RFXANK, Ankyrin repeat containing regulatory factor X-associated protein deficiency

GENERAL INFORMATION

Description:

Defects in RFXANK are a cause of hereditary MHC class II deficiency, also known as Bare Lymphocyte Syndrome (BLS) or HLA class II-deficient combined immunodeficiency); a form of Severe Combined Immunodeficiency disease (SCID). RFXANK is linked with BLS complementation group B. The disease is very rare, only approximately 70 patients from 57 unrelated families have been reported worldwide.

Alternative names:

- MHC class II deficiency
- Bare Lymphocyte Syndrome type II (BLS)
- RFXANK (complementation group B)

Classification:

- Combined B and T cell immunodeficiencies
  - Major histocompatibility complex class II deficiency

Inheritance:

Autosomal recessive

OMIM:

- #209920 Bare lymphocyte syndrome, type II
- 603200 Regulatory factor X, ankyrin repeat-containing; RFXANK

Cross references:

Incidence:

Incidence is not known yet.

CLINICAL INFORMATION

Description:

Patients have extreme susceptibility to bacterial, viral, and fungal infections in the first year of life and usually results in death by age of four. It principally affects children born to cosanguineous families of nothern African or Mediterranean origin. Patients also can have liver diseases associated with chronic Cryptosporidium infection. Recurrent bronchopulmonary infections have been observed in all patients. The infectious agents include viruses (CMV, respiratory syncytial virus, enterovirus), bacteria (Steptococcus, Haemophilus, Proteus, Pseudomonas), Pneumocystis carinii, and Candida albicans. Neurological manifestation due to viral infections have been diagnosed in a number of patients. Hematologic manifestations are characterized by neutropenia and severe autoimmune cytopenia.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Defective expression of HLA class 2, ORPHANET

Therapeutic options:

- Patients can be cured with bone marrow transplantations of haematopoietic stem cells. Other recommendations include treatment of infections with antibacterials, antifungals, and antivirals, intravenous gamma-globulin infusion, irradiation of all blood products.
- Bone marrow transplant, UCSF Medical Center
- Stem Cell Transplant, National Marrow Donor Program (NMDP)

Research programs, clinical trials:

- Pilot Study of Allogeneic Bone Marrow Transplantation Plus Cyclosporine and Mycophenolate Mofetil to Induce Mixed Hematopoietic Chimerism in Patients With Primary T-Cell Immunodeficiency Disorders, ClinicalTrial.gov
- Beckman Research Institute
- University of Califonia
- Defective expression of HLA class 2, ORPHANET
- Leiden University Medical Center

GENE INFORMATION

Names:

HUGO name: RFXANK
Alias(es): ANKRA1, BLS, RFX-B, RFXB, regulatory factor X-associated ankyrin-containing protein, DNA-binding protein RFXANK, Regulatory factor X subunit B

Localization:

Reference sequences:

DNA: RFXANK_DNA (IDRefSeq) , **cDNA:** AF094760 (EMBL) , **Protein:** O14593 (SWISSPROT) Other Sequences

Chromosomal Location:

19p12

Maps:

RFXANK (Map View)

Variations / Mutations:

- ; RFXANKbase: Mutation registry for Ankyrin repeat containing regulatory factor X-associated protein deficiency.

Other gene-based resources:

Ensembl: ENSG00000064490, GENATLAS: RFXANK, GeneCard: RFXANK, UniGene: 296776, Entrez Gene: 8625, euGenes: 8625, GDB: 9956049

PROTEIN INFORMATION

Description:

Protein function:

Activates transcription from class II MHC promoters. Activation requires the activity of the MHC class II transactivator (CIITA). May regulate other genes in the cell. RFX binds the x1 box of MHC-II promoters. Isoform RFX-b-delta5 is not involved in the positive regulation of MHC class II genes.

Subunit:

RFX consists of at least three different subunits; RFXAP, RFX5 and RFX-b/ RFXANK; with each subunit representing a separate complementation group. RFX forms cooperative DNA binding complexes with x2bp and cbf/nf-y. RFX associates with CIITA to form an active transcriptional complex.

Subcellular location:

Nuclear

Protein function:

2 isoforms; a long form and RFX-b-delta5; are produced by alternative splicing

Other features:

Other related resourses:

InterPro: IPR002110; ANK, Pfam: PF00023; ank, SMART: SM00248; ANK, PROSITE: PS50088; ANK_REPEAT, PROSITE: PS50297; ANK_REP_REGION

Expression pattern for human:

Tissue	Exp. (%)	Clones
skin, epithelium	14.65	1:351
nasopharynx	7.96	1:646
head and neck	5.39	1:954
adipose, white adipose tissue	5.21	1:987
lung with fibrosis	3.48	1:1479
synovial membrane	3.39	1:1518
human lung epithelial cell lines untreated lps 6hr to lps	2.46	3:6278
ovary (pool of 3)	2.35	2:4380
colon, 2 pooled adenocarcinomas	2.33	4:8815
blood	2.03	5:12646

Animal models:

Mouse:

MGD: ; Rfxank

Fly:

euGenes: ; Rfx

C. elegans:

euGenes: ; daf-19

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:

- Birth disorders information directory