p56 Lck deficiency

GENERAL INFORMATION

Description:

p56 Lck deficiency is a unique form of SCID with selective CD4 lymphopenia and reduced production of the p56lck protein. A chromosomal aberration involving LCK is found also in leukemias.

Alternative names:

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- CD4 deficiency-LCK

Classification:

- Combined B and T cell immunodeficiencies
  - Other

Inheritance:

Autosomal recessive

OMIM:

- *153390 Lymphocyte-specific protein-tyrosine kinase; LCK

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for JAK3 deficiency
- IDR factfile for X-linked SCID(gamma-chain deficiency)

Incidence:

Incidence is not known.

CLINICAL INFORMATION

Description:

Patients have in the first year of life failure to thrive, opportunistic infections, and low or absent immunoglobulin levels.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Severe combined immunodeficiency, X-linked, eMedicine

Genetic:

- IDdiagnostics, LCK

Therapeutic options:

- Bone marrow transplantation is the only treatment of SCID. Other recommendations include intravenous gamma-globulin infusion, irradiation of all blood products, antibiotherapy.
- eMedicine

Research programs, clinical trials:

- European Initiative for Primary Immunodeficiencies

GENE INFORMATION

Names:

HUGO name: LCK
Alias(es): Lymphocyte-specific protein tyrosine kinase, Proto-oncogene tyrosine-protein kinase, P56-LCK, LSK, T cell-specific protein-tyrosine kinase

Localization:

Reference sequences:

DNA: X14055 (EMBL) , **cDNA:** X13529 (EMBL) , **Protein:** P06239 (SWISSPROT) Other Sequences

Chromosomal Location:

1p35-p34.3

Maps:

LCK (Map View)

Other gene-based resources:

Ensembl: ENSG00000182866, GENATLAS: LCK, GeneCard: LCK, UniGene: 470627, Entrez Gene: 3932, euGenes: 3932, GDB: 119360, HomoloGene: 3911

PROTEIN INFORMATION

Description:

Protein function:

May participate in antigen-induced T-cell activation.

Catalytic activity:

ATP + a protein tyrosine = ADP + a protein tyrosine phosphate.

Subunit:

Binds to phosphatidylinositol 3'-kinase (PI3k) from T lymphocytes through its SH3 domain and to the tyrosine phosphorylated form of khdrbs1/p70 through its SH2 domain. Binds to HIF-1 nef through its SH3 domain. This interaction inhibits its tyrosine-kinase activity.

Subcellular location:

Bound to the cytoplasmic domain of either CD4 or CD8.

Similarity:

Belongs to the tyr protein kinase family. Src subfamily.

Structures (PDB):

1BHF	P56Lck Sh2 Domain Inhibitor Complex
1BHH	Free P56Lck Sh2 Domain
1CWD	Human P56Lck Tyrosine Kinase Complexed With Phosphonopeptide
1CWE	Human P56Lck Tyrosine Kinase Complexed With Phosphonopeptide
1FBZ	Structure-Based Design Of A Novel, Osteoclast-Selective, Nonpeptide Src Sh2 Inhibitor With In Vivo Anti-Resorptive Activity
1H92	Sh3 Domain Of Human Lck Tyrosine Kinase
1IJR	Crystal Structure Of Lck Sh2 Complexed With Nonpeptide Phosphotyrosine Mimetic
1KIK	Sh3 Domain Of Lymphocyte Specific Kinase (Lck)
1LCJ	Sh2 (Src Homology-2) Domain Of Human P56-Lck Tyrosine Kinase Complexed With The 11 Residue Phosphotyrosyl Peptide Epqpyeeipiyl
1LCK	Sh3-Sh2 Domain Fragment Of Human P56-Lck Tyrosine Kinase Complexed With The 10 Residue Synthetic Phosphotyrosyl Peptide Tegqpyqpqpa
1LKK	Human P56-Lck Tyrosine Kinase Sh2 Domain In Complex With The Phosphotyrosyl Peptide Ac-Ptyr-Glu-Glu-Ile (Pyeei Peptide)
1LKL	Human P56-Lck Tyrosine Kinase Sh2 Domain In Complex With The Phosphotyrosyl Peptide Ac-Ptyr-Glu-Glu-Gly (Pyeeg Peptide)
1Q68	Solution Structure Of T-Cell Surface Glycoprotein Cd4 and Proto-Oncogene Tyrosine-Protein Kinase Lck Fragments
1Q69	Solution Structure Of T-Cell Surface Glycoprotein Cd8 Chain and Proto-Oncogene Tyrosine-Protein Kinase Lck Fragments
1QPC	Structural Analysis Of The Lymphocyte-Specific Kinase Lck In Complex With Non-Selective and Src Family Selective Kinase Inhibitors
1QPD	Structural Analysis Of The Lymphocyte-

Domains:

SH3 domain: 60-120

SH2 domain: 126-223

Protein kinase domain: 244-497

Other features:

ATP nucleotide phosphate-binding region: 250-258

Atp binding site: 272

Other related resourses:

PIR: OKHULK, InterPro: IPR000719; Prot_kinase, InterPro: IPR000980; SH2, InterPro: IPR001452; SH3, InterPro: IPR001245; Tyr_pkinase, InterPro: IPR008266; Tyr_pkinase_AS, Pfam: PF00017; SH2, Pfam: PF00018; SH3_1, PRINTS: PR00401; SH2DOMAIN, PRINTS: PR00452; SH3DOMAIN, PRINTS: PR00109; TYRKINASE, ProDom: PD000001; Prot_kinase, ProDom: PD000093; SH2, SMART: SM00252; SH2, SMART: SM00326; SH3, SMART: SM00219; TyrKc, PROSITE: PS00107; PROTEIN_KINASE_ATP, PROSITE: PS50011; PROTEIN_KINASE_DOM, PROSITE: PS00109; PROTEIN_KINASE_TYR, PROSITE: PS50001; SH2, PROSITE: PS50002; SH3

Expression pattern for human:

Tissue	Exp. (%)	Clones
thymus	25.04	3:5542
thymus	20.57	1:2249
human embryonic stem cells	19.24	3:7214
lymph_node	12.71	32:116453
spleen	5.96	2:15523
pancreatic islet	3.35	1:13811
blood	2.90	3:47876
vascular	2.37	1:19518
pluripotent cell line derived from blastocyst inner cell mass	2.01	1:23025
other	1.36	13:442392

Animal models:

Mouse:

NCBI Gene: ; 16818 (96.66 % aminoacid similarity to human)

Rat:

NCBI Gene: ; 313050 (96.46 % aminoacid similarity to human)

OTHER RESOURCES

Societies:

General:

- IPOPI, International Patient Organization for Primary Immunodeficiencies
- The Jeffrey Modell Foundation
- National Center for Biotechnology Information
- Immune Deficiency Foundation
- European Society for Immunodeficiencies

Other information sources:

- Immunodeficiencies