X-linked lymphoproliferative syndrome 2

GENERAL INFORMATION

Description:

The X-linked lymphoproliferative syndrome (XLP) is a rare, inherited immunodeficiency that is characterized by lymphohystiocytosis, hypogammaglobulinaemia and lymphomas, and that usually develops in response to infection with Epstein-Barr virus (EBV). Mutations in the signalling lymphocyte activation molecule (SLAM)-associated protein SAP, a signalling adaptor molecule, underlie 60% of cases of familial XLP. Another procent of cases is due to defects in in the gene that encodes the X-linked inhibitor-of-apoptosis XIAP (BIRC4) required for the survival and/or differentiation of NKT cells and also a potent regulator of lymphocyte homeostasis in vivo. BIRC4 are the cause of lymphoproliferative syndrome x-linked type 2 (XLP2).

Alternative names:

- XLP2
- Lymphoproliferative syndrome X-linked type 2, XIAP deficiency

Classification:

- Other well-defined immunodeficiency syndromes

Inheritance:

X-linked

OMIM:

- #300635 Lymphoproliferative syndrome, x-linked, 2; XLP2
- #308240 Lymphoproliferative syndrome
- *300079 Baculoviral IAP repeat-containing protein 4; BIRC4

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for X-linked lymphoproliferative disease (Duncan disease)

Incidence:

XLP affects about 3 out of every 1,000,000 males,

CLINICAL INFORMATION

Description:

Most of the patients developed a lymphohystiocytosis, related to EBV infection . In addition symptoms include severe or fatal mononucleosis, acquired hypogammaglobulinemia, pancytopenia and malignant lymphoma, splenomegaly.

Diagnosis:

Diagnostic laboratories:

Clinical:

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

Genetic:

- IDdiagnostics
- BIRC4, GeneTest

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: BIRC4

Localization:

Reference sequences:

DNA: D0120 (IDRefSeq) , **cDNA:** U45880 (EMBL) , **Protein:** P98170 (SWISSPROT) Other Sequences

Chromosomal Location:

Maps:

BIRC4 (Map View)

Variations / Mutations:

- BIRC4base; Mutation registry for XIAP deficiency/lymphoproliferative syndrome X-linked type 2

Other gene-based resources:

Ensembl: ENSG00000101966, GENATLAS: BIRC4, GeneCard: BIRC4, UniGene: 356076, Entrez Gene: 331, euGenes: 331, GDB: 9848649, HomoloGene: 901

PROTEIN INFORMATION

Description:

Protein function:

Apoptotic suppressor. Inhibitor of caspase-3, -7 and -9

Subunit:

Interacts with smac and with prss25; these interactions inhibit apoptotic suppressor activity

Subcellular location:

Cytoplasm

Tissue specificity:

Ubiquitous, except peripheral blood leukocytes

Similarity:

Belongs to the iap family

Structures (PDB):

1C9Q .
1F9X .
1G3F .
1G73 .
1I3O .
1I4O .
1I51 .
1KMC .
1NW9 .
1TFQ .

Other features:

Baculoviral iap repeat-containing protein 4: 1-497

Zinc finger region Ring-type: 450-485

Other related resourses:

PIR: S69544, InterPro: IPR001370; Prot_inh_I32_IAP, InterPro: IPR001841; Znf_RING, Pfam: PF00653; BIR, SMART: SM00238; BIR, SMART: SM00184; RING, PROSITE: PS01282; BIR_REPEAT_1, PROSITE: PS50143; BIR_REPEAT_2, PROSITE: PS00518; ZF_RING_1, PROSITE: PS50089; ZF_RING_2

Expression pattern for human:

Tissue	Exp. (%)	Clones
pharynx	13.74	1:4158
esophagus	5.89	2:19405
cochlea	4.58	1:12466
lymph_node	4.33	6:79183
kidney	4.15	14:192682
stomach	3.91	5:73010
nerve	3.65	1:15651
vascular	3.60	3:47560
colon	3.47	6:98776
lung	3.41	17:284571

Animal models:

Mouse:

MGD: ; Birc4

OTHER RESOURCES

Societies:

General:

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

Other information sources:

- Immunodeficiencies+BIRC4 deficiency