

Gene Section

Mini Review

USP6 (ubiquitin specific protease 6 (Tre-2 oncogene))

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Identity

Other names: TRE2; TRE17

HGNC (Hugo): USP6

Location: 17p13

Note

The gene is the result of a recent evolutionary fusion of two other genes - TBC1D3 (PRC17) on chromosome 17q12 and USP32 (NY-REN-60) on chromosome 17q22 (see below).

DNA/RNA

Description

30 exons spanning 47 kb of genomic DNA. Exons 1 to 14 are derived from the TBC1D3 (PRC17), and exons 15 to 30 are derived from the USP32 (NY-REN-60).

Transcription

The gene is transcribed from telomere to centromere. The coding region starts on exon 2 but

many splicing variants have been identified in the untranslated exon 1. There are at least two major transcripts with an approximate length of 8 kb.

Protein

Description

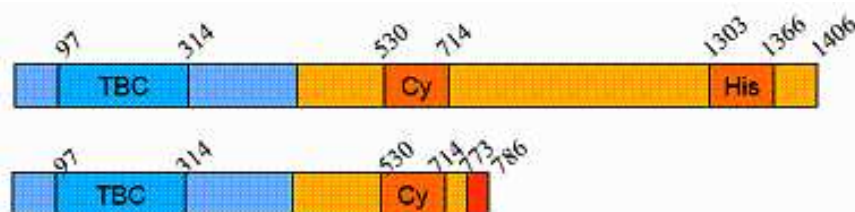
USP6 encodes for a 1406 aminoacid protein containing two major domains: TBC (from TRE2-Bub2-Cdc16), which encodes a GTPase-activating protein of the Rab family of GTPases, and a UBP domain with a ubiquitin specific protease activity. A USP6 splicing variant, also known as 'onco-TRE17 or TRE17-onco', encodes a 786 aminoacid protein with a truncated UBP domain. See figure 1.

Expression

Among normal tissues, USP6 seems to primarily expressed in testes.

Localisation

Cytoplasmic protein.



Numbers indicate amino acids demarcating the various domains. TRE17(long) and TRE17(onco) are identical through the first 773 amino acids; the last 13 amino acids of TRE17(onco) are unique (indicated in orange). Blue regions are PRC17 homologous, gold regions are USP32 homologous.

Function

USP6 function is still poorly understood but recent evidence has shown that USP6 is involved in endocytic trafficking. USP6 seems to operate in the same pathway controlled by Arf6 GTPase, which has been linked to mitogenic signaling and invasive behavior.

Homology

While the N-terminal portion of USP6 is highly homologous to PRC17 (89% identity), the C-terminal end is highly homologous to USP32 (97% identity).

Implicated in

Aneurysmal Bone Cyst or Aneurysmal Bone Tumor

Cytogenetics

Rearrangements of 17p13 with different partner chromosomes.

Hybrid/Mutated gene

USP6 fusion genes are formed by juxtaposition of USP6 coding sequences to the promoter regions of several partner genes, which lead to USP6 transcriptional upregulation. There is no fusion protein.

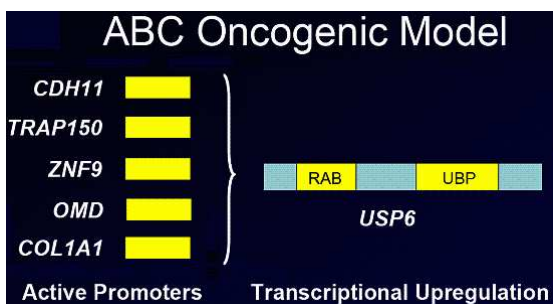
THRAP3 -USP6 in t(1;17)(p34;p13)

ZNF9 -USP6 in t(3;17)(q21;p13)

OMD -USP6 in t(9;17)(q22;p13)

CDH11 -USP6 in t(16;17)(q22;p13)

COL1A1 -USP6 in t(17;17)(q12;p13)



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