

Gene Section

Mini Review

LPHN2 (Iatrophilin 2)

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Identity

Other names: LPHH1; LEC1; KIAA0786

HGNC (Hugo): LPHN2

Location: 1p31.1

Local order: --ELTD1---LPHH1----FLJ23033----
PRKACB--

DNA/RNA

Description

LPHH1 consists of 19 commonly used coding exons. A further seven exons have been identified which may be alternatively spliced into the core backbone with variable frequencies and tissue specificities. At least a number of these additional exons are highly conserved in mammalian species. The core exons (ATG, exon 1 to stop, exon 19) span a region of about 154 kb. However, the 5'end

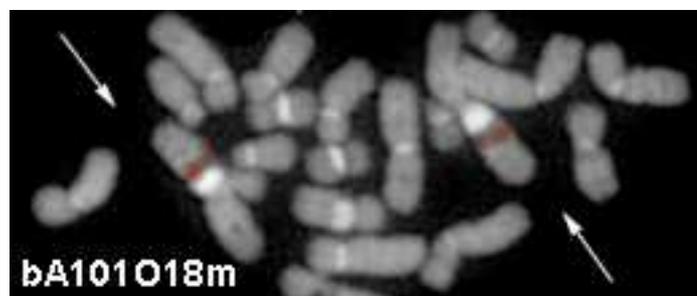
of the gene is not precisely defined with transcripts in different tissues apparently initiating from specific locations over an extensive region. The most distant leader exon identified (foetal lung) lies approximately 390 kb from exon 1 which makes the total size of the gene at least 550 kb.

Transcription

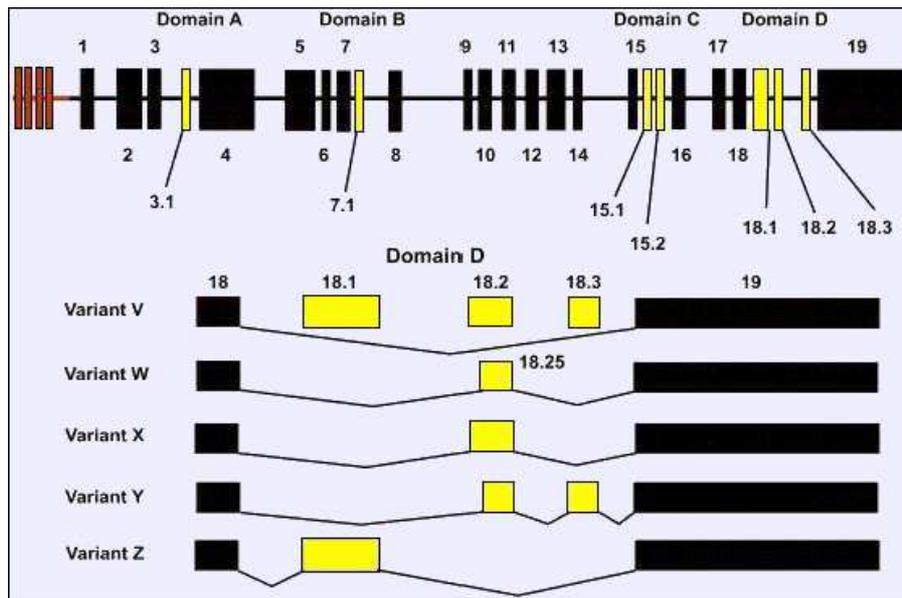
Expression has been observed by RT-PCR in all normal tissues and lines tested with the clear exception of lymphocytes and lymphoblastoid cells. Strongest expression was observed in foetal lung, normal adult lung and thyroid. Alternative splicing to some degree in at least one domain (minimally the carboxy-terminal domain D) was seen in each tissue and line examined with human brain showing a characteristic pattern and additional variability in the other three coding sequence domains.

Pseudogene

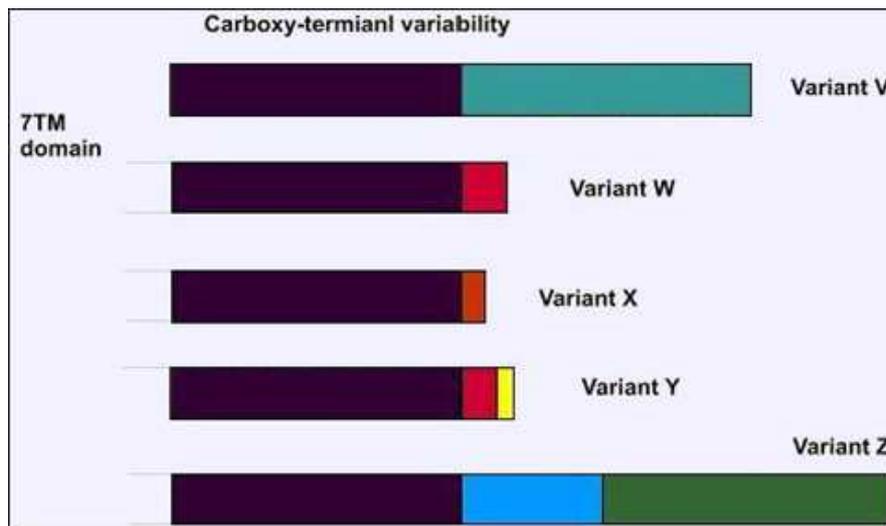
No known pseudogene.



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



Representation of the genomic structure of LPHN1. Black blocks represent core exons which are present in the majority of gene transcripts. The yellow blocks represent alternatively spliced coding exons which may be incorporated variably in transcripts derived from different cell types/tissues or as a consequence of differing cellular states. The red boxes represent the presence of multiple, in some cases tissue-specific, leader exons that have been identified for this gene, an observation consistent with the existence of multiple dispersed promoter elements. The most variably spliced region of the coding sequence was the carboxy-terminal domain D.



Alternative splicing in domain D dramatically alters the structure of the carboxy-terminus of the encoded protein, latrophilin 2. Variable splicing in this region occurs in all tissues and cell lines tested.

Protein

Description

LPHN1 encodes a putative seven-span transmembrane receptor with atypically large extra membrane N (predicted to be extra-cellular) and C termini. In addition to the seven hydrophobic membrane spanning domains, a putative lectin-like region is present near the N-terminus.

Expression

Protein likely to be ubiquitously expressed in adherent

cells but that has not so far been confirmed. Human brain-specific alternative splices alter the structure of the extra-membrane, intra-cellular loop between TM domains 5 and 6, a region thought to be critical for G-protein/receptor interactions.

Localisation

Likely to be plasma membrane.

Function

Likely role in coupling cell adhesion to cell signalling.

Homology

Latrophilin 2 is part of a small sub-family of 7 TMs which includes latrophilins 1 and 3. Latrophilin 1 is the receptor for Black Widow spider toxin: -latrotoxin.

Mutations**Note**

None reported.

Implicated in**Breast carcinoma****Note**

Analysis of breast cancer cell lines has demonstrated dramatic differences in transcript levels between certain lines. In one case, strong expression was allelically imbalanced.

Lung carcinoma**Note**

Strong expression in normal lung was reduced in 55% (35/64) of matched primary non-small cell lung carcinomas (NSCLC). Over-representation was not scored in any tumour, nor in any lung cancer cell line tested and transcript was undetectable by RT-PCR in one line (1/15) and very low in a further two. Loss of heterozygosity was scored in 8/16 informative NSCLC lesions. Primary and SCLC lines showed a characteristic pattern of alternative splicing.

References

Hayflick JS. A family of heptahelical receptors with adhesion-like domains: a marriage between two super families. *J Recept Signal Transduct Res.* 2000 May-Aug;20(2-3):119-31

White GR, Varley JM, Heighway J. Genomic structure and expression profile of LPHH1, a 7TM gene variably expressed in breast cancer cell lines. *Biochim Biophys Acta.* 2000 Apr 25;1491(1-3):75-92

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