Interleukin-12 receptor β1 deficiency

GENERAL INFORMATION

Description:

IL12 is a cytokine secreted by phagocytes and dendritic cells and that induces interferon-gamma production by natural-killer and T lymphocytes. It consists of two subunits encoded by IL12A and IL12B. The clinical syndrome is rare and its inheritance may differ between kindreds. Although autosomal recessive in most cases, autosomal dominant and X-linked recessive inheritance have been reported. These disorders generally manifest in childhood, although they may become apparent during adulthood. IL12RB1 deficiency is associated with immunity impairment which leads to a predisposition to severe mycobacterial and salmonella infections in otherwise healthy individuals.

Alternative names:

- IL12Rβ1 deficiency
- Mendelian susceptibility to mycobacterial infections due to IL12 deficiency

Classification:

- Defects of innate immune system, receptors and signaling components

Inheritance:

Autosomal recessive

OMIM:

- #209950 Atypical mycobacteriosis, familial
- *601604 Interleukin 12 receptor, beta-1; IL12RB1

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for IFNγ1-receptor deficiency
- IDR factfile for IFNγ2-receptor deficiency
- IDR factfile for Interleukin-12 p40 deficiency
- IDR factfile for STAT1 deficiency

Incidence:

Incidence is not known.

CLINICAL INFORMATION

Description:

Patients with IL-12 and IL-12 Receptor deficiencies have mild symptoms, with delayed but good granuloma in response to BCG vaccination and impaired granuloma formation following NTM infection. Patients with complete IL-12Rb1 deficiencies presented with curable BCG infection upon vaccination and NTM infections after the age of three years. In one patient, the infection was fatal. The sister of one of the patients with BCG infection was resistant to three inoculations of BCG, but developed abdominal tuberculosis at the age of 18. In IL-12Rg1 deficiency there is a phenotypic heterogeneity for a given genotype.

Diagnosis:

Diagnostic laboratories:

Clinical:

- ORPHANET

Therapeutic options:

- ORPHANET
- Antibiotic therapy based on the susceptibilities of the mycobacterial species. Antimycobacterial therapy may have to be continued for extended periods and suplementary measures like drainage of the pus, attention to nutrition and growth can also be requiered. For those who not respond well to antibiotic treatment , additional IFNg therapy is effective.

Research programs, clinical trials:

- European Initiative for Primary Immunodeficiencies
- Molecular and Clinical Studies of Primary Immunodeficiency diseases, ClinicalTrials.gov

GENE INFORMATION

Names:

HUGO name: IL12RB1
Alias(es): IL12R, IL12RB, interleukin 12 receptor, beta 1, Interleukin-12 receptor beta-1 chain precursor, IL-12R-beta1, IL-12 receptor beta component, IL-12RB1

Localization:

Reference sequences:

DNA: IL12RB_DNA (IDRefSeq) , **cDNA:** U03187 (EMBL) , **Protein:** P42701 (SWISSPROT) Other Sequences

Chromosomal Location:

19p13.1

Maps:

IL12RB1 (Map View)

Variations / Mutations:

- IL12RB1base; Mutation registry for Interleukin-12 receptor b1 deficiency

Other gene-based resources:

Ensembl: ENSG00000096996, GENATLAS: IL12RB1, GeneCard: IL12RB1, UniGene: 223894, Entrez Gene: 3594, euGenes: 3594, GDB: 375777

PROTEIN INFORMATION

Description:

Protein function:

Involved in IL-12 transduction. Binds to IL-12 with a low affinity.

Subunit:

Dimer/oligomer; disulfide-linked. The functional high affinity IL-12 receptor is composed of at least IL12rb1 and IL12rb2.

Subcellular location:

Type I membrane protein.

Protein function:

2 isoforms; a long form and a short form; may be produced by alternative splicing.

Domains:

Extracellular domain.: 24-545

Cytoplasmic domain: 571-662

Fibronectin type-III 1 domain: 43-133

Fibronectin type-III 2 domain: 143-236

Fibronectin type-III 3 domain: 237-337

Fibronectin type-III 4 domain: 338-444

Fibronectin type-III 5 domain: 445-540

Other features:

Signal peptide: 1-23

Interleukin-12 receptor beta-1 chain: 24-662

Disulfide bonds: 52-62

Other related resourses:

InterPro: IPR003961; FN_III, InterPro: IPR003529; Hemtopoptn_L_F2, Pfam: PF00041; fn3, SMART: SM00060; FN3, PROSITE: PS01353; HEMATOPO_REC_L_F2

Expression pattern for human:

Tissue	Exp. (%)	Clones
leukopheresis	45.38	2:4557
leukocyte	23.02	2:8982
lymph, T-cell	12.16	1:8503
blood	8.18	1:12646
bone marrow	5.21	1:19854
mixed	3.43	2:60341
lymph	1.61	1:64395
skin	1.01	1:102017

Animal models:

Mouse:

MGD: ; Il12rb1

Fly:

euGenes: ; CG10535

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