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Gene Section
Mini Review

L1CAM (L1 cell adhesion molecule)

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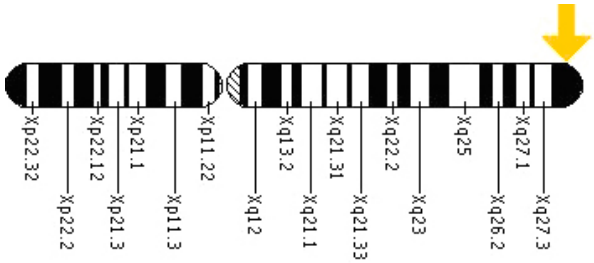
Identity

Other names: CAML1; CD171; HSAS; HSAS1; MASA; MIC5; N-CAML1; S10; SPG1

HGNC (Hugo): L1CAM

Location: Xq28



Picture from Genetics Home Reference; Reviewed March 2008.

DNA/RNA

Description

The L1CAM gene is 24,657 bp in length, consisting of 28 exons according to Ensembl and Entrez-gene.

Transcription

There are 7 transcripts of the gene according to Ensembl.

Protein

Description

L1CAM (L1) is a 200-220 kD glycoprotein and a member of the immunoglobulin superfamily. This type-1 transmembrane protein consists of six immunoglobulin like domains at the amino terminal end of the molecule followed by five fibronectin type III homologous repeats, a single trans-membrane region and a short intracellular domain (Moos et al., 1988). Two splicing variants are known encoding for 1257 and 1253 amino acids proteins.

Expression

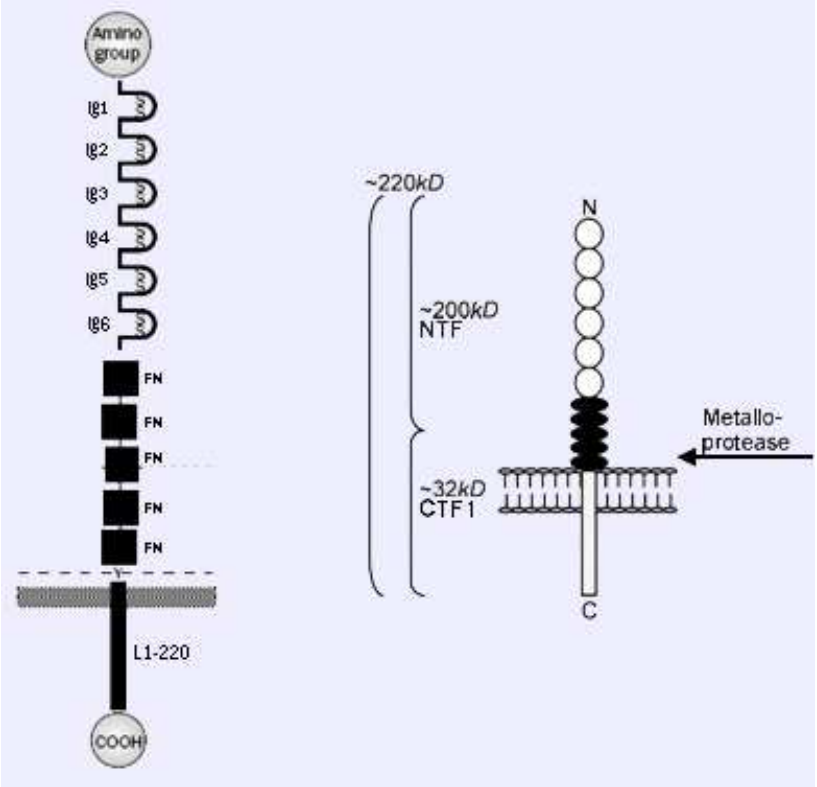
Neural, hematopoietic and transformed epithelial cells.

Localisation

Cell surface, extracellular matrix and nucleus (C-terminal fragment).

Function

L1 plays a critical role in axon outgrowth and fasciculation, neuronal migration and survival, synaptic plasticity and regeneration after trauma (Maness et al., 2007). L1 can interact with itself (homophilic) but also with a variety of heterophilic ligands such as integrins, CD24, neurocan, neuropilin-1 and other members of the neural cell adhesion family. In many incidences the binding sites in the L1 molecule have been mapped. The RGD site in the sixth Ig domain supports α5β1, αvβ3,5 integrin-mediated cell binding and the first Ig domain can bind to the proteoglycan neurocan or the VEGF-R2-coreceptor neuropilin-1.
Beside its cell surface localization, L1CAM can also be cleaved by several proteases, i.e. the matrix metalloproteinases ADAM10 and ADAM17, metalloprotease PC5A proprotein convertase or by γ-secretases (Maretzky et al., 2005). Soluble L1CAM has been reported to be important for migration of neuronal as well as of tumor cells (Maretzky et al., 2005; Mechtersheimer et al., 2001), and several studies support a role for L1CAM in tumor growth (Arlt et al., 2006), tumor cell invasion, metastasis of melanoma, ovarial and



Protein domain structure (left) and cleavage sites (right) of L1CAM. NTF, 200 kDa N-terminal cleavage product; CTF1, 32 kDa C-terminal cleavage product; Ig, immunoglobulin like domain; FN, fibronectin like domain (From Fogel et al., 2003 and Maretzky et al., 2005).

colon cancer (Mechtersheimer et al., 2001; Gavert et al., 2005; Fogel et al., 2003) and chemoresistance (Sebens Müerköster et al., 2007; Stoeck et al., 2007).
L1 transiently activates pp60$^{c\text{-}src}$, phosphoinositide 3-kinase (PI3 kinase), the VAV2 guanine nucleotide exchange factor, the RAC1 GTPase and p21-activated kinase (PAK1) in a pathway culminating in MEK and ERK activation.

Homology

NrCAM/BRABO, CHL1, neurofascin; in invertebrates, neuroglian and sax-7.

Mutations

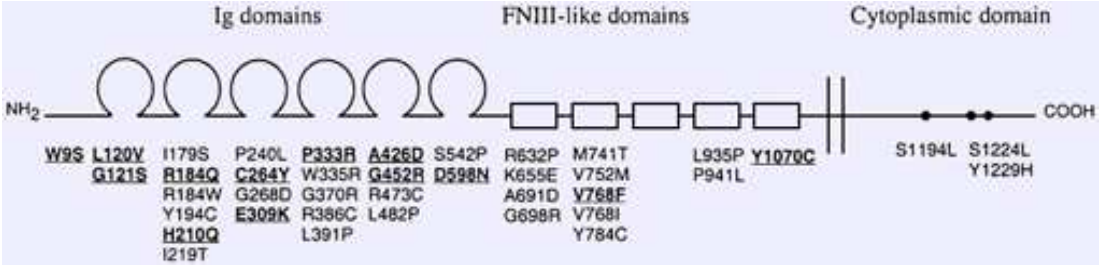
Germinal

Numerous mutations in the L1CAM gene are known (De Angelis et al., 1999) accounting for X-linked neurological syndromes (corpus callosum hypoplasia, retardation, aphasia, spastic paraplegia and hydrocephalus). Alternative splicing of a neuron-specific exon is thought to be functionally relevant.

Implicated in

Note
Various cancers.

Disease
Overexpression of L1 has been reported in ovarian cancer, colon cancer, glioma, renal cell cancer, neuroblastoma, endometrial cancer, melanoma, pancreatic cancer. L1 expression promotes invasiveness of the tumor as well as chemoresistance. Thus, L1 expression is mainly found in the invasive front of coloretal cancer and blockade of L1 reduces tumor growth in mouse models. Blockade of L1 dimishes resistance of ovarian and pancreatic cancer towards anti-cancer drugs.



Prognosis

In ovarian cancer, L1 expression associates with poor prognosis. Other L1 expressing tumor entities include those with extremely poor prognosis, i.e. pancreatic or renal cell cancer.

Various diseases

Disease

L1 mutations associate with X-linked mental retardation (=L1 syndrome: mental retardation, hydrocephalus, aphasia, spastic paraplegia, agenesis of corpus callosum, optic nerve atrophy), Hirschprung's disease and schizophrenia in some populations.

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