X-linked lymphoproliferative disease (Duncan disease)

GENERAL INFORMATION

Description:

X-linked lymphoproliferative disorder is initiated after an infection with the Epstein-Barr virus (EBV). EBV is the causative agent of infectious mononucloeosis, and may produce one or more of the following: signs of activation in lymphocytes and histiocytes and/or progressive hypogammaglobulinemia and/or lymphomas.

Alternative names:

- Lyp
- Lymphoproliferative disease; XLPD; XLP
- Immunodeficiency, X-linked progressive combined variable
- Duncan disease
- Familial fatal Epstein-barr virus infection
- EBV susceptibility; EBVS
- Susceptibility to infectious mononucleosis
- Immunodeficiency 5; IMD5
- Purtilo syndrome
- X-linked lymphoproliferative syndrome (SH2D1A/SLAM-associated protein (SAP)

Classification:

- Other well-defined immunodeficiency syndromes

Inheritance:

X-linked

OMIM:

- #308240 Lymphoproliferative syndrome
- *300490 SH2 domain protein 1A; SH2D1A

Incidence:

Incidence is not known.

CLINICAL INFORMATION

Description:

Many boys carrying the defective gene for XLP, before exposure to EBV infection are clinically healthy. After exposure to EBV patients can present: fulminant and often fatal infectious mononucleosis, lymphoproliferative disorders including malignant lymphoma, and dysgammaglobulinemia, pancytopenia. Less frequent manifestations are aplastic anemia, vasculitis, and lymphoid granulomatosis. Several phenotypes (hypogamaglobulinemia, lymphoma, aplastic anemia) may manifest within the XLP patient over time.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Lymphoproliferative Syndrome, X-linked, eMedicine
- X-linked lymphoproliferative disease, ORPHANET

Genetic:

- SH2D1A, IDdiagnostics
- Laboratorio di Genetica Pediatrica Angelo Nocivelli - University of Brescia, EDDNAL
- North East Thames Regional Clinical Molecular Genetics Laboratory (London), EDDNAL

Therapeutic options:

- Regular intravenous immunoglobulins should be used for the hypogammaglobulinemia. Early transplantation of allogeneic hematopoietic stem cells prevent EBV and non-EBV related complications in later life. Genetic therapy may be an option in the future.
- Lymphoproliferative Syndrome, X-linked, eMedicine
- Lymphoproliferative disorder, eMedicine

Research programs, clinical trials:

- European Initiative for Primary Immunodeficiencies.

GENE INFORMATION

Names:

HUGO name: SH2D1A
Alias(es): DSHP, EBVS, IMD5, LYP, MTCP1, SAP, XLP, XLPD, SH2 domain protein 1A, SLAM-associated protein, T cell signal transduction molecule SAP, Duncan's disease SH2-protein

Localization:

Reference sequences:

DNA: AL022718 (EMBL) , **cDNA:** AL023657 (EMBL) , **Protein:** O60880 (SWISSPROT) Other Sequences

Chromosomal Location:

Xq25-q26

Maps:

SH2D1A (Map View)

Variations / Mutations:

- SH2D1Abase; Mutation registry for X-linked lymphoproliferative syndrome (XLP)

Other gene-based resources:

Ensembl: ENSG00000183918, GENATLAS: SH2D1A, GeneCard: SH2D1A, UniGene: 349094, Entrez Gene: 4068, euGenes: 4068, GDB: 120701

PROTEIN INFORMATION

Description:

Protein function:

Inhibitor of the SLAM self-association. Acts by blocking recruitment of the SH2-domain-containing signal-transduction molecule SHP-2 to a docking site in the SLAM cytoplasmic region.

Subcellular location:

Cytoplasmic (potential).

Protein function:

6 isoforms; a, b, c, d, e and f; are produced by alternative splicing.

Structures (PDB):

1D1Z Crystal Structure Of The Xlp Protein Sap

Domains:

Sh2 domain: 6-104

Other features:

Other related resourses:

InterPro: IPR000980; SH2, Pfam: PF00017; SH2, ProDom: PD000093; SH2, SMART: SM00252; SH2, PROSITE: PS50001; SH2

Expression pattern for human:

Tissue	Exp. (%)	Clones
human spinal cord	62.60	1:488
thymus, pooled	19.28	2:3169
lymph, T-cell	7.19	2:8503
blood	2.42	1:12646
uterus, epithelium	2.31	1:13207
pool, lung+testis+B-cell	2.19	4:55714
lung	0.98	5:155782
pool, melanocyte+heart +uterus	0.93	1:32944
germ cell, pooled	0.85	1:35870
unclassified	0.59	1:51898

OTHER RESOURCES

Societies:

General:

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

Other information sources:

- Immunodeficiencies+SH2D1A deficiency