Interleukin-12 (IL-12) p40 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.

Alternative names:

- IL12 p40 deficiency

Classification:

- Defects of innate immune system, receptors and signaling components

Inheritance:

Autosomal recessive

OMIM:

- #209950 Atypical mycobacteriosis, familial
- *161561 Interleukin 12B; IL12B

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for IFNγ1-receptor deficiency
- IDR factfile for IFNγ2-receptor deficiency
- IDR factfile for Interleukin-12 receptor beta 1 deficiency
- IDR factfile for STAT1 deficiency

Incidence:

Incidence is not known.

CLINICAL INFORMATION

Description:

For all patients known to date, mycobacterial infection has been the principal clinical presentation and none have clinical atopy or serological evidence of sensitization to common aero-allergens or signs of autoimmunity. Generally, patients with IL-12 and IL-12 Receptor deficiencies have mild symptoms, with delayed but good granuloma formation in response to BCG vaccination and impaired granuloma formation following NTM infection. The child with complete IL-12p40 deficiency presented with curable BCG- and Salmonella enteritidis- infections.

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: IL12B
Alias(es): CLMF, NKSF2, interleukin 12B (natural killer cell stimulatory factor 2, cytotoxic lymphocyte maturation factor 2, p40), Interleukin-12 beta chain precursor, Cytotoxic lymphocyte maturation factor 40 kDa subunit, NK cell stimulatory factor chain 2

Localization:

Reference sequences:

DNA: AY008847 (EMBL) , **cDNA:** M65290 (EMBL) , **Protein:** P29460 (SWISSPROT) Other Sequences

Chromosomal Location:

5q31.1-q33.1

Maps:

IL12B (Map View)

Variations / Mutations:

- IL12Bbase; Mutation registry for Interleukin-12 (IL-12) p40 deficiency

Other gene-based resources:

Ensembl: ENSG00000113302, GENATLAS: IL12B, GeneCard: IL12B, Entrez Gene: 3593, euGenes: 3593, GDB: 127870

PROTEIN INFORMATION

Description:

Protein function:

Cytokine that can act as a growth factor for activated T and NK cells, enhance the lytic activity of NK/lymphokine-activated killer cells, and stimulate the production of IFN-gamma by resting pbmc.

Subunit:

Disulfide-bonded heterodimer of 40 kda and 35 kda subunits. NKsf is essentially a complex of cytokine and soluble receptor.

Subcellular location:

Secreted.

Post-translational modification:

Known to be C-mannosylated in the recombinant protein; it is not yet known for sure if the wild-type protein is also modified.

Domains:

Ig-like C2-type domain: 43-97

Fibronectin type-III domain: 235-320

Other features:

Signal peptide: 1-22

Interleukin-12 beta chain: 23-328

Disulfide bond interchain: 199

Disulfide bonds: 50-90

Other related resourses:

InterPro: IPR002996; CR1A, InterPro: IPR003961; FN_III, InterPro: IPR003530; Hemtopoptn_L_F3, InterPro: IPR003006; Ig_MHC, InterPro: IPR003598; Ig_c2, Pfam: PF00041; fn3, Pfam: PF00047; Ig, SMART: SM00408; IGc2, PROSITE: PS01354; HEMATOPO_REC_L_F3

Expression pattern for human:

Tissue	Exp. (%)	Clones

Animal models:

Mouse:

MGD: ; Il12b

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