Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL INIST-CNRS

# Gene Section
## Short Communication

# USP32 (ubiquitin specific peptidase 32)

**Aysegul Sapmaz, Ayse Elif Erson-Bensan**

Netherlands Cancer Institute-Antoni van Leeuwenhoek hospital (NKI-AVL), Amsterdam, Netherlands (AS), Department of Biological Sciences, Middle East Technical University, Ankara, Turkey (AS, AEEB)

Published in Atlas Database: July 2013

Online updated version : http://AtlasGeneticsOncology.org/Genes/USP32ID52046ch17q23.html
DOI: 10.4267/2042/52076



**Abstract:** Short communication on USP32, with data on DNA/RNA, on the protein encoded and where the gene is implicated.

## Identity

**Other names:** NY-REN-60, USP10

**HGNC (Hugo):** USP32

**Location:** 17q23.1

**Local order:** Based on Mapviewer (Master Map: Gene on sequence, gene flanking USP32 oriented from centromere on 17q23.3 are:

- TBC1D3P1-DHX40P1 (17q23): TBC1D3P1-DHX40P1 read through transcribed pseudogene
- MIR4737: MicroRNA 4737
- HEATR6 (17q23.1): Heat repeat containing 6
- LOC100422693 (Chr.17): UDP-N-acetyl-alpha-D-galactosamine :polypeptide N-acetylgalactosamyltransferase 1 (GalNAc-T1) pseudogene
- LOC6456338 (17q23.1): WDNM1-like pseudogene
- LOC653653(17q23.1): adaptor-related protein complex 1 sigma 2 subunit pseudogene
- CA4 (17q23): carbonic anhydrase IV
- FAM106DP (Chr. 17): family with sequence similarity 106 memberD pseudogene
- SCARNA20 (17q23.2): small cajal body specific RNA 20
- RPL32P32 (17q23.2): ribosomal protein L32 pseudogene 32
- LOC100418753 (Chr.17): septin 7 pseudogene
- **USP32 (17q23.3): ubiquitin specific protease 32**
- LOC100506882 (Chr.17): uncharacterized LOC100506882
- C17orf64 (17q23.2): chromosome 17 open reading frame 64
- RPL12P38 (17q23.2): ribosomal protein L12 pseudogene 38
- HMGN2P42 (Chr.17) high mobility group nucleosomal binding domain 2 pseudogen 42
- APPBP2 (17q23.2): amyloid beta precursor protein (cytoplasmic tail binding protein 2.

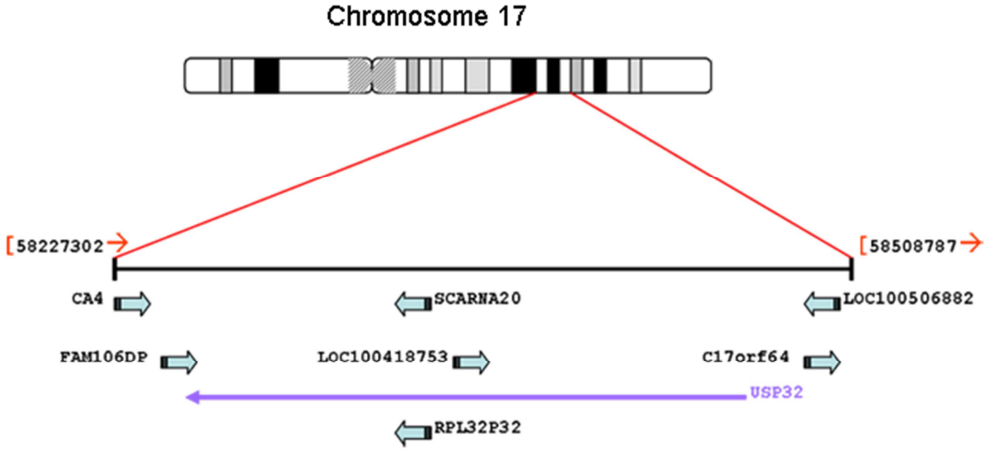


**Figure 1.** Genes flanking USP32 gene on 17q23.3. → stands for positive strand , ← stands for negative strand.

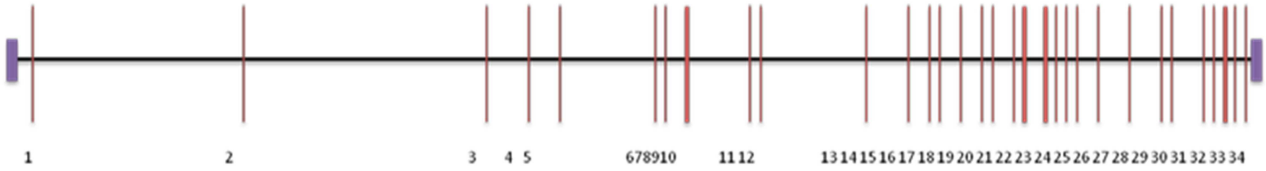


**Figure 2.** 34 exons of USP32.

# DNA/RNA

## Description

USP32 gene is located on a prominent gene amplification region, 17q23, in breast cancers (Bärlund et al., 1997; Erson et al., 2001) and has 34 exons (figure 2).

## Transcription

USP32 mRNA is 7026 bp long. Coding sequence of USP32 starts at the 287$^{th}$ bp and ends at the 5101$^{st}$ bp of the mRNA. Total length of USP32 coding sequence is 4815 bp.

## Pseudogene

No pseudogene has been reported for USP32.

# Protein

**Note**

Three independent studies reported USP32 to be phosphorylated at the 1173$^{rd}$ tyrosine and 1372$^{nd}$ serine residues (Dephoure et al., 2008; Rigbolt et al., 2011; Mayya et al., 2009).

## Description

USP32 (ubiquitin specific protease 32 - accession number: NT_010783 and mRNA accession number: NM_032582) encodes for a protein consisting of 1604 amino acids and the resulting protein's predicted molecular weight is approximately 182 kDa. The N-terminal region contains calcium binding domain with EF-hand and DUSP domains.

The EF-hand calcium binding domains, consisting of a helix (E), a loop and a second helix (F) motif, are generally found in calcium binding proteins.

DUSP domain is common among ubiquitin specific proteases. The function of this domain in USP32 remains unclear but is predicted be functional in protein-protein interactions. In addition, USP32 harbors Cys, His and Asp triad which is common in USP subfamily of DUBs (figure 3). Recently, active deubiquitination function of USP32 has been established (Akhavantabasi et al., 2010).

## Expression

Overexpressed transcript was detected in malignant breast ephitelium (Grigoriadis et al., 2006). Another study showed overexpression of USP32 in 50% (9 of 18) of breast cancer cell lines and 22% (9 of 41) of primary breast tumors compared to mammary epithelial cells (Akhavantabasi et al., 2010).

## Localisation

Golgi (Akhavantabasi et al., 2010).

## Function

USP32 is an active deubiquitinating enzyme (Akhavantabasi et al., 2010).

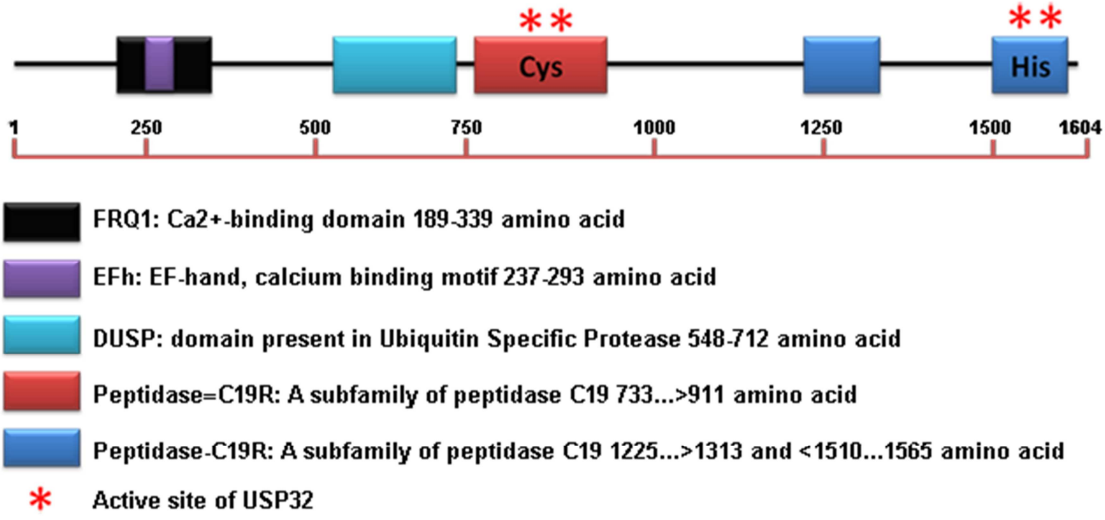


**Figure 3.** Domains of USP32.

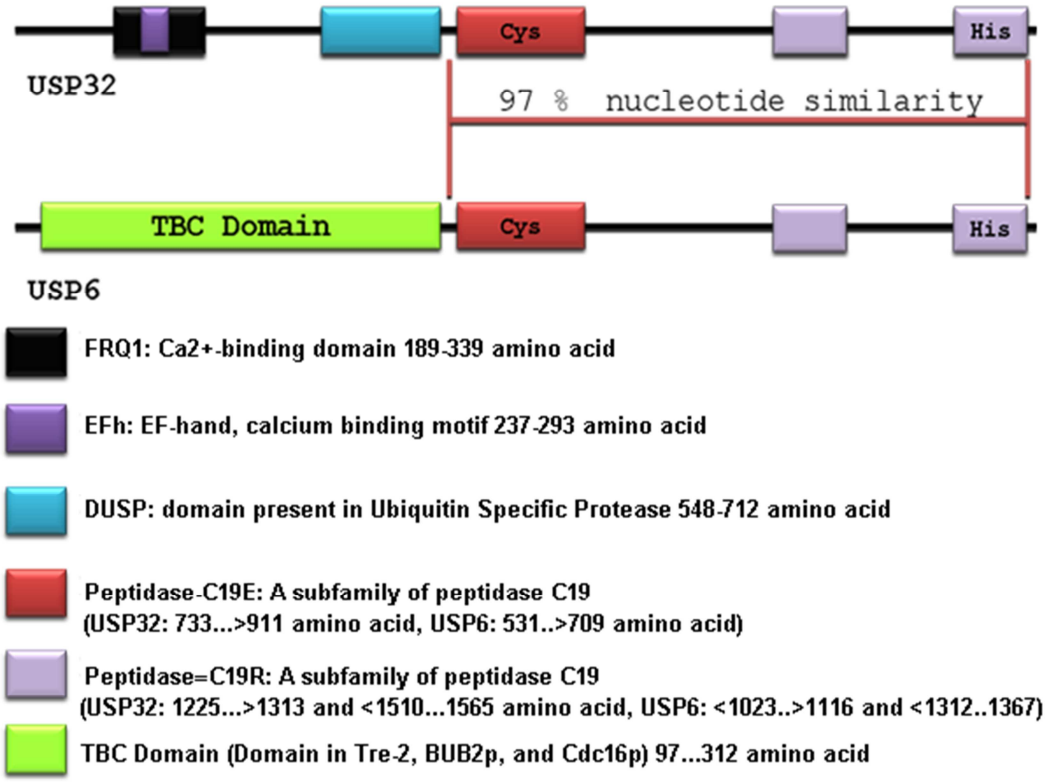


**Figure 4.** Sequence homology between USP32 and USP6.

### *Homology*

C-terminal of USP32 shows 97% nucleotide homology with USP6 (ubiquitin specific protease 6 (Tre-2 oncogene)) (Paulding et al., 2003) (figure 4).

## Mutations

**Note**

In the Parkinson disease, CNVs in USP32 gene were suggested. However, these variations in USP32 were not confirmed with Multiplex ligation-dependent probe amplification (MLPA) and real time PCR (Pankratz et al., 2011).

## Implicated in

### *Breast cancer*

**Note**

USP32 is located on 17q23 chromosomal region which is amplified in breast cancer (Sinclair et al., 2003; Haverty et al., 2008). Real-time PCR analysis in breast cancer cell lines determined that USP32 transcript is amplified more than two-fold in 50% of breast cancer cell lines and in 22% of (9 of 41) primary breast tumors compared to normal breast tissue samples. Moreover, silencing of USP32 leads to a decrease in the proliferation and migration properties of HeLa and MCF7 cells (Akhavantabasi et al., 2010).

In estrogen receptor (ER) positive tumors, USP32 may have a higher copy number than ER negative tumors (Zhang et al., 2009). Scafoglio et al. (2006) suggest USP32 to be an estrogen responsive gene.

**Hybrid/Mutated gene**

RT-PCR and transcriptome sequencing analysis determined USP32 to be one of the twelve expressed fusion genes in breast cancer cell line ZR-75-30. USP32 is found to be expressed with CCDC49 as a fusion transcript (Schulte et al., 2012).

## References

Bärlund M, Tirkkonen M, Forozan F, Tanner MM, Kallioniemi O, Kallioniemi A. Increased copy number at 17q22-q24 by CGH in breast cancer is due to high-level amplification of two separate regions. Genes Chromosomes Cancer. 1997 Dec;20(4):372-6

Erson AE, Niell BL, DeMers SK, Rouillard JM, Hanash SM, Petty EM. Overexpressed genes/ESTs and characterization of distinct amplicons on 17q23 in breast cancer cells. Neoplasia. 2001 Nov-Dec;3(6):521-6

Paulding CA, Ruvolo M, Haber DA. The Tre2 (USP6) oncogene is a hominoid-specific gene. Proc Natl Acad Sci U S A. 2003 Mar 4;100(5):2507-11

Sinclair CS, Rowley M, Naderi A, Couch FJ. The 17q23 amplicon and breast cancer. Breast Cancer Res Treat. 2003 Apr;78(3):313-22

Grigoriadis A, Mackay A, Reis-Filho JS, Steele D, Iseli C, Stevenson BJ, Jongeneel CV, Valgeirsson H, Fenwick K, Iravani M, Leao M, Simpson AJ, Strausberg RL, Jat PS, Ashworth A, Neville AM, O'Hare MJ. Establishment of the epithelial-specific transcriptome of normal and malignant human breast cells based on MPSS and array expression data. Breast Cancer Res. 2006;8(5):R56

Scafoglio C, Ambrosino C, Cicatiello L, Altucci L, Ardovino M, Bontempo P, Medici N, Molinari AM, Nebbioso A, Facchiano A, Calogero RA, Elkon R, Menini N, Ponzone R, Biglia N, Sismondi P, De Bortoli M, Weisz A. Comparative gene expression profiling reveals partially overlapping but distinct genomic actions of different antiestrogens in human breast cancer cells. J Cell Biochem. 2006 Aug 1;98(5):1163-84

Dephoure N, Zhou C, Villén J, Beausoleil SA, Bakalarski CE, Elledge SJ, Gygi SP. A quantitative atlas of mitotic phosphorylation. Proc Natl Acad Sci U S A. 2008 Aug 5;105(31):10762-7

Haverty PM, Fridlyand J, Li L, Getz G, Beroukhim R, Lohr S, Wu TD, Cavet G, Zhang Z, Chant J. High-resolution genomic and expression analyses of copy number alterations in breast tumors. Genes Chromosomes Cancer. 2008 Jun;47(6):530-42

Mayya V, Lundgren DH, Hwang SI, Rezaul K, Wu L, Eng JK, Rodionov V, Han DK. Quantitative phosphoproteomic analysis of T cell receptor signaling reveals system-wide modulation of protein-protein interactions. Sci Signal. 2009 Aug 18;2(84):ra46

Zhang Y, Martens JW, Yu JX, Jiang J, Sieuwerts AM, Smid M, Klijn JG, Wang Y, Foekens JA. Copy number alterations that predict metastatic capability of human breast cancer. Cancer Res. 2009 May 1;69(9):3795-801

Akhavantabasi S, Akman HB, Sapmaz A, Keller J, Petty EM, Erson AE. USP32 is an active, membrane-bound ubiquitin protease overexpressed in breast cancers. Mamm Genome. 2010 Aug;21(7-8):388-97

Pankratz N, Dumitriu A, Hetrick KN, Sun M, Latourelle JC, Wilk JB, Halter C, Doheny KF, Gusella JF, Nichols WC, Myers RH, Foroud T, DeStefano AL. Copy number variation in familial Parkinson disease. PLoS One. 2011;6(8):e20988

Rigbolt KT, Prokhorova TA, Akimov V, Henningsen J, Johansen PT, Kratchmarova I, Kassem M, Mann M, Olsen JV, Blagoev B. System-wide temporal characterization of the proteome and phosphoproteome of human embryonic stem cell differentiation. Sci Signal. 2011 Mar 15;4(164):rs3

Schulte I, Batty EM, Pole JC, Blood KA, Mo S, Cooke SL, Ng C, Howe KL, Chin SF, Brenton JD, Caldas C, Howarth KD, Edwards PA. Structural analysis of the genome of breast cancer cell line ZR-75-30 identifies twelve expressed fusion genes. BMC Genomics. 2012 Dec 22;13:719

*This article should be referenced as such:*

Sapmaz A, Erson-Bensan AE. USP32 (ubiquitin specific peptidase 32). Atlas Genet Cytogenet Oncol Haematol. 2014; 18(1):46-49.