

Natural killer deficiency

GENERAL INFORMATION

Description:

Natural killer cells are large granular lymphocytes capable of killing tumor cells and certain virally infected cells in a manner not restricted by the major histocompatibility complex (MHC). Fc receptor III is encoded by 2 separate genes: one for the neutrophil receptor, or CD16 (FCGR3A), and another for the transmembrane receptor on natural killer cells and macrophages. Neutrophil-Fc receptor III deficiency is due to deletion of the Fc receptor III-1 gene (CD16), while the Fc receptor III-2 gene (CD32) is normally present.

Alternative names:

- NK cell deficiency
- CD16 deficiency

Classification:

- Other well-defined immunodeficiency syndromes? Immunodeficiency with dermatological defects/Cellular immunodeficiency?

Inheritance:

Autosomal recessive

OMIM:

- *146740 Fc fragment of IgG, low affinity IIIa, receptor for; FCGR3A

Cross references:

Incidence:

Incidence is not known.

CLINICAL INFORMATION

Description:

Patients have susceptibility to herpes virus infections, recurrent viral respiratory tract infections and, NK cytopenia. Also, patients have severe clinical problems after Bacille Calmette-Guerin (BCG) vaccination and following Epstein-Barr virus and Varicella Zoster virus infections.

Diagnosis:

Diagnostic laboratories:

Therapeutic options:

- Specific antibiotics are used for the infections.

Research programs, clinical trials:

- European Initiative for Primary Immunodeficiencies 2001-2004, coord.Edvard Smith.

GENE INFORMATION

Names:

HUGO name: FCGR3A

Alias(es): CD16 , FCG3 , FCGR3 , IGFR3, Fc fragment of IgG, low affinity III, receptor for CD16 , Fc fragment of IgG, low affinity IIIa, receptor for CD16, Low affinity immunoglobulin gamma Fc region receptor III-A precursor , IgG FC receptor III-2, Fc-gamma RIII-alpha, Fc-gamma RIIIA, FcRIIIA, Fc-gamma RIII, FcRIII, CD16-A, FcR-10

Localization:

Reference sequences:

DNA: X52645 (EMBL) Z46222 (EMBL) ,
cDNA: X58957 (EMBL) , **Protein:** P08637
(SWISSPROT)

Chromosomal Location:

1q23

Maps:

FCGR3A (Map View)

Markers:

WI-16134, RH11453, GDB:190042,
PMC20248P1

Variations / Mutations:

- FCGR3Abase; Mutation registry for Natural killer deficiency

Other gene-based resources:

Ensembl: ENSG00000162747, GENATLAS:
FCGR3A, GeneCard: FCGR3A, UniGene:
372679, Entrez Gene: 2214, euGenes: 2214,
GDB: 119904, HomoloGene: 477

PROTEIN INFORMATION

Description:

Protein function:

Receptor for the Fc region of IgG. Binds complexed or aggregated IgG and also monomeric IgG. Mediates antibody-dependent cellular cytotoxicity (adcc) and other antibody-dependent responses, such as phagocytosis.

Subunit:

Exists as a hetero-oligomeric receptor complex with Fc epsilon receptor I gamma subunit and / or the CD3 zeta subunit.

Subcellular location:

Type I membrane protein (potential). Exists also as a soluble receptor.

Post-translational modification:

Glycosylated. Contains high mannose- and complex-type oligosaccharides.

Miscellaneous:

Encoded by one of two nearly identical genes: FCGR3A and FCGR3B which are expressed in a tissue-specific manner. The PHE-203 in III-a determines the transmembrane domains whereas the SER-203 in III-b determines the GPI-anchoring.

Polymorphism:

Isoform VAL-157 shows a higher binding capacity of IgG1, IgG3 and IgG4 compared with isoform PHE-157. Alleles LEU-66 and PHE-157, and alleles HIS-66 / ARG-66 and VAL-157 are in linkage disequilibrium.

Tissue specificity:

Expressed on natural killer cells, macrophages, subpopulation of T cells, immature thymocytes and placental trophoblasts.

Similarity:

Contains 2 immunoglobulin-like C2-type domains.

Domains:

Extracellular domain: 17-208

Cytoplasmic domain: 230-254

Ig-like C2-type 1 domain: 24-105

Ig-like C2-type 2 domain: 107-189

Other features:

Signal peptide: 1-16

Low affinity immunoglobulin gamma fc region receptor iii-a: 17-254

N-linked (glcnac...) glycosylation sites: 56,63,92,180,187

Disulfide bonds: 47-89, 128-172

Other related resources:

PIR: JL0107, InterPro: IPR003599; Ig, InterPro: IPR007110; Ig-like, Pfam: PF00047; ig, SMART: SM00409; IG, PROSITE: PS50835; IG_LIKE

Expression pattern for human:

Tissue	Exp. (%)	Clones
colon	12.32	6:82275
placenta	9.48	8:142648
ovary	9.44	4:71634
peripheral_nervous_system	8.04	1:21019
pancreas	7.50	3:67592
kidney	7.41	5:113979
prostate	7.00	4:96523
other	5.98	15:423795
mixed	5.91	11:314320
brain	5.82	11:319574

Animal models:**Mouse:**

MGD: ; Fcgr3, NCBI Gene: ; 246256 (62.25 % aminoacid similarity to human)

Rat:

NCBI Gene: ; 304966 (60.64 % aminoacid similarity to human)

OTHER RESOURCES**Societies:****General:**

- International Patient Organization for Primary Immunodeficiencies
- Immune Deficiency Foundation
- European Society for Immunodeficiencies