Familial haemophagocytic lymphohistiocytosis type 4

GENERAL INFORMATION

Description:

Familial hemophagocytic lymphohistiocytosis is a lethal disorder of immune regulation. It is a disorder of early childhood characterized by excessive, uncontrolled T-lymphocyte and macrophage activation. Infiltration of the liver, spleen, bone marrow, and central nervous system by activated T cells and macrophages results in a multisystem disorder.

Alternative names:

- FHL4, FHLH
- HPLH4, HLH; Familial erythrophagocytic lymphohistiocytosis 4; Familial histiocytic reticulosis 4; Hemophagocytic lymphohistiocytosis

Classification:

- Phagocytic disorders
  - Familial haemophagocytic lymphyohistiocytosis

Inheritance:

Autosomal recessive

ICD code:

ICD D76.1

OMIM:

- #267700 Reticulosis, familial histiocytic
- %603552 Hemophagocytic lymphohistiocytosis, familial, 1
- *605014 Syntaxin 11; STX11

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for Familial haemophagocytic lymphohistiocytosis type 1
- IDR factfile for Familial haemophagocytic lymphohistiocytosis type 2
- Familial haemophagocytic lymphohistiocytosis type 3

Incidence:

1:50,000

CLINICAL INFORMATION

Description:

The symptoms may vary widely. The most common findings are unexplained high fever, irritability, general pain, oedema, hepatosplenomegaly, cytopenia (thrombocytopenia, anemia). This macrophage activation syndrome occur after a healthy period of several months after the birth to more rarely several years, and is usually triggered by viral infection. Other early symptoms include skin rash, lymph node enlargement, and neurologic abnormalities (bulging fontanel, neck stiffness, hypotonia, hypertonia, convulsions, cranial nerve palsy, ataxia, hemiplagia/tetraplagia, blindness and unconsciousness).

Diagnosis:

Diagnostic laboratories:

Clinical:

- ORPHANET

Genetic:

- IDdiagnostics, STX11
- GeneTests

Therapeutic options:

- Treatment with epipodophyllotoxins, immunosuppressive agents, corticotherapy and anti thymocyte immunoglobulin (ATG) control macrophage activation and precede bone marrow transplantation. Intrathecal injections of methotrexate prevent or cure neuromeningeal disorders.
- Lymphohistiocytosis, eMedicine
- The Role of Blood and Marrow Transplantation as Treatment for Hemophagocytic Lymphohistiocytosis (HLH)

Research programs, clinical trials:

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GENE INFORMATION

Names:

HUGO name: STX11

Localization:

Reference sequences:

DNA: D0083 (IDRefSeq) , **cDNA:** AF071504 (EMBL) , **Protein:** O75558 (SWISSPROT) Other Sequences

Chromosomal Location:

6q24

Maps:

STX11 (Map View)

Variations / Mutations:

- STX11base; Mutation registry for Familial haemophagocytic lymphohistiocytosis 4 (FHL4)

Other gene-based resources:

Ensembl: ENSG00000135604, GENATLAS: STX11, GeneCard: STX11, UniGene: 118958, Entrez Gene: 8676, euGenes: 8676, GDB: 9956241, HomoloGene: 2792

PROTEIN INFORMATION

Description:

Protein function:

Snare that acts to regulate protein transport between late endosomes and the trans-golgi network.

Subunit:

Interacts with the snare proteins SNAP-23 and VAMP.

Subcellular location:

Membrane; peripheral membrane protein (potential).

Similarity:

Belongs to the syntaxin family.

Domains:

t-SNARE coiled-coil homology domain: 204-266

Other features:

Syntaxin-11: 1-287

Other related resourses:

InterPro: IPR006012; Syntaxin, InterPro: IPR006011; Syntaxin_N, InterPro: IPR010989; t-snare, InterPro: IPR000727; T_SNARE, Pfam: PF05739; SNARE, Pfam: PF00804; Syntaxin, SMART: SM00503; SynN, SMART: SM00397; t_SNARE, PROSITE: PS00914; SYNTAXIN, PROSITE: PS50192; T_SNARE

Expression pattern for human:

Tissue	Exp. (%)	Clones
lymph_node	34.66	15:83039
bone_marrow	18.56	4:41353
placenta	11.08	11:190488
mixed	8.64	13:288723
uncharacterized_tissue	5.34	6:215582
small_intestine	4.48	1:42840
unclassified	4.08	2:94133
blood	3.12	1:61437
lung	2.66	4:288686
connective_tissue	2.00	1:96057

Animal models:

Mouse:

MGD: ; 4

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

Disease specific:

- Histiocyte Society
- Histiocytosis Association of America
- Histiocyte Society of Germany
- The Histiocytosis Association of Canada
- Artemis Society, Greek histiocytosis support group
- Associazione Italiana Ricerca Istiocitos (AIRI)

Other information sources:

- Familial haemophagocytic lymphohistiocytosis