Autoimmune lymphoproliferative syndrome, type 1B

GENERAL INFORMATION

Description:

Defects in TNFSF6 are a cause of autoimmune lymphoproliferative syndrome (ALPS), a childhood syndrome. There are several types of ALPS: type I ALPS (a and b) is associated with Fas and Fas ligand defects and type II ALPS is caused by defects in other apoptosis genes (CASP10). ALPS can be caused by autosomal recessive (ALPS 0) or by autosomal dominant inheritance of Fas mutations (ALPS Ia) and Fas ligand (ALPS Ib).

Alternative names:

- ALPS1B, ALPS Ib, ALPS type Ib
- APO-1 ligand/Fas ligand defect type Ib,defective CD178

Classification:

- Defects in lymphocyte apoptosis
  - Autoimmune lymphoproliferative syndrome

Inheritance:

Autosomal dominant

OMIM:

- #601859 Autoimmune lymphoproliferative syndrome
- *134638 Tumor necrosis factor ligand superfamily, member 6; TNFSF6

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for Apopotosis mediator APO-1/ Fas defects

Incidence:

Incidence unknown.

CLINICAL INFORMATION

Description:

In most cases, the disease is revealed early in life, usually before 5 years of age. This syndrome associates lymphoproliferative manifestations, such as splenomegaly and polyadenopathy with a specific immunological disorder. The latter consists of serum hyper-gammaglobulinemia G (hyper IgG) sometimes associated with hyper IgA, accumulations of a particular T-cell population i.e., #/# T-cell receptor (TCR)(+) CD4(-) CD8(-). Autoimmune manifestations are observed in most cases. Lymphoproliferative manifestations resolve with age, whereas immunological disorders frequently persist.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Autoimmune lymphoproliferative syndrome, ORPHANET
- Lymphoproliferative disorders, eMedicine

Genetic:

- TNFRSF6, IDdiagnostics

Therapeutic options:

- In patients with massive lymphoproliferation, chemotherapy with prednisone, cyclophosphamide and vincristine has been unsuccessful. Allogenic bone-marrow transplantation is the only cure for complete Fas deficiency. In case of hypersplenism, splenectomy is often performed. Severe autoimmune manifestation can be treated with steroids and cyclophosphamide.
- Lymphoproliferative disorders, eMedicine

Research programs, clinical trials:

- European Initiative for Primary Immunodeficiencies
- APLSbase, Jennifer Puck, National Human Genome Research Institute

GENE INFORMATION

Names:

HUGO name: FASLG
Alias(es): APT1LG1, CD95L, TNFSF6, FASL, FasL, apoptosis (APO-1) antigen ligand 1, tumor necrosis factor (ligand) superfamily, member 6, FAS antigen ligand, Apoptosis antigen ligand, APTL, CD178 antigen

Localization:

Reference sequences:

DNA: Z96050 (EMBL) , **cDNA:** X89102 (EMBL) , **Protein:** P48023 (SWISSPROT) Other Sequences

Chromosomal Location:

1q23-q23

Maps:

TNFSF6 (Map View)

Variations / Mutations:

- FASLGbase; Mutation registry for Autoimmune lymphoproliferative syndrome, type 1B (ALPS1B)
- ALPSbase at NHGRI; ALPSbase

Other gene-based resources:

Ensembl: ENSG00000117560, GENATLAS: TNFSF6, GeneCard: TNFSF6, UniGene: 2007, Entrez Gene: 356, euGenes: 356, GDB: 132671

PROTEIN INFORMATION

Description:

Protein function:

Cytokine that binds to TNFRSF6/Fas, a receptor that transduces the apoptotic signal into cells. May be involved in cytotoxic T cell mediated apoptosis and in T cell development. TNFRFSF6/Fas-mediated apoptosis may have a role in the induction of peripheral tolerance, in the antigen-stimulated suicide of mature T cells, or both. Binding to the decoy receptor TNFRSF6b/dcr3 modulates its effects.

Subunit:

Homotrimer (probable)

Subcellular location:

Type II membrane protein. May be released into the extracellular fluid, probably by cleavage form the cell surface.

Post-translational modification:

N-glycosylated

Protein function:

2 isoforms are produced by alternative splicing.

Domains:

Cytoplasmic domain: 1-80

Extracellular domain: 103-281

Pro-rich domain: 4-70

Poly-pro domain: 45-65

Other features:

Tumor necrosis factor ligand superfamily member 6, membrane form: 1-281

Tumor necrosis factor ligand superfamily member 6, soluble form: 130-281

Disulfide bonds: 202-233

Other related resourses:

InterPro: IPR003636; TNF_abc, Pfam: PF00229; TNF, SMART: SM00207; TNF, PROSITE: PS00251; TNF_1, PROSITE: PS50049; TNF_2

Expression pattern for human:

Tissue	Exp. (%)	Clones
blood	37.63	2:12646
lymph, T-cell	27.99	1:8503
leukocyte	26.49	1:8982
mixed	7.89	2:60341

Animal models:

Mouse:

MGD: ; Tnfsf6

Fly:

euGenes: ; CG10465

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

Other information sources:

- Autoimmune lymphoproliferative syndromes: genetic defects of apoptosis pathways