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Gene Section
Mini Review

LCK (lymphocyte-specific protein tyrosine kinase)

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Identity

Other names: P56-LCK LSK (T cell-specific protein-tyrosine kinase); lck tyrosine kinase (AA 1-142); membrane associated protein tyrosine kinase proto-oncogene LCK; protein-tyrosine kinase put. ptk (135aa); tyrosine kinase

HGNC (Hugo): LCK

Location: 1p34.3

DNA/RNA

Description

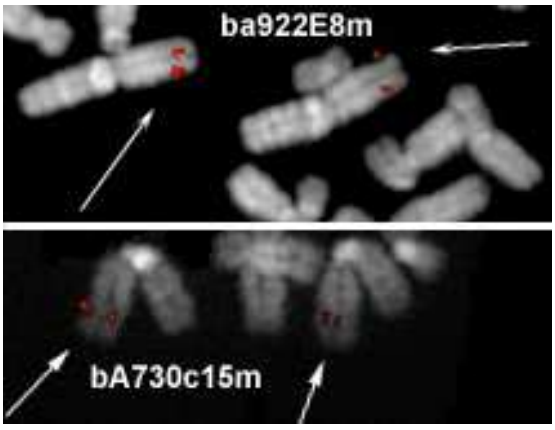
DNA sequence is located on chromosome no.1 on the arm 1(p).

Transcription

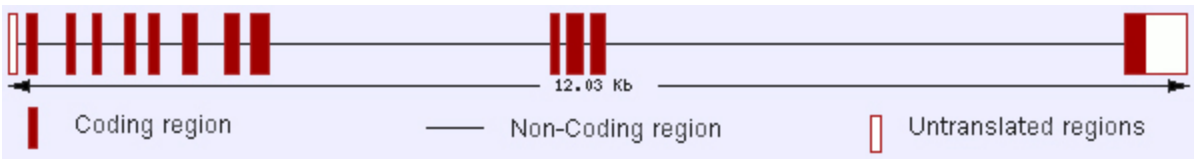
Consists of 13 exons and 12 introns spanning 12.3 kb.

Pseudogene

Unknown



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



Protein

Description

The kinase p56lck (509 aa) is a T-lymphocyte-specific member of the Src family of non-receptor protein tyrosine kinase. Lck is a 56 kDa phosphoprotein expressed in variety of lymphoid and non-lymphoid cell lineages. Lck contain myristylation sequence, unique amino-terminal regions, followed by Src homology domains SH3 and SH2, a tyrosine kinase catalytic domain, and C-terminal regulatory domain. Lck associates with the inner face of the plasma membrane through its amino-terminus. This interaction is mediated by both myristic acid and palmitic acid that are bound to the amino terminal glycine and Cys-3 and/or Cys-5. The Unique region of Lck represents the domain possessing the greatest sequence diversity within this group of enzymes. This domain is thought to be involved in the interaction of the Lck with specific cellular proteins including Lck substrate. In T-cells it is known, to mediate association with the cytoplasmic tail of T-cell coreceptors CD4 and CD8a. SH3 (Src homology 3) domain is mainly implicated in the regulation of protein-protein interactions, recognizing proline-rich region found in guanine nucleotide exchange factors and GTPase activating proteins. SH2 (Src homology 2) domain of Lck recognizes phosphorylated tyrosine residues on other proteins thereby facilitating the formation of tyrosine phosphorylation-induced multimeric complexes. The tyrosine kinase domain is the catalytic domain of Lck catalyzing the transfer of the gamma-phosphate from ATP to tyrosine residues on proteins. The catalytic domain contains a site of autophosphorylation (Tyr-394), which plays an important role in regulating the protein kinase activity. A C-terminal regulatory domain is also seen containing the major site of tyrosine phosphorylation in vivo (Tyr-505). Phosphorylation of Csk (C-terminal Src kinase) at Tyr-505 leads to inactivation of Lck. Lck is also activated by oxidative stress. Reoxygenation after hypoxia induces Lck kinase activity.

Expression

Expressed in variety of lymphoid and non-lymphoid cell lineages (Breast cancer tissues and other cancers too).

Localisation

Cell membrane.

Function

T-cell development.

T-cell activation.

Homology

Shares sequence homology with other Src family kinases (Src, Hck, Fyn, Blk, Lyn, Fgr, Yes, and Yrk).

Mutations

Note

Not reported yet.

Implicated in

Breast cancer, T-cell Leukemia, Colon carcinoma

Oncogenesis

Upregulation of Lck is seen in many cases of Breast cancer. It is also overexpressed in lymphoma, colon cancer. Rearrangement of LCK gene is also reported in murine lymphoma cell line. Oncogenic activation of Lck due translocation of the LCK gene is reported in the human HSB2 T-cell leukemia with t(1;7)(p34;q34) with LCK/ TCRB involvement. Lck regulates cell motility through NF-KB mediated uPA secretion following hypoxia and reoxygenation in Breast cancer.

Disease

Type 1 Diabetes.

Prognosis

T-cell mediated Type diabetes (Autoimmune disease) shows defect in TCR/CD3-mediated T-cell activation due to the abnormal expression of LCK.

References

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