Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

Gene Section
Mini Review

LASP1 (LIM and SH3 protein)

Sabine Strehl

Children's Cancer Research Institute, Kinderspitalgasse 6, A-1090 Vienna, Austria (SS)

Published in Atlas Database: August 2005

Online updated version: http://AtlasGeneticsOncology.org/Genes/Lasp1ID203.html
DOI: 10.4267/2042/38246

This article is an update of: Rio MC. LASP1 (LIM, actin binding and SH3 protein). Atlas Genet Cytogenet Oncol Haematol.2000;4(2):51.

Identity

Other names: MLN50, EVI149

HGNC (Hugo): LASP1

Location: 17q12-21

Local order: from centromere to telomere are: TRAF4 (alias MLN62/CART1), MLLT6 (alias AF17), LASP1, STARD3 (alias MLN64), ERBB2 (alias c-erbB2), and RARA.

DNA/RNA

Description

LASP1 encompasses 51.65 kb on the genomic level and consists of 7 exons.

Transcription

3845 bp mRNA, 783 bp coding sequence.

Protein

Description

261 amino acids; 29 kDa. LASP1 encodes a member of a LIM (Lin-11, Isl-1 and Mec-3) protein subfamily and is characterized by a LIM motif (cysteine-rich LIM/double zinc finger motif) at the N-terminus, an SH3 domain (Src homology region 3) at the C-terminus, and two actin-binding domains in the core of the protein

Expression

Ubiquitous.

Localisation

Intracellular, cytoplasmic; associated with the F-actin rich cortical cytoskeleton.

Function

LASP1 plays an important role in the regulation of dynamic actin-based, cytoskeletal activities and cell motility. Agonist-dependent changes in LASP1 phosphorylation may also serve to regulate actin-associated ion transport activities, not only in the parietal cell but also in certain other F-actin-rich secretory epithelial cell types. Together, (LIM-) nebulette, Lasp-1, and zyxin may play an important role in the organization of focal adhesions.

Homology

LASP family of proteins: actin-binding repeats similar to those in LASP1 are also present in other nebulin-related proteins such as NEBL (nebulette, 107 kD actin-binding Z-disk protein) and NRAP (nebulin-related anchoring protein); NRAP also contains an N-terminal LIM domain and NEB (nebulin) a C-terminal SH3 domain, both of which are highly homologous to the respective domains of LASP1.

Implicated in

t(11;17)(q23;q12) --> MLL-LASP1

Disease

Infant AML-M4; only one case described so far.

Abnormal protein

The MLL-LASP1 chimeric protein consists of the AT-hook DNA-binding domain and the methyltransferase motif including the CXXC zinc-finger domain of MLL and the SH3 domain of LASP1.

Breast carcinomas

Disease

17q11-q21 amplification is found in about 25% of primary breast carcinomas; simultaneous amplification

and overexpression of LASP1 and ERBB2.

Prognosis

Poor clinical outcome; increase risk of relapse.

References

Tomasetto C, Moog-Lutz C, Régnier CH, Schreiber V, Basset P, Rio MC. Lasp-1 (MLN 50) defines a new LIM protein subfamily characterized by the association of LIM and SH3 domains. FEBS Lett. 1995 Oct 16;373(3):245-9

Tomasetto C, Régnier C, Moog-Lutz C, Mattei MG, Chenard MP, Lidereau R, Basset P, Rio MC. Identification of four novel human genes amplified and overexpressed in breast carcinoma and localized to the q11-q21.3 region of chromosome 17. Genomics. 1995 Aug 10;28(3):367-76

Bièche I, Tomasetto C, Régnier CH, Moog-Lutz C, Rio MC, Lidereau R. Two distinct amplified regions at 17q11-q21 involved in human primary breast cancer. Cancer Res. 1996 Sep 1;56(17):3886-90

Chew CS, Parente JA Jr, Zhou C, Baranco E, Chen X. Lasp-1 is a regulated phosphoprotein within the cAMP signaling pathway in the gastric parietal cell. Am J Physiol. 1998 Jul;275(1 Pt 1):C56-67

Schreiber V, Masson R, Linares JL, Mattei MG, Tomasetto C, Rio MC. Chromosomal assignment and expression pattern of the murine Lasp-1 gene. Gene. 1998 Jan 30;207(2):171-5

Schreiber V, Moog-Lutz C, Régnier CH, Chenard MP, Boeuf H, Vonesch JL, Tomasetto C, Rio MC. Lasp-1, a novel type of actin-binding protein accumulating in cell membrane extensions. Mol Med. 1998 Oct;4(10):675-87

Chew CS, Parente JA Jr, Chen X, Chaponnier C, Cameron RS. The LIM and SH3 domain-containing protein, lasp-1, may link the cAMP signaling pathway with dynamic membrane restructuring activities in ion transporting epithelia. J Cell Sci. 2000 Jun;113 (Pt 11):2035-45

Chew CS, Chen X, Parente JA Jr, Tarrer S, Okamoto C, Qin HY. Lasp-1 binds to non-muscle F-actin in vitro and is localized within multiple sites of dynamic actin assembly in vivo. J Cell Sci. 2002 Dec 15;115(Pt 24):4787-99

Butt E, Gambaryan S, Göttfert N, Galler A, Marcus K, Meyer HE. Actin binding of human LIM and SH3 protein is regulated by cGMP- and cAMP-dependent protein kinase phosphorylation on serine 146. J Biol Chem. 2003 May 2;278(18):15601-7

Strehl S, Borkhardt A, Slany R, Fuchs UE, König M, Haas OA. The human LASP1 gene is fused to MLL in an acute myeloid leukemia with t(11;17)(q23;q21). Oncogene. 2003 Jan 9;22(1):157-60

Keicher C, Gambaryan S, Schulze E, Marcus K, Meyer HE, Butt E. Phosphorylation of mouse LASP-1 on threonine 156 by cAMP- and cGMP-dependent protein kinase. Biochem Biophys Res Commun. 2004 Nov 5;324(1):308-16

Li B, Zhuang L, Trueb B. Zyxin interacts with the SH3 domains of the cytoskeletal proteins LIM-nebulette and Lasp-1. J Biol Chem. 2004 May 7;279(19):20401-10

Lin YH, Park ZY, Lin D, Brahmbhatt AA, Rio MC, Yates JR 3rd, Klemke RL. Regulation of cell migration and survival by focal adhesion targeting of Lasp-1. J Cell Biol. 2004 May 10;165(3):421-32

Phillips GR, Anderson TR, Florens L, Gudas C, Magda G, Yates JR 3rd, Colman DR. Actin-binding proteins in a postsynaptic preparation: Lasp-1 is a component of central nervous system synapses and dendritic spines. J Neurosci Res. 2004 Oct 1;78(1):38-48

This article should be referenced as such:

Strehl S. LASP1 (LIM and SH3 protein). Atlas Genet Cytogenet Oncol Haematol. 2005; 9(4):310-311.