALL and one T-ALL), and four cases were found in young adults (aged 25, 26, 32, 33) (Lacronique et al., 1997; Peeters et al., 1997; Najfeld et al. 2007; Zhou et al., 2012).

Prognosis

Three patients did not reach complete remission (two B-ALL and one T-ALL); one patient died 6 months after diagnosis (the a-CML case), and one patient achieved CR, relapsed; a second CR was diagnosis (a B-ALL case). obtained and the patient was alive 31 months after

Cytogenetics

Cytogenetics morphological

The t(9;12)(p24;p13) was the sole abnormality in three cases, accompanied with a t(3;12) ETV6/MECOM in one case, with numerical abnormalities in one case, and part of a complex karyotype in one case (the MDS case). Del(6q) was found in two cases.

Genes involved and proteins

JAK2

Location

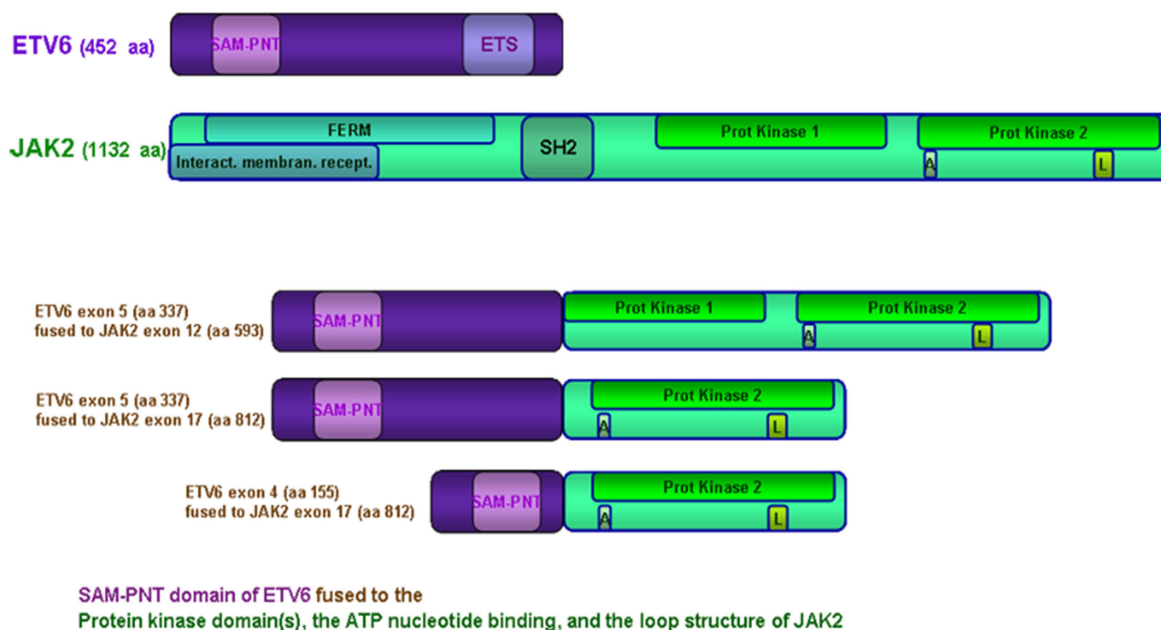
9p24.1

DNA/RNA

24 exons.

Protein

1132 amino acids (aa); from N-term to C-term, JAK2 contains: an interaction region with cytokine/interferon/growth hormone receptors: aa 1-239, a FERM domain: aa 37-380, a SH2 domain: aa 401-482, two protein kinase domains: aa 545-809 and 849-1124, an ATP nucleotide binding site: aa 855-863, and a loop structure: aa 1056-1078 (JAK2 kinase insertion loop). JAK homology domains are the following: JH7: aa 25-137; JH6: aa 144-284; JH5: aa 288-309; JH4: aa 322-440; JH3: aa 451-538; JH2: aa 543-824; JH1: 836-1123. Phosphotyrosines are located at aa 119, 372, 373, 523, 813, 868, 966, 972, 1007, and 1008 (Harpur et al., 1992; Saltzman et al., 1998; Lucet et al., 2006).



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t(9;12)(p24;p13) ETV6/JAK2 (475, 654, or 876 aa)
Jean Loup Huret, 2014

ETV6/JAK2 fusion protein.

Protein tyrosine kinase of the non-receptor type that associates with the intracellular domains of cytokine receptors; mediates signaling transduction.

ETV6

Location

12p13.2

DNA/RNA

9 exons; alternate splicing.

Protein

452 amino acids. ETV6 is composed of a HLH domain responsible for hetero- and homodimerization in N-term, and an ETS domain responsible for sequence specific DNA-binding in C-term (binds to the DNA sequence 5'-CCGGAAGT-3'). Transcriptional regulator; tumor suppressor. Involved in bone marrow hematopoiesis.

Result of the chromosomal anomaly

Hybrid gene

Description

5' ETV6 - 3' JAK2. Three different hybrids have been found: fusion of ETV6 exon 4 to JAK2 exon 17 (Peeters et al., 1997), fusion of ETV6 exon 5 to JAK2 exon 17 (Lacronique et al., 1997), and fusion of ETV6 exon 5 to JAK2 exon 12 (Peeters et al., 1997).

Fusion protein

Description

The HLH domain of ETV6 is fused to the protein kinase domain(s), the ATP nucleotide binding, and the loop structure of JAK2; according to the different possible breakpoints, the resulting protein contains 475, 654, or 876 amino acids. Furthermore, other products result from splicing (Peeters et al., 1997). The reciprocal JAK2-ETV6 may not be expressed.

Oncogenesis

It may be speculated that the HLH domain of ETV6 induces oligomerization, resulting in constitutive activation of the kinase domain of JAK2.

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This article should be referenced as such:

Huret JL. t(9;12)(p24;p13) ETV6/JAK2. *Atlas Genet Cytogenet Oncol Haematol.* 2014; 18(10):757-759.
