**Leukaemia Section**

**Short Communication**

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

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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).
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).

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**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.

**References**


Najfeld V, Cozza A, Berkofsky-Fessler W, Prcchal J, Scalise A. Numerical gain and structural rearrangements of JAK2, identified by FISH, characterize both JAK2617V>F-positive and -negative patients with Ph-negative MPD, myelodysplasia, and B-lymphoid neoplasms. Exp Hematol. 2007 Nov;35(11):1668-76


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