**t(12;13)(p13;q12) ETV6/FLT3**

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**Clinics and pathology**

**Disease**

Acute lymphoblastic leukemia (ALL) and myeloid malignancies are described in cases of t(12;13)(p13;q12).

Note

The translocation t(12;13)(p13;q12) is molecularly heterogeneous:

The t(12;13)(p13;q12) with ETV6 and FLT3 involvement, herein described, was found in only one case so far, a case of myeloproliferative disorder (MPD) with eosinophilia (Vu et al., 2006).

On the other hand, a t(12;13)(p13;q12) ETV6 / CDX2 has been described in another case (Chase et al., 1999).

Finally, other cases of t(12;13)(p13;q12) without molecular ascertainment may or may not involve FLT3, CDX2, or even ETV6.

**Epidemiology**

All together, nine cases of t(12;13)(p13;q12) were described:

**Clinics**

The t(12;13)(p13;q12) ETV6/FLT3 case was a female patient aged 68 years, with a MPD with eosinophilia; she died 21 months after diagnosis. Another case presents with a similar phenotype: a 49 year-old male patient, also with a MDP with eosinophilia; he died 11 months after diagnosis (and with a history of leukocytosis for last two years before diagnosis) (Chiyoda et al., 1994).

The case with ETV6/CDX2 involvement was a 66 year old male patient with M1 acute myeloid leukaemia (AML); he died 40 months after diagnosis.

The six other known patients with a t(12;13)(p13;q12) were two children and one 17 year-old female patient with acute lymphoblastic leukemia (ALL) (Keene et al., 1987; Wlodarska et al., 1998; Heerema et al., 2000) and three adult patients with myeloid diseases (one refractory anemia with excess of blasts (RAEB) and two AMLs; one of which was a treatment-related AML (t-AML)) (Knapp et al., 1985; Tosi et al., 1998; Clavio et al., 2001).

**Cytogenetics**

**Cytogenetics morphological**

The t(12;13)(p13;q12) was the sole anomaly in five cases (the two MPD with eosinophilia, one ALL, the RAEB and a M0-AML). The t(12;13)(p13;q12) was accompanied with -5 and -7 in the t-AML, and with major karyotypic anomalies (MAKA) in the CD10+ ALL in the 17 year-old female patient.

**Genes involved and proteins**

Note

In only one patient, the ETV6/FLT3 implication was found (Vu et al., 2006). Following this report, transgenic mice expressing ETV6-FLT3 were used (Baldwin et al., 2007). Expression of the fusion protein in the transgenic mice was found in spleen, bone marrow, thymus, and liver. A significant increase in the number of CFU-GM, BFU-E, CFU-S and CFU-GEMM was produced. Mice developed MPD with a high incidence but did not succumbed to leukemia (Baldwin et al., 2007).

**ETV6**

**Location**

12p13

**Protein**

HLH domain responsible for hetero- and homodimerization in N-term, and an ETS domain responsible for sequence specific DNA-binding in C-
term. Transcriptional regulator; involved in bone marrow hematopoiesis.

**FLT3**

**Location**

13q12

**Protein**

Contains five immunoglobulin-like domains in the extracellular region involved in protein-ligand interaction, a transmembrane domain, and an intracellular tyrosine kinase domain. Dimerization induces kinase domain activation, leading to the activation of intracellular signalling pathways. Receptor tyrosine kinase. Receptor for the FL cytokine. Expressed on early hematopoietic progenitor cells.

**Result of the chromosomal anomaly**

**Hybrid gene**

**Description**

Both ETV6/FLT3 and FLT3/ETV6 transcripts were detected. However, FLT3/ETV6 transcripts were out of frame. Various in frame fusion products of ETV6/FLT3 were found. Fusion of exon 5 of ETV6 5' term to exon 14 of FLT3 3' term (and exon 4 and 16 in one transcript).

**Fusion protein**

**Description**

N-term Helix-loop-helix (HLH) oligodimerization domain of ETV6 fused to the transmembrane and tyrosine kinase domains of FLT3.

**Oncogenesis**

Constitutive tyrosine kinase activation.

**References**


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