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Identity

Other names: FLJ16691
HGNC (Hugo): PXN
Location: 12q24.23
Local order: Information about the local order of PXN can be found at ensembl.org.

DNA/RNA

Description
The PXN gene is 55.314 kb and consists of 12 exons. This gene is a member of the Human CCDS set: CCDS44996, CCDS44997, CCDS44998.

Transcription
The transcript is 3788 base pairs long. 4 isoforms have been identified.

Pseudogene
Not known.

Protein

Description
4 isoforms have been identified by alternative splicing. The 1st isoform is the normal variant and is comprised of 591 AA and weighs 68 kDa. The amino terminus region contains 5 LD-motifs, while the carboxy terminus contains 4 LIM-zinc binding domains. The protein also contains a proline rich region and several potential phosphorylation sites.

Expression
Epithelium.

Localisation
Found in the cytoplasm closely apposed to the plasma membrane at sites of focal adhesion to the extracellular matrix.
Function

**Focal adhesion protein:** This protein is a cytoskeletal component involved in focal actin-membrane attachments to the extracellular matrix. PXN can interact with multiple structural molecules and regulatory proteins to modulate adhesion, motility and survival of the cell by changing actin dynamics. Some PXN binding proteins have oncogenic equivalents, allowing cells to bypass normal adhesion and GF signaling cascades.

**Regulation:** PXN activity is regulated by various kinases. Adhesion and GF’s stimulate these kinases to phosphorylate LD motifs or LIM domains. Molecules such as Vinculin, FAK and SRC phosphorylate tyrosine residues of the N-terminal LD motifs. This results in recruitment of downstream effectors (like CRK) to mediate changes in cell motility or in modulation of gene expression via MAPK pathways. N-terminal serine phosphorylation has also been identified. Phosphorylation of serine and threonine residues of C-terminal LIM domains results in recruitment to focal adhesions. Identification of the C-terminal kinases is currently under investigation.

**Abbreviations:** CRK (CT10 sarcoma oncogene cellular homolog); FAK (focal adhesion kinase); GF (growth factor); MAPK (mitogen activated protein kinase); SRC (Rous sarcoma oncogene cellular homolog).

Homology

Member of the paxillin family, containing the 4 LIM-zinc binding domains.

Mutations

**Germinal**
Not known.

**Somatic**
Several single nucleotide polymorphisms have been identified. Point mutations between the LD1 and LD2 motifs have been associated with lung cancer, the A127T mutation being the most frequent mutation (Jagadeeswaran et al., 2008).

Implicated in

**Head and neck cancers**

**Note**
PXN overexpression has been reported in various head and neck cancers (Li et al., 2008; Dai et al., 2010; Shi et al., 2010). Metallopanstimulin-I expression has been associated with reduced PXN levels and tumor growth rate (Dai et al., 2010).

**Lung cancer**

**Note**
A significant correlation was found between the presence of the A127T mutation between the LD1 and LD2 regions of PXN with non small cell lung cancer (Jagadeeswaran et al., 2008). A possible mechanism is that mutations between the LD1 and 2 regions confer resistance to calpain mediated proteolysis of PXN (Cortesio et al., 2011). However, two later studies did not find this mutation to exist in lung cancer or any other solid tumor (Pallier et al., 2009; Kim et al., 2011). Overexpression of PXN in non small cell lung cancer has been reported with less controversy (Jagadeeswaran et al., 2008; Zhao et al., 2010; Mackinnon et al., 2011). The overexpression could possibly be due to rearrangements on chromosome 12 (Wu et al., 2010).

Breast cancer

**Note**
Metastatic potential was found to be directly related to PXN levels (Cai et al., 2010). The relationship between PXN and Her-2 expression is controversial. A study in 2007 found a direct relationship between the 2 markers (Short et al., 2007) while a 2011 study found no such link (Panousis et al., 2011).

Prostate cancer

**Note**
PXN up regulation was found to promote adhesion and motility of prostate cancer cells (Bokobza et al., 2010).

To be noted

**Note**
The link between PXN mutations and increased growth rate and invasion of cancer cells is controversial. On the contrary, amplification and/or overexpression of PXN has been consistently reported in the literature.

References


This article should be referenced as such: