

Gene Section

Mini Review

ETV6 (ETS variant gene 6 (TEL oncogene))

Stevan Knezevich

BC Cancer Research Centre (BCCRC), Vancouver, British Columbia, Canada. (SK)

Published in Atlas Database: June 2005

Online updated version: <http://AtlasGeneticsOncology.org/Genes/ETV6ID38.html>

DOI: 10.4267/2042/38233

This article is an update of: Romana SP. ETV6 (ETS variant gene 6 (TEL oncogene)). *Atlas Genet Cytogenet Oncol Haematol.* 1999;3(4):181-182.

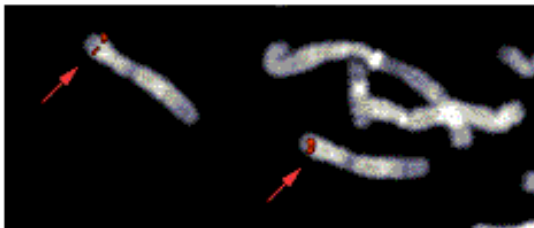
This work is licensed under a Creative Commons Attribution-Noncommercial-No Derivative Works 2.0 France Licence.
© 2005 *Atlas of Genetics and Cytogenetics in Oncology and Haematology*

Identity

Other names: TEL (translocation ets leukemia)

HGNC (Hugo): ETV6

Location: 12p13.1



ETV6 (12p13.1) in normal cells: clone dJ852F10 - Courtesy Mariano Rocchi, Resources for Molecular Cytogenetics.

DNA/RNA

Description

A member of the ets (E-26 transforming specific) family of transcription factors; the gene spans a region of 240 kb and consists of 8 exons.

Transcription

Transcription is from telomere to centromere; there are

three species of transcripts: 2400kb, 4300kb and 6200 kb; the gene encodes for a 1356 kb cDNA.

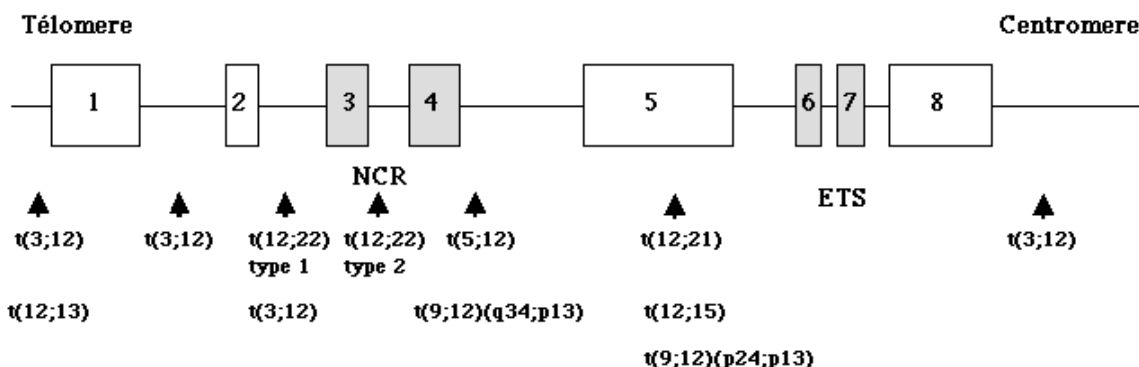
Protein

Description

There are two alternative start codons that correspondingly result in two isoforms. Codon 1 gives rise to a 57kDa protein while codon 43 gives rise to a 53 kDa protein. It has been demonstrated that these two isoforms are phosphorylated. ETV6 shares homology at the 5' and 3' ends with other ets family members, namely the helix-loop-helix (HLH) and ETS domains, respectively. HLH domain is encoded by exons 3 and 4 and has also been referred to as the pointed or sterile alpha motif (SAM) domain. It is responsible for hetero- and homodimerization with other ETV6 proteins and possibly other ets family members. The ETS domain is encoded by exons 6 through 8 and is responsible for sequence specific DNA-binding. It is positively charged, allowing it to bind to purine rich segments of DNA. A central domain also exists that is involved in the recruitment of a repression complex including NCOR2 and SIN3.



SAM-PNT: Sterile alpha motif/pointed domain
ETS: ETS domain



Expression

Expression arrays and Northern analysis have shown ubiquitous expression with greater expression in bone marrow, spleen and thymus.

Localisation

Immunofluorescence has shown a nuclear localization.

Function

Acts as a transcriptional regulator; important in vitelline angiogenesis and in bone marrow hematopoiesis.

Mutations

Note

ETV6 is implicated in leukemia, myelodysplastic syndromes and sarcoma.

Implicated in

t(1;12)(p36;p13) --> MDS2/ETV6

Disease

One CML with t(9;22) and one refractory anemia with excess of blasts in transformation.

t(1;12)(q21;p13) --> ARNT/ETV6

Disease

AML-M2.

t(1;12)(q25;p13) --> ABL2/ETV6

Disease

AML-M3, -M4, T-cell ALL.

t(3;12)(q26;p13) --> EVI1/ETV6

Disease

CML.

t(4;12)(p16;p13) --> FGFR3/ETV6

Disease

Peripheral T-cell lymphoma.

t(4;12)(q11;p13) --> CHIC2 (BTL)/ETV6

Disease

AML (FAB type M0)

t(5;12)(q31;p13) --> FACI6/ETV6

Disease

Acute myelogenous leukemia with eosinophilia.

t(5;12)(q33;p13) --> PDGFRb/ETV6

Disease

CMML.

t(6;12)(q23;p13) --> STL/ETV6

Disease

B-cell ALL.

t(7;12)(q36;p13) --> HLXB9/ETV6

Disease

AML (FAB type M1).

dic(9;12)(p13;p13) --> PAX5/ETV6

Disease

ALL.

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

Disease

Leukemias.

t(9;12)(q22;p13) --> SYK/ETV6

Disease

MDS.

t(9;12)(q34;p13) --> ABL1/ETV6

Disease

Acute myeloblastic leukemia (AML), chronic myelogenous leukemia (CML), acute lymphocytic leukemia (ALL).

t(10;12)(q24;p13) --> ?/ETV6

Disease

CMML.

t(12;13)(p13;q12) --> ETV6/CDX2

Disease

CML in transformation, myelodysplastic syndrome (MDS), acute non lymphocytic leukemia (ANLL), B and T- ALL.

t(12;13)(p13;q14) --> ETV6/TTL

Disease
ALL.

t(12;15)(p13;q25) --> ETV6/NTRK3

Disease
Congenital Fibrosarcoma, Congenital Mesoblastic Nephroma (cellular and mixed variants), Secretory Ductal Carcinoma of Breast, AML.

t(12;17)(p13;p12-p13) --> ETV6/PER1

Disease
AML.

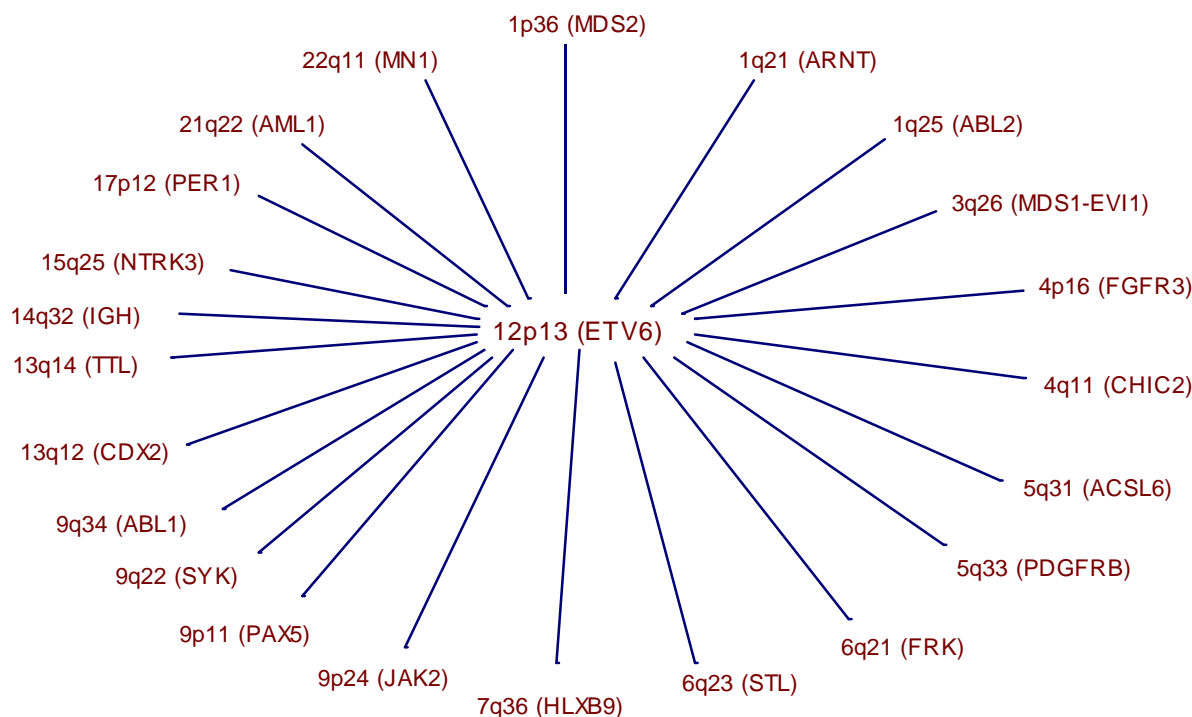
t(12;21)(p13;q22) --> ETV6/AML1

Disease
Childhood B-cell (ALL).

t(12;22)(p13;q11) --> ETV6/MN1

Disease
Refractory Anemia with Excess Blasts.

Breakpoints



ETV6 and partners. Editor 08/2004.

References

Wessels JW, Fibbe WE, van der Keur D, Landegent JE, van der Plas DC, den Ottolander GJ, Roozendaal KJ, Beverstock GC. t(5;12)(q31;p12). A clinical entity with features of both myeloid leukemia and chronic myelomonocytic leukemia. *Cancer Genet Cytogenet.* 1993 Jan;65(1):7-11

Golub TR, Barker GF, Bohlander SK, Hiebert SW, Ward DC, Bray-Ward P, Morgan E, Raimondi SC, Rowley JD, Gilliland DG. Fusion of the TEL gene on 12p13 to the AML1 gene on 21q22 in acute lymphoblastic leukemia. *Proc Natl Acad Sci U S A.* 1995 May 23;92(11):4917-21

Peeters P, Raynaud SD, Cools J, Wlodarska I, Grosgeorge J, Philip P, Monpoux F, Van Rompaey L, Baens M, Van den Berghe H, Marynen P. Fusion of TEL, the ETS-variant gene 6 (ETV6), to the receptor-associated kinase JAK2 as a result of

t(9;12) in a lymphoid and t(9;15;12) in a myeloid leukemia. *Blood.* 1997 Oct 1;90(7):2535-40

Peeters P, Wlodarska I, Baens M, Criel A, Selleslag D, Hagemeyer A, Van den Berghe H, Marynen P. Fusion of ETV6 to MDS1/EVI1 as a result of t(3;12)(q26;p13) in myeloproliferative disorders. *Cancer Res.* 1997 Feb 15;57(4):564-9

Suto Y, Sato Y, Smith SD, Rowley JD, Bohlander SK. A t(6;12)(q23;p13) results in the fusion of ETV6 to a novel gene, STL, in a B-cell ALL cell line. *Genes Chromosomes Cancer.* 1997 Apr;18(4):254-68

Chase A, Reiter A, Burci L, Cazzaniga G, Biondi A, Pickard J, Roberts IA, Goldman JM, Cross NC. Fusion of ETV6 to the

caudal-related homeobox gene CDX2 in acute myeloid leukemia with the t(12;13)(p13;q12). *Blood*. 1999 Feb 1;93(3):1025-31

Cools J, Bilhou-Nabera C, Wlodarska I, Cabrol C, Talmant P, Bernard P, Hagemeijer A, Marynen P. Fusion of a novel gene, BTL, to ETV6 in acute myeloid leukemias with a t(4;12)(q11-q12;p13). *Blood*. 1999 Sep 1;94(5):1820-4

Yagasaki F, Jinnai I, Yoshida S, Yokoyama Y, Matsuda A, Kusumoto S, Kobayashi H, Terasaki H, Ohyashiki K, Asou N, Murohashi I, Bessho M, Hirashima K. Fusion of TEL/ETV6 to a novel ACS2 in myelodysplastic syndrome and acute myelogenous leukemia with t(5;12)(q31;p13). *Genes Chromosomes Cancer*. 1999 Nov;26(3):192-202

Buijs A, van Rompaey L, Molijn AC, Davis JN, Vertegaal AC, Potter MD, Adams C, van Baal S, Zwarthoff EC, Rousset MF, Grosveld GC. The MN1-TEL fusion protein, encoded by the translocation (12;22)(p13;q11) in myeloid leukemia, is a transcription factor with transforming activity. *Mol Cell Biol*. 2000 Dec;20(24):9281-93

Iijima Y, Ito T, Oikawa T, Eguchi M, Eguchi-Ishimae M, Kamada N, Kishi K, Asano S, Sakaki Y, Sato Y. A new ETV6/TEL partner gene, ARG (ABL-related gene or ABL2), identified in an AML-M3 cell line with a t(1;12)(q25;p13) translocation. *Blood*. 2000 Mar 15;95(6):2126-31

Salomon-Nguyen F, Della-Valle V, Mauchauffe M, Busson-Le Coniat M, Ghysdael J, Berger R, Bernard OA. The t(1;12)(q21;p13) translocation of human acute myeloblastic leukemia results in a TEL-ARNT fusion. *Proc Natl Acad Sci U S A*. 2000 Jun 6;97(12):6757-62

Beverloo HB, Panagopoulos I, Isaksson M, van Wering E, van Drunen E, de Klein A, Johansson B, Slater R. Fusion of the homeobox gene HLXB9 and the ETV6 gene in infant acute myeloid leukemias with the t(7;12)(q36;p13). *Cancer Res*. 2001 Jul 15;61(14):5374-7

Cazzaniga G, Daniotti M, Tosi S, Giudici G, Aloisi A, Pogliani E, Kearney L, Biondi A. The paired box domain gene PAX5 is fused to ETV6/TEL in an acute lymphoblastic leukemia case. *Cancer Res*. 2001 Jun 15;61(12):4666-70

Yagasaki F, Wakao D, Yokoyama Y, Uchida Y, Murohashi I, Kayano H, Taniwaki M, Matsuda A, Bessho M. Fusion of ETV6 to fibroblast growth factor receptor 3 in peripheral T-cell lymphoma with a t(4;12)(p16;p13) chromosomal translocation. *Cancer Res*. 2001 Dec 1;61(23):8371-4

Keung YK, Beaty M, Steward W, Jackle B, Pettrati M. Chronic myelocytic leukemia with eosinophilia, t(9;12)(q34;p13), and ETV6-ABL gene rearrangement: case report and review of the literature. *Cancer Genet Cytogenet*. 2002 Oct 15;138(2):139-42

Odero MD, Vizmanos JL, Román JP, Lahortiga I, Panizo C, Calasanz MJ, Zeleznik-Le NJ, Rowley JD, Novo FJ. A novel gene, MDS2, is fused to ETV6/TEL in a t(1;12)(p36.1;p13) in a patient with myelodysplastic syndrome. *Genes Chromosomes Cancer*. 2002 Sep;35(1):11-9

Tognon C, Knezevich SR, Huntsman D, Roskelley CD, Melnyk N, Mathers JA, Becker L, Carneiro F, MacPherson N, Horsman D, Poremba C, Sorensen PH. Expression of the ETV6-NTRK3 gene fusion as a primary event in human secretory breast carcinoma. *Cancer Cell*. 2002 Nov;2(5):367-76

Murga Penas EM, Cools J, Algenstaedt P, Hinz K, Seeger D, Schafhausen P, Schilling G, Marynen P, Hossfeld DK, Dierlamm J. A novel cryptic translocation t(12;17)(p13;p12-p13) in a secondary acute myeloid leukemia results in a fusion of the ETV6 gene and the antisense strand of the PER1 gene. *Genes Chromosomes Cancer*. 2003 May;37(1):79-83

Qiao Y, Ogawa S, Hangaishi A, Yuji K, Izutsu K, Kunisato A, Imai Y, Wang L, Hosoya N, Nannya Y, Sato Y, Maki K, Mitani K, Hirai H. Identification of a novel fusion gene, TTL, fused to ETV6 in acute lymphoblastic leukemia with t(12;13)(p13;q14), and its implication in leukemogenesis. *Leukemia*. 2003 Jun;17(6):1112-20

Uren A, Toretsky JA. Pediatric malignancies provide unique cancer therapy targets. *Curr Opin Pediatr*. 2005 Feb;17(1):14-9

This article should be referenced as such:

Knezevich S. ETV6 (ETS variant gene 6 (TEL oncogene)). *Atlas Genet Cytogenet Oncol Haematol*. 2005; 9(4):272-275.
