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Gene Section
Short Communication

PRUNE (prune exopolyphosphatase)

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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 drosopterins "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 exopolyphospatases (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 (α2 and α3) 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 being 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 (GSK3β), 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 accociated 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.

References

Banfi S, Borsani G, Rossi E, Bernard L, Guffanti A, Rubboli F, Marchitiello A, Giglio S, Coluccia E, Zollo M, Zuffardi O, Ballabio A. Identification and mapping of human cDNAs homologous to Drosophila mutant genes through EST database searching. Nat Genet. 1996 Jun;13(2):167-74

Reymond A, Volorio S, Merla G, Al-Maghtheh M, Zuffardi O, Bulfone A, Ballabio A, Zollo M. Evidence for interaction between human PRUNE and nm23-H1 NDPKinase. Oncogene. 1999 Dec 2;18(51):7244-52

D'Angelo A, Garzia L, André A, Carotenuto P, Aglio V, Guardiola O, Arrigoni G, Cossu A, Palmieri G, Aravind L, Zollo M. Prune cAMP phosphodiesterase binds nm23-H1 and promotes cancer metastasis. Cancer Cell. 2004 Feb;5(2):137-49

D'Angelo A, Zollo M. Unraveling genes and pathways influenced by H-prune PDE overexpression: a model to study cellular motility. Cell Cycle. 2004 Jun;3(6):758-61

Zollo M, Andrè A, Cossu A, Sini MC, D'Angelo A, Marino N, Budroni M, Tanda F, Arrigoni G, Palmieri G. Overexpression of h-prune in breast cancer is correlated with advanced disease status. Clin Cancer Res. 2005 Jan 1;11(1):199-205

Kobayashi T, Hino S, Oue N, Asahara T, Zollo M, Yasui W, Kikuchi A. Glycogen synthase kinase 3 and h-prune regulate cell migration by modulating focal adhesions. Mol Cell Biol. 2006 Feb;26(3):898-911

Garzia L, D'Angelo A, Amoresano A, Knauer SK, Cirulli C, Campanella C, Stauber RH, Steegborn C, Iolascon A, Zollo M. Phosphorylation of nm23-H1 by CKI induces its complex formation with h-prune and promotes cell motility. Oncogene. 2008 Mar 20;27(13):1853-64

Tammenkoski M, Koivula K, Cusanelli E, Zollo M, Steegborn C, Baykov AA, Lahti R. Human metastasis regulator protein H-prune is a short-chain exopolyphosphatase. Biochemistry. 2008 Sep 9;47(36):9707-13

Galasso A, Zollo M. The Nm23-H1-h-Prune complex in cellular physiology: a 'tip of the iceberg' protein network perspective. Mol Cell Biochem. 2009 Sep;329(1-2):149-59

Virgilio A, Spano D, Esposito V, Di Dato V, Citarella G, Marino N, Maffia V, De Martino D, De Antonellis P, Galeone A, Zollo M. Novel pyrimidopyrimidine derivatives for inhibition of cellular proliferation and motility induced by h-prune in breast cancer. Eur J Med Chem. 2012 Nov;57:41-50

Carotenuto M, Pedone E, Diana D et al.. Neuroblastoma tumorigenesis is regulated through the Nm23-H1/h-Prune C-terminal interaction. Sci Rep. 2013;3:1351

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