

# Gene Section

## Short Communication

# PRUNE (prune exopolyphosphatase)

**Massimo Zollo**

Department of Molecular Medicine and Medical Biotechnology, Federico II, Naples, Italy and CEINGE, Biotecnologie Avanzate, Naples, Italy (MZ)

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## Abstract

Short communication on PRUNE, with data on DNA/RNA, on the protein encoded and where the gene is implicated.

## Identity

**Other names:** DRES-17, DRES17, HTCD37

**HGNC (Hugo):** PRUNE

**Location:** 1q21.3

### Note

Prune stands for the human homologue of the *Drosophila* prune gene. Prune protein was initially identified in *Drosophila*, in which its mutation caused a brownish-purple "prune" eye color due to significant loss of drospterins "red pigments", compared to the bright red eye of the wild-type fly, thus explaining its mutant name. Then the human homologue gene was identified (the human clone, DRES17).

## DNA/RNA

### Description

The prune gene is approximately 1,4 kb in length, consisting of 8 exons and 7 introns.

### Transcription

11 transcripts.

### Pseudogene

A Prune pseudogene, missing exon 4, is located in the 13q12 chromosomal region (acc. no. AF126025) (Reymond et al., 1999).

## Protein

### Description

Prune, a 62 kDa protein, belongs to the DHH family phosphoesterase proteins including RecJ DNA repair exonucleases, pyrophosphatases (PPASEs) and exopolyphosphatases (PPX). The DHH super-family can be divided into two main groups on the basis of a C-terminal motif that is very well conserved within each group, but not across the groups. All the members of this super-family possess four other motifs that contain highly conserved charged residues predicted to be responsible for binding ions and catalyzing the phosphoesterase reaction. The most characteristic of these is the third motif, with the signature DHH (Asp-His-His), after which this superfamily was named. Prune is a cyclic nucleotides phosphodiesterase. Due to its protein similarities, Prune might possess other biochemical functionalities within the DHH family of proteins.

The region between amino acids 353-370 of the h-Prune C-terminal is part of the h-Prune DHH2 domain, and in particular constitutes the second part of the last helix and a turned region that interacts with the preceding helix; accordingly, this region in the h-Prune C-terminal has a clear helical propensity. Therefore, the IDP h-Prune C-terminal domain that does not have specific interactions with the globular portions of the whole protein begins at residue 371 and retains the secondary structure propensities ( $\alpha 2$  and  $\alpha 3$ ) indicated by the NMR analysis, with a more compact C-terminal region (amino acids 410-440) (Carotenuto et al., 2013).

## Expression

H-prune overexpression in breast, colorectal and gastric cancers correlates with the degree of lymph-node and distant metastases.

## Localisation

Prune is localized intracellularly to the cytoplasm.

## Function

Prune has a role in the metastatic processes through specific inhibition of the anti-metastasis function of nm23-H1 *in vivo*.

Acting as a cytoplasmic cyclic nucleotides phosphodiesterases (cNMP-PDE), Prune is involved in both promoting cellular mobility and stimulating expression of genes involved in metastatic pathways.

An additional function has been discovered linking to the first mammalian exopolyphosphatase activity homologue protein, by degrading Poly-P in the cytoplasm, as a source of energy within the cell.

## Homology

The PRUNE gene is conserved in Rhesus monkey, dog, cow, mouse, rat, chicken, zebrafish, fruit fly, mosquito, *S. cerevisiae*, *K. lactis*, *E. gossypii*, *S. pombe*, *M. oryzae*, and *N. crassa*.

## Implicated in

### Various cancers

#### Note

Prune participates in the complex network of interactions with proteins involved in cell cycle and cell motility.

It is known that: (i) Prune together with glycogen synthase kinase-3 (GSK3 $\beta$ ), a kinase involved in WNT signaling pathway, cooperatively regulates the disassembly of focal adhesions to promote cell migration; (ii) Prune via interaction with Gelsolin, an ATP-severing protein acting in focal adhesions, leads to invasive properties for cancer cells. (iii) the h-prune interaction with NM23 in breast cells results in an increase in h-prune PDE activity, thus inducing negative regulation of nm23-H1 antimetastatic function.

### Colorectal and gastric cancers

#### Note

H-Prune overexpression correlates with T and N stages in colorectal cancer and its expression is an independent predictor of survival of patients with gastric cancer.

### Breast cancer

#### Note

In breast carcinoma, the overexpression of h-prune is associated with lymph node status and metastasis formation.

## Brain development

#### Note

Interestingly, Prune has also been shown to be highly expressed in brain development together with nm23-H1, expression was observed in cortex, hippocampus, midbrain and during cerebellum development.

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