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Gene Section
Mini Review

ETV4 (ets variant 4)

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Identity

Other names: E1A-F; E1AF; PEA3; PEAS3

HGNC (Hugo): ETV4

Location: 17q21.31

DNA/RNA

Description

The gene spans approximately 30 kb and contained 14 exons. The largest exon (901 bp) contains the end of the ETS domain, the carboxy-terminal domain and the 3'-untranslated region. The remaining exons varied from 48 bp (exon 5) to 266 bp (exon 9).

Protein

Description

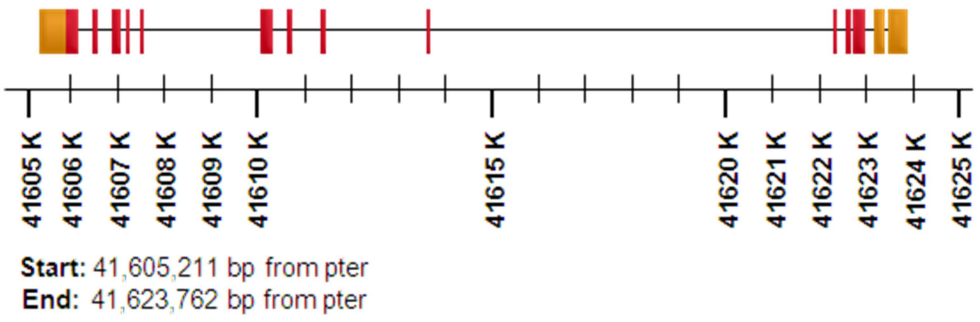
ETV4 is a member of ets-oncogene family transcription factors that were cloned by the ability to bind to enhancer motifs of the adenovirus E1A gene (Lavia et al., 2003). It is composed of 555 amino acids, which has a molecular weight ranging 61~70 kDa.

Localisation

Nuclear (Monté et al., 1994; Takahashi et al., 2005). Ubiquitinated protein is localized in the dot-like structure in the nuclear (Takahashi et al., 2005).

Function

ETV4 is capable of regulating transcription by binding to the Ets-binding site in the promoter of its target genes. Biologically, it contributes in a number of processes including neuronal pathfinding, mammary gland development, and male sexual function (Laing et al., 2000; Ladle et al., 2002; Kurpios et al., 2003). In various malignancies, its over-expression has been observed and it was also associated with tumor progression and outcome of patients with these malignancies. As mechanism of such function, regulation of hepatocyte growth factor (HGF)-induced cell migration (Hakuma et al., 2005), HER2-mediated malignant potential (Benz et al., 1997), and other ETV4-related factors including cyclooxygenase (COX)-2 and matrix metalloproteinases (MMPs) have been reported (Higashino et al., 1995; Horiuchi et al., 2003; Shindoh et al., 2004).



GeneLoc map region.

In addition, ETV4 promotes cell cycle progression via upregulation of cyclin D3 transcription in breast cancer cell (MDA231 cell) (Jiang et al., 2007). In contrast, ETV4 function as negative regulator of sonic hedgehog expression (Mao et al., 2009).

Implicated in

Breast cancer

Disease

Over-expression of ETV4 has been detected in human cancer cell lines (Baert et al., 1997). In animal model and human tissues, its over-expression was also found and it was associated with malignant potential including invasion and metastasis (Trimble et al., 1993; De Launoit et al., 2000; Benz et al., 1997; Bièche et al., 2004). Such ETV4-related functions are controlled via regulation of cyclin D3 transcription (Jiang et al., 2007), HER-2/Neu (Benz et al., 1997), and MMPs (Bièche et al., 2004).

Gastric cancer

Disease

Correlated with tumor progression via up-regulation of matrilysin in human tissues (Yamamoto et al., 2004).

Lung cancer

Disease

ETV4 expression was not detected in normal lung tissues. On the other hand, it is expressed in distal lung epithelium during lung development and in human lung cancer cells (Hiroumi et al., 2001; Liu et al., 2003). It was reported to be associated with cell invasion (Hiroumi et al., 2001) and metastasis via regulation of caveolin-1 transcription (Sloan et al., 2009) and Met-related factors (Hakuma et al., 2005).

Malignant melanoma

Disease

In cell lines, ETV4 plays important roles for malignant behavior including invasion and metastasis thorough up-regulation of MT1-MMP (Hata et al., 2008).

Prostate cancer

Disease

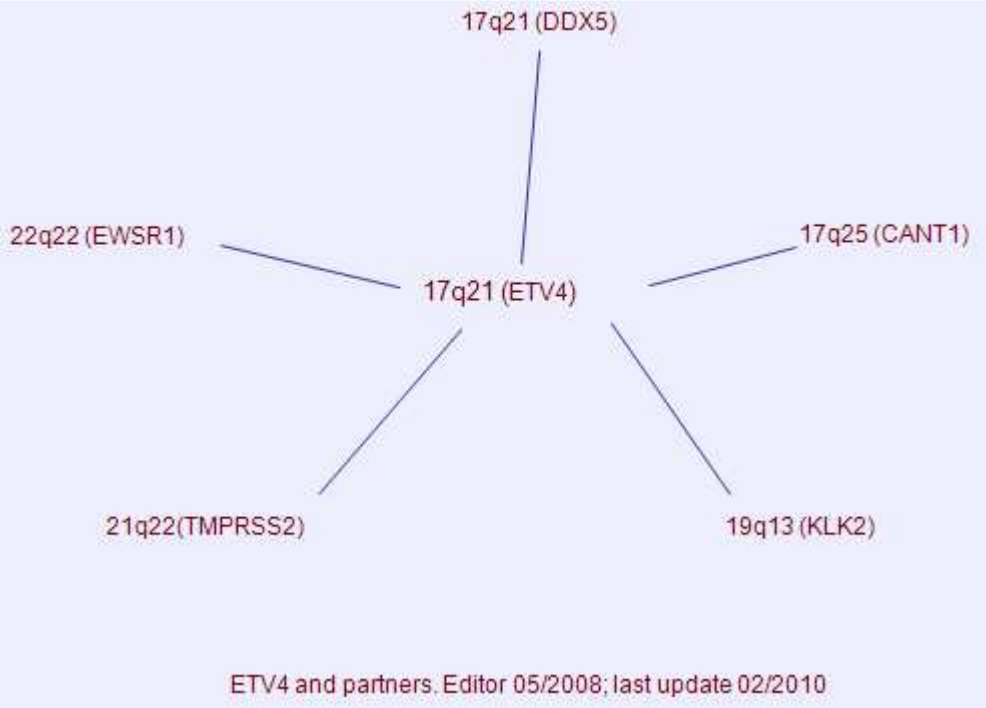
In human tissues, its expression in cancer cell was significantly higher than that in normal cells and it was also positively associated with pT stage. This finding was influenced with regulation of MMP-7 and MMP-9, but not of MMP-1, MMP-3, and MMP-14 (MT1-MMP) (Maruta et al., 2009).

Colorectal cancer

Disease

In early stage of colorectal carcinogenesis, its over-expression plays important roles through MMPs, COX-2, and iNos (Nosho et al., 2005).

Breakpoints



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