ZAP-70 deficiency

GENERAL INFORMATION

Description:

ZAP-70 deficiency is a rare autosomal recessive form of severe combined immunodeficiency characterized by the selective absence of CD8+ T cells and by abundant CD4+ T cells in the peripheral blood that are unresponsive to T cell receptor (TCR)-mediated stimuli in vitro. Eight children from five families were described in the literature.

Alternative names:

- Zeta associated protein of 70kDa

Classification:

- Combined B and T cell immunodeficiencies
  - Other

Inheritance:

Autosomal recessive

OMIM:

- #600802 Severe combined immunodeficiency, autosomal recessive, T-negative/B-positive type
- +176947 Zeta-chain-associated protein kinase; ZAP70

Cross references:

Phenotype related immunodeficiencies:

- TMEM142 deficiency

Incidence:

Incidence is not known.

CLINICAL INFORMATION

Description:

Nearly all patients with ZAP-70 defects presented with typical clinical features of SCID in early life: severe pulmonary infection often sustained by opportunistic pathogens (Pneumocystis Carinii), chronic diarrhea, failure to thrive, and persistent candidiasis. Most patients have detectable lymphoid tissue since peripheral blood lymphocyte counts are normal or elevated.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Severe Combined Immunodeficiency, eMedicine
- ZAP70 deficiency, ORPHANET

Genetic:

- ZAP70, IDdiagnostics

Therapeutic options:

- Bone marrow transplantation have been successful. Isolation in a protected environment. Regular use of antibiotic prophylaxis (trimethoprim 5mg/kg, sulfamethoxazole 21mg/kg 21 days) and intravenous immunoglobulins (400mg/kg/21 days).
- Severe Combined Immunodeficiency, eMedicine
- National Marrow Donor Program

Research programs, clinical trials:

- European Initiative for Primary Immunodeficiencies 2001-2004, coord.Edvard Smith.
- Preclinical gene therapy studies for ZAP70 deficiency, ORPHANET

GENE INFORMATION

Names:

HUGO name: ZAP70
Alias(es): SRK, STD, ZAP-70, syk-related tyrosine kinase, zeta-chain (TCR) associated protein kinase, Tyrosine-protein kinase ZAP-70

Localization:

Reference sequences:

DNA: AC016699 (EMBL) , **cDNA:** L05148 (EMBL) , **Protein:** P43403 (SWISSPROT)

Chromosomal Location:

2q12

Maps:

ZAP70 (Map View)

Variations / Mutations:

- ZAP70base; Mutation registry for autosomal recessive severe combined ZAP70 deficiency

Other gene-based resources:

Ensembl: ENSG00000115085, GENATLAS: ZAP70, GeneCard: ZAP70, UniGene: 234569, Entrez Gene: 7535, euGenes: 7535, GDB: 433738

PROTEIN INFORMATION

Description:

Protein function:

Associates with the T-cell antigen receptor zeta chain. Plays a role in lymphocyte activation.

Catalytic activity:

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

Post-translational modification:

Undergoes tyrosine phosphorylation following TCR stimulation.

Domains:

SH2 1 domain: 10-102

SH2 2 domain: 163-254

Protein kinase domain: 338-600

Other features:

ATP nucleotide phosphate-binding region: 344-352

ATP binding site: 369

Other related resourses:

InterPro: IPR000719; Euk_pkinase, InterPro: IPR000980; SH2, InterPro: IPR001245; Tyr_pkinase, Pfam: PF00017; SH2, Pfam: PF00069; pkinase, SMART: SM00252; SH2, SMART: SM00219; TyrKc, PROSITE: PS00107; PROTEIN_KINASE_ATP, PROSITE: PS00109; PROTEIN_KINASE_TYR, PROSITE: PS50011; PROTEIN_KINASE_DOM, PROSITE: PS50001; SH2

Expression pattern for human:

Tissue	Exp. (%)	Clones
blood, white cells	31.34	1:910
leukopheresis	18.78	3:4557
blood	13.53	6:12646
leukocyte	9.53	3:8982
thymus, pooled	9.00	1:3169
blood, lymphocyte	7.55	3:11328
germ cell, pooled	2.39	3:35870
uterus, epithelium	2.16	1:13207
germ cell	1.42	1:20077
unclassified	1.10	2:51898

OTHER RESOURCES

Societies:

General:

- International Patient Organization for Primary Immunodeficiencies
- Immune Deficiency Foundation
- March of Dimes Birth Defects Foundation
- NIH/National Institute of Allergy and Infectious Diseases
- European Society for Immunodeficiencies