ETV1 (ets variant 1)
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**Identity**
- Other names: ER81
- HGNC (Hugo): ETV1
- Location: 7p21.2

**DNA/RNA**

**Description**
The ETV1 (ETS-translocation variant 1) gene belongs to the PEA3-subfamily of erythroblast transformation-specific (ETS)-family of transcription factors. It is located on chromosome 7p21.3, consisting of 13 exons and spanning approximately 100 kb DNA in length (Coutte et al., 1999).

**Transcription**
ETV1 has 7 Refseq transcripts that are generated by alternative splicing and alternative transcriptional initiation.

**Pseudogene**
No pseudogene reported.

**Protein**

**Description**
ETV1 belongs to the PEA3-subfamily of erythroblast transformation-specific (ETS)-family of transcription factors. There are 7 protein isoforms of ETV1, ranging from 374 amino acids to 477 amino acids (~55 kD).

**Expression**
The ETV1 protein is physiologically expressed in the central nervous system including the developing proprioceptive neurons, the motor neurons and the dopaminergic neurons (Arber et al., 2000; Flames and Hobert, 2009). ETV1 is also expressed in the inner core cells of the Pacinian corpuscle (Sedy et al., 2006) and in the interstitial cells of Cajal (Chen et al., 2007; Chi et al., 2010). Pathologically, the ETV1 protein is aberrantly expressed in a subset of melanoma and prostate cancer through genomic rearrangements (Jané-Valbuena et al., 2010; Tomlins et al., 2005), or abnormally highly expressed in gastrointestinal stromal tumor (GIST) through high endogenous expression and protein stabilization by active MAP kinase signaling (Chi et al., 2010), or partially highly expressed as part of an oncogenic fusion protein-EWSR1-ETV1-in Ewing sarcoma (Jeon et al., 1995).

**Localisation**
Nucleus.

**Function**
ETV1 belongs to the ETS (E-twenty-six) family of transcription factors and the PEA3 subfamily transcription factors (ETV1, ETV4 and ETV5). It specifically recognizes the GGAA core consensus DNA motif in the genome and mediates transcriptional activation and repression of target genes in cell type and cell lineage-specific contexts.
ETV1 is critical in the normal development of a functional sensory-motor circuitry in the spinal cord (Arber et al., 2000), the specification of a group of specialized dopaminergic neurons in the central nervous system (Flames and Hobert, 2009), the normal development of the Pacinian corpuscle (Sedy et al., 2006), and the normal development and specification of the subclasses of interstitial cells of Cajal localized in the circular muscle and in the myenteric plexus (Chi et al., 2010).

ETV1 contributes to the pathogenesis of a number of cancer types through 1) aberrantly overexpression in melanoma and prostate cancer via genomic rearrangement (Jané-Valbuena et al., 2010; Tomlins et al., 2007; Tomlins et al., 2005), 2) abnormal protein stabilization in GIST (Chi et al., 2010), 3) formation of the oncogenic fusion protein EWSR1-ETV1 in Ewing sarcoma (Jeon et al., 1995).

**Homology**

A member of the ETS-family transcription factor and the PEA3 subfamily transcription factors, with most sequence homology to ETV5 and ETV4.

**Mutations**

**Note**

No validated known mutations.

**Implicated in**

**Ewing sarcoma**

**Prognosis**

The prognostic relevance remains to be determined.

**Cytogenetics**

Ewing sarcoma translocation, t(7;22)(p22;q12) that fused EWSR1 to the ETV1 gene (Jeon et al., 1995).

**Hybrid/Mutated gene**

EWSR1-ETV1 fusion gene accounts for ~1% of all Ewing sarcomas. The majority of Ewing sarcoma fusion genes are EWSR1-FLI1 (~85%) and EWSR1-ERG (~10%).

**Abnormal protein**

EWSR1-ETV1 fusion protein that fuses the first 7 exons of EWSR1 to the last 3-4 exons of ETV1 (exons 10 or 11-exon 13).
Typical breakpoint in prostate cancer fusions.

**Oncogenesis**
The EWSR1-ETS (EWSR1-FLI1, EWSR1-ETV1, EWSR1-ERG, etc) fusion proteins are thought to be the "oncogenic drivers" in Ewing sarcoma. EWSR1-FLI1 and EWSR1-ERG have been modeled in cell lines demonstrating the requirement of the oncogenic fusion proteins for Ewing sarcoma cell line growth and survival. The EWSR1-ETV1 fusion protein has not been modeled.

**Prostate cancer**
**Prognosis**
ETV1 fusion seems to confer a poorer prognosis in several studies.

**Oncogenesis**
ETV1 is aberrantly overexpressed in prostate cancer through genomic rearrangements that result in overexpression of a truncated ETV1 or full-length ETV1.
ETV1 is required for the growth of ETV1-positive prostate cancer cells and ETV1 overexpression confers invasiveness prostate cancer cells (Tomlins et al., 2007; Tomlins et al., 2005).

**Melanoma**
**Prognosis**
The prognostic relevance remains to be determined.

**Oncogenesis**
ETV1 is amplified in 13% of primary and 18% of metastatic melanomas, which results in aberrant overexpression. ETV1 is required for growth and proliferation of melanoma cells with ETV1 amplification and it cooperates with oncogenic NRAS (G12D) for tumorigenesis in mice (Jané-Valbuena et al., 2010).

**Gastrointestinal stromal tumor (GIST)**
**Prognosis**
The prognostic relevance remains to be determined.

**Oncogenesis**
ETV1 is naturally highly expressed and is required for the development of the interstitial cells of Cajal (ICCs) in the gastrointestinal tract that are the precursor cells of GIST. It is also highly expressed and required for the growth, survival and tumorigenesis of GISTs. It drives a core transcriptional program that is conserved in ICC and GIST. ETV1 protein level is stabilized by active KIT and downstream MAP kinase signaling pathways and cooperates with mutant KIT in GIST pathogenesis (Chi et al., 2010).

**Breakpoints**
See Figure below.
References

Jeon IS, Davis JN, Braun BS, Sublett JE, Roussel MF, Denny CT, Shapiro DN. A variant Ewing's sarcoma translocation (7;22) fuses the EWS gene to the ETS gene ETV1. Oncogene. 1995 Mar 16;10(6):1229-34


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