LPP (lipoma preferred partner)

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Published in Atlas Database: May 2004

Online updated version: http://AtlasGeneticsOncology.org/Genes/LPPID72.html

DOI: 10.4267/2042/38093

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Identity

HGNC (Hugo): LPP

Location: 3q27-q28

DNA/RNA

Description

At least 11 exons; predicted start codon in exon 3, stop codon in exon 11; the protein coding region is covered by the overlapping “CEPH Mark 1” YAC clones 135H6 and 192B10 (start codon in 135H6, stop codon in 192B10) and is dispersed over at least 400 kb genomic DNA; the LIM domains are encoded by separate exons: LIM 1 is encoded by exon 8, LIM 2 by exon 9, and LIM 3 by exon 10 and part of exon 11.

Transcription

mRNA: ubiquitously: > 10 kb; testis: additional transcripts of 1.8 kb and 1.25 kb.

Pseudogene

No pseudogenes.

Probe(s) - Courtesy Mariano Rocchi, Resources for Molecular Cytogenetics.

![Image of LPP gene and protein](image-url)
Protein

Description
612 amino acids; proline-rich region (amino-terminal 2/3 of the protein) followed by three LIM domains (carboxy-terminal 1/3 of the protein). Proline-rich region contains an alpha-actinin binding site, two VASP-binding motifs, and a nuclear export signal.

Expression
Smooth muscle marker; readily detected on Western blot with an LPP-antibody in all fibroblastic and epithelial cell lines tested to date.

Localisation
LPP is present in the cytoplasm of cells as well as at sites of cell adhesion such as focal adhesions (attachments sites to the extracellular matrix) and cell-cell contacts; LPP also shuttles to the nucleus and its nuclear-cytoplasmic localisation is regulated in part by a nuclear export signal (NES) which is sensitive to the drug leptomycin B.

Function
Because of their structural features (many protein-protein interaction domains) and their characteristic to shuttle between the nucleus and the cytoplasm, LPP and its family members (see below) have been proposed to be scaffolding proteins involved in signal transduction from sites of cell adhesion to the nucleus; LPP has been shown to harbour transcriptional activation capacity in luciferase reporter assays, suggesting that LPP may be directly involved in the regulation of gene expression; LPP was found to be highly expressed in smooth muscle, and a role for LPP in regulating cell motility was proposed; the precise function of LPP remains to be elucidated.

Homology
LPP is a member of the zyxin family of proteins, which contains five members: ajuba, LIMD1, LPP, TRIP6 and zyxin. The family hallmark of these proteins are three clustered LIM domains at the carboxy-terminus, which are protein interaction domains. All family members are present at sites of cell adhesion and have the ability to shuttle to the nucleus, and all family members have one or more nuclear export signals.

Mutations

Somatic
HMGA2/LPP fusion proteins and MLL/LPP fusion proteins (Fig2).

Implicated in

Solitary lipomas
Disease
Benign tumors of adipose tissue.

Prognosis
Can be surgically removed with no recurrence in most cases.

Cytogenetics
More than 60% of solitary lipomas have an aberrant karyotype; 2/3 of these carry 12q15 rearrangements, most often translocations, affecting the HMGA2 gene; 1/4 of the latter have chromosomal region 3q27-q28 (containing LPP) as 12q15 translocation partner as such creating an HMGA2/LPP fusion gene.

Hybrid/Mutated gene
HMGA2/LPP hybrid gene containing the first three exons of HMGA2 and exons 8-11 or 9-11 of LPP; under the regulation of the HMGA2 promoter.

Abnormal protein
HMGA2/LPP fusion transcripts encode the three DNA-binding domains of HMGA2 followed by two LIM domains (LIM 2 and LIM 3) or a portion of the proline-rich region and all three LIM domains of LPP.

Pulmonary chondroid hamartomas
Disease
Benign mesenchymal tumors of the lung.

Prognosis
Good

Cytogenetics
More than 70% of pulmonary chondroid hamartomas have an aberrant karyotype; 70% of these carry 12q15 rearrangements, most often translocations, affecting the HMGA2 gene; 1/8 of the latter have chromosomal region 3q27-q28 (containing LPP) as 12q15 translocation partner as such creating an HMGA2/LPP fusion gene.

Hybrid/Mutated gene
HMGA2/LPP hybrid gene containing the first three exons of HMGA2 and exons 9-11 of LPP; under the regulation of the HMGA2 promoter.

Abnormal protein
HMGA2/LPP fusion transcripts encode the three DNA-binding domains of HMGA2 followed by the two most carboxy-terminal LIM domains (LIM 2 and LIM 3) of LPP.

Parosteal lipoma
Disease
Rare deep-seated benign tumor of adipose tissue comprising less than 0.5% of all lipomas; parosteal lipomas exhibit a contiguous relationship with the periostium; because of their intimate relationship to the bone, they are considered as lipomas of bone.

Prognosis
Most often asymptomatic; in some cases: loss of motor and/or sensory function as a result of the compression or stretching of a nerve.
Hybrid/Mutated gene
HMGA2/LPP hybrid gene containing the first three exons of HMGA2 and exons 9-11 of LPP; under the regulation of the HMGA2 promoter.

Abnormal protein
HMGA2/LPP fusion transcripts encode the three DNA-binding domains of HMGA2 followed by the two most carboxy-terminal LIM domains (LIM 2 and LIM 3) of LPP.

Soft tissue chondroma
Disease
Benign tumor of cartilage; rare entity.

Cytogenetics
Only 31 cases with abnormal karyotypes have been reported (11-2003); 12q15 nonrandomly involved; one case reported with rearrangement of LPP t(3;12)(q27;q15).

Hybrid/Mutated gene
HMGA2/LPP hybrid gene containing the first three exons of HMGA2 and exons 9-11 of LPP; under the regulation of the HMGA2 promoter.

Abnormal protein
HMGA2/LPP fusion transcripts encode the three DNA-binding domains of HMGA2 followed by the two most carboxy-terminal LIM domains (LIM 2 and LIM 3) of LPP.

AML-M5
Disease
Secondary leukemia following treatment with DNA topoisomerase II inhibitors.

Cytogenetics
MLL gene on 11q23 frequently involved; one case reported with rearrangement of LPP t(3;11)(q28;q23).
Hybrid/Mutated gene

MLL/LPP hybrid gene containing the first 8 exons of MLL and exons 9-11 of LPP; under the regulation of the MLL promoter.

Abnormal protein

MLL/LPP fusion transcripts encode the three DNA-binding domains and the methyltransferase-like domain of MLL followed by the two most carboxy-terminal LIM domains (LIM 2 and LIM 3) of LPP.

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