t(8;12)(q13;p13) ETV6/NCOA2

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Published in Atlas Database: November 2013
Online updated version: http://AtlasGeneticsOncology.org/Anomalies/t0812q13p13ID1503.html
DOI: 10.4267/2042/53771
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Abstract
Short Communication on t(8;12)(q13;p13) ETV6/NCOA2, with data on clinics, and the genes implicated.

Clinics and pathology

Disease
T-cell acute lymphoblastic leukemia (T-ALL), B-cell acute lymphoblastic leukemia (B-ALL), biphenotypic acute leukemia (BAL), and acute myeloid leukemia (AML).

Phenotype/cell stem origin
This entity most often appears as a childhood leukemia expressing both T-lymphoid and myeloid antigens. Eleven cases are available to date: one case of common B-ALL, 6 cases of T-ALL, 3 cases of BAL, and one M4-AML (Pui et al., 1987; Schneider et al., 2000; Yamamoto et al., 2002; Strehl et al., 2008; Zhou et al., 2012).

Epidemiology
There were 5 male and 6 female patients, aged 2, 2, 2, 7, 8, 11, 14, 23, 75 years, and two additional cases came from a series of “childhood leukemia”.

Prognosis
Although the sample is far too small for definitive conclusions, the prognosis does not seem bad (see Figure).

Cytogenetics

Cytogenetics morphological
Breakpoints were difficult to assign accurately by conventional cytogenetics, with cases described with a t(8;12)(q10;p10), a t(8;12)(q11;p11), a t(8;12)(q12;p12), a t(8;12)(q12;p13), or a t(8;12)(q13;p13), but all exhibiting an ETV6/NCOA2 fusion transcript (Strehl et al., 2008). The t(8;12) was the sole anomaly in five cases (four ALLs and one M1-AML/BAL), and was accompanied with a del(5q) in two ALL cases, a del(6q), a +9, and a del(11q) in an ALL each, a t(11;19)(q23;p13) in the M4-AML, and a +22 in a M1-AML/BAL.

Genes involved and proteins

Note
Heterozygous NOTCH1 mutations were found in five of six samples where they were studied (Strehl et al., 2008; Zhou et al., 2012).

NCOA2
Location
8q13.3
Protein
1464 amino acids. NCOA2 is composed of a basic helix-loop-helix (HLH), a PAS (Per/Arnt/Sim) region, four LXXLL motifs (L=leucine, X=any amino acid) that are critical for interaction with nuclear receptors, a LLXXLXXXL motif is involved in transcriptional coactivation and CREBBP/CBP binding, and a polyglutamine tract. Transcriptional coactivator for steroid receptors and nuclear receptors. Involved in skeletal muscle differentiation (Chen et al., 2000). Acts as a tumor suppressor in liver cancer (O’Donnell et al., 2012).
**ETV6**

**Location**
12p13.2

**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**
There was fusion of ETV6 exon 4 with NCOA2 exon 15 in five of six cases, and fusion of ETV6 exon 5 with NCOA2 exon 14 in one case (Strehl et al., 2008).

**Fusion protein**

**Description**
Fuses the pointed or sterile alpha motif (SAM) oligomerization domain of ETV6 to the C-term poly Gin of NCOA2 (with or without the LLXXLXXXL motif of NCOA2).

**References**

Pui CH, Williams DL, Raimondi SC, Rivera GK, Look AT, Dodge RK, George SL, Behm FG, Crist WM, Murphy SB.


This article should be referenced as such: