IFNγ1-receptor deficiency

GENERAL INFORMATION

Description:

The clinical syndrome is rare and is due to impaired immunity against mycobacteria. Parental consanguinity 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. Three molecular forms of IFNγ-receptor deficiency have been described. Complete deficiency of IFNγ1-receptor is associated with severe and often fatal mycobacterial infection, mostly at an early age. These mutations preclude cell surface expression of the receptor or prevent cellular responses to IFNγ, and the type of mutation accounts for clinical heterogeneity. Two forms of partial deficiency in IFNγ1-receptor have been identifiend, associated with milder clinical infections. The more common form of partial deficency in IFNγ1-receptor is due to heterozygous frameshift deletions at exon 6 of the gene, which result in abnormal receptors that accumulates at high levels at the cell surface, exerting a dominativ negative effect. One form of partial IFNγ1-receptor deficiency has been described in two siblings. They expressed the receptor at the cell surface, reduced but did not completely abrogate IFNγ binding, signalling or both.

Alternative names:

- IFNGR1D
- IFNGR1 deficiency
- IL12/IL23-IFN-gama axis deficiencies
- Mendelian susceptibility to mycobacterial infection
- AVP, type II
- Antiviral protein, type II
- Immune interferon receptor 1
- CD119 antigen; CD119

Classification:

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

Inheritance:

Autosomal recessive

OMIM:

- #209950 Atypical mycobacteriosis, familial
- *107470 Interferon, gamma, receptor 1; IFNGR1
- #600263 Helicobacter pylori infection, susceptibility to

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for IFNγ2-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:

The opportunistic infections constitute the hallmark of inherited IFN#1-receptor deficiency. Other features of immune dysregulation are asthma, atopy, glomerulonephritis, vasculitis and positive rheumatoid factor. The clinical phenotype of patients with partial IFNgR deficiency is generally mild like that in IL-12R deficiency. One patient with partial recessive IFNgR1 deficiency presented with clinical BCG and Salmonella enteridis infections and the other patient, not vaccinated, had symptomatic tuberculosis. 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. A pathological feature characteristic for IFN#1-receptor deficiency is the failure to form mature granulomas in response to Mycobacterium.

Diagnosis:

Diagnostic laboratories:

Genetic:

- Laboratory of Human Genetics of Infectious Diseases - INSERM, Paris, EDDNAL

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
- Recherche de mutation du gene du recepteur de l'intereferon gamma
- Molecular and Clinical Studies of Primary Immunodeficiency diseases, ClinicalTrials.gov

GENE INFORMATION

Names:

HUGO name: IFNGR1
Alias(es): IFNGR, interferon gamma receptor 1, Interferon-gamma receptor alpha chain precursor (CDw119)

Localization:

Reference sequences:

DNA: AL050337 (EMBL) , **cDNA:** J03143 (EMBL) , **Protein:** P15260 (SWISSPROT) Other Sequences

Chromosomal Location:

6q23-24

Maps:

IFNGR1 (Map View)

Variations / Mutations:

- IFNGR1base; Mutation registry for IFN#1-receptor deficiency

Other gene-based resources:

Ensembl: ENSG00000027697, GENATLAS: IFNGR1, GeneCard: IFNGR1, Entrez Gene: 3459, euGenes: 3459, GDB: 120688

PROTEIN INFORMATION

Description:

Protein function:

Receptor for interferon gamma. Two receptors bind one interferon-gamma dimer.

Subunit:

Monomer.

Subcellular location:

Type I membrane protein.

Post-translational modification:

Phosphorylated at SER/THR residues.

Structures (PDB):

1JRH	Complex (Antibody/Antigen)
1FG9	3:1 Complex Of Interferon-γ Receptor With Interferon-γ Dimer

Domains:

Extracellular domain: 18-245

Cytoplasmic domain: 267-489

Other features:

Signal peptide: 1-17

Interferon-gamma receptor alpha chain: 18-489

Disulfide bonds: 77-85, 122-167, 195-200, 214-235

Other related resourses:

PIR: A31555, InterPro: IPR000282; Cytok_receptor_2

Expression pattern for human:

Tissue	Exp. (%)	Clones
gall bladder	12.46	4:2435
sciatic nerve	8.65	1:877
human skeletal muscle	6.35	9:10746
colonic mucosa with ulcerative colitus	6.23	1:1218
connective tissue	5.83	1:1301
esophagus	5.14	2:2949
pheochromocytoma	4.86	1:1560
cns, multiple sclerosis lesions	3.88	4:7823
T cells from T cell leukemia	3.16	1:2397
whole blood	3.10	1:2445

Animal models:

Mouse:

MGD: ; Ifngr

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