IFNγ2-receptor deficiency

GENERAL INFORMATION

Description:

The clinical syndrome is rare and is due to impaired immunity against mycobacteria. Parental cosanguinity and familial forms are frequent and the syndrome is often described as Mendelian susceptibility to mycobacterial infection. In most cases the inheritance is autosomal recessive, but also autosomal dominant and X-linked inheritence have been found. A child with disseminated Mycobacterium fortuitum and M. avium complex infections and absent IFNγ signaling was found to due to a mutation in the extracellular domain of IFNγ2-receptor.

Alternative names:

- IFNGR2D
- IFGR2
- IL12/IL23-IFN-gama axis deficiencies
- Mendelian susceptibility to mycobacterial infection
- Interferon, gamma, transducer 1; IFNGT1
- Interferon, gamma, accessory factor for receptor

Classification:

- Defects of innate immune system, receptors and signaling components
  - Interferon-# (IFN#) receptor deficiency

Inheritance:

Autosomal recessive

OMIM:

- #209950 Atypical mycobacteriosis, familial
- *147569 Interferon, gamma, receptor 2; IFNGR2

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for IFNγ1-receptor deficiency
- IDR factfile for Interleukin-12 p40 deficiency
- IDR factfile for Interleukin-12 receptor beta 1 deficiency
- IDR factfile for STAT1 deficiency

Incidence:

Incidence is not known.

CLINICAL INFORMATION

Description:

Patients with complete IFNgR1 or IFNgR2 have a severe form of the syndrome, with BCG infection after immunization and early onset NTM infection. Also lepromatous-like lesions, in response to BCG vaccination, were observed and are suggestive. The clinical phenotype of patients with partial IFNgR deficiency is generally mild like that in IL-12R deficiency. The patient with partial recessive IFNgR2 deficiency had a history of BCG and Mycobacterium abcessus infections.

Diagnosis:

Diagnostic laboratories:

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: IFNGR2
Alias(es): AF-1, IFGR2, IFNGT1, interferon gamma receptor 2, interferon-gamma receptor beta chain precursor, Interferon-gamma receptor accessory factor-1 Interferon-gamma transducer-1, Interferon-gamma transducer-1

Localization:

Reference sequences:

DNA: AP001717 (EMBL) , **cDNA:** U05875 (EMBL) , **Protein:** P38484 (SWISSPROT) Other Sequences

Chromosomal Location:

21q22.1-q22.2

Maps:

IFNGR2 (Map View)

Variations / Mutations:

- IFNGR2base; Mutation registry for IFN#2-receptor deficiency

Other gene-based resources:

Ensembl: ENSG00000159128, GENATLAS: IFNGR2, GeneCard: IFNGR2, Entrez Gene: 3460, euGenes: 3460, GDB: 142306

PROTEIN INFORMATION

Description:

Protein function:

Part of the receptor for interferon gamma. Required for signal transduction. This accessory factor is an integral part of the IFN-gamma signal transduction pathway and is likely to interact with GAF, JAK1, and/or JAK2.

Subcellular location:

Type I membrane protein.

Domains:

Extracellular domain: 28-247

Cytoplasmic domain: 269-337

Other features:

Signal peptide: 1-27

Interferon-gamma receptor beta chain: 28-337

Other related resourses:

InterPro: IPR000282; Cytok_receptor_2, InterPro: IPR003961; FN_III, Pfam: PF00041; fn3, SMART: SM00060; FN3

Expression pattern for human:

Tissue	Exp. (%)	Clones
normal gingiva (cell line from immortalized keratinocytes)	13.45	1:517
head and neck	7.29	1:954
synovial membrane	4.58	1:1518
leukopheresis	4.58	3:4557
pheochromocytoma	4.46	1:1560
lung metatastic chondrosarcoma	4.31	4:6448
B cells from Burkitt lymphoma	3.24	1:2143
heart	2.45	13:36928
pool, placenta	2.36	4:11794
osteoarthritic cartilage	2.32	1:2999

Animal models:

Mouse:

MGD: ; Ifngr2

Fly:

euGenes: ; CG6201

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