p67^{phox} deficiency

GENERAL INFORMATION

Description:

Neutrophil cytosolic factor 2 (NCF2) is absent in 5% of patients with autosomal recessive chronic granulomatous disease (AR-CGD). The disease is characterized by a defect of intracellular bacterial killing in neutrophils and monocytes, due to a failure of superoxide, oxygen radical, and peroxide production. Organisms that are catalase negative are killed normally, whereas catalase-positive organisms (Staphylococcus aureus, Aspergillus, Nocardia, and Serratia) cause major problems.

Alternative names:

- CGD, autosomal cytochrome-b-positive, type II
- Chronic granulomatous disease, due to NCF2 deficiency
- Deficiency of neutrophil cytosol factor 2
- Deficiency of NCF2
- P67-phox, deficiency of neutrophil cytosolic factor 2

Classification:

- Defects of phagocyte function
  - Chronic granulomatous disease

Inheritance:

Autosomal recessive

OMIM:

- #233710 Granulomatous disease, chronic, autosomal cytochrome-b-positive form II
- *608515 Neutrophil cytosolic factor 2; NCF2

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for X-linked chronic granulomatous disease
- IDR factfile for p22phox deficiency
- IDR factfile for p47phox deficiency

Incidence:

1: 200,000-250,000 live births in USA. Internationally 1: 500,000.

CLINICAL INFORMATION

Description:

The hallmark of disease are infections with catalase-positive organisms, especially deep-seated abscesses, osteomyelitis, and chronic granulomata. It may mimic inflammatory bowel disease and lead to malabsorption and obstruction of the bowel. Liver abcess is a common first presentation. Early manifestations include chronic and recurrent pyogenic infections during first 2 years of life, lymphadenopathy, recurrent enlargement of lymph nodes of neck. Later manifestations include gastrointestinal symptoms: hepatomegaly/hepatosplenomegaly, esophageal outlet, pyloric, and/or urethral obstruction, persistent diarrhea - granulomatous colitis, perianal abscesses or rectal fistulous tracts. Skin manifestations include eczematoid dermatitis, impetigo, recurrent skin furunculosis, subcutaneous abscesses. Other symptoms include mucous membrane infections, conjunctivitis, rhinitis, stomatitis, chronic or recurrent pneumonias, chronic cough, osteomyelitis.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Chronic granulomatous disease, eMedicine
- Chronic granulomatous disease, eMedicine

Genetic:

- GeneTest
- EDDNAL
- EDDNAL

Therapeutic options:

- Long-term antibiotic therapy (co-trimoxazole, itraconazole). Low-dose prophylactic #-interferon widely used in USA. Acute infections are treated promptly with intravenous antibiotics, supplemented with high dose #-interferon. Drainage of large abcesses may be required. The inflammatory bowel disease is helped by high-dose of steroids. Bone marrow transplantation should be carried out early.
- Chronic granulomatous disease, eMedicine
- Chronic granulomatous disease, eMedicine

Research programs, clinical trials:

- Use of G-CSF to Obtain Blood Cell Precursors, Clinical.Trials.gov
- Posaconazole to Treat Invasive Fungal Infections, Clinical.Trials.gov
- Modified Stem Cell Transplantation Procedure for Treating Chronic Granulomatous Disease
- European Initiative for Primary Immunodeficiencies

GENE INFORMATION

Names:

HUGO name: NCF2
Alias(es): p67phox, neutrophil cytosolic factor 2, Neutrophil NADPH oxidase factor 2, 67 kDa neutrophil oxidase factor

Localization:

Reference sequences:

DNA: NCF2_DNA (IDRefSeq) , **cDNA:** M32011 (EMBL) , **Protein:** P19878 (SWISSPROT) Other Sequences

Chromosomal Location:

1q25

Maps:

NCF2 (Map View)

Variations / Mutations:

- NCF2base; Mutation registry for autosomal recessive p67 phox deficiency

Other gene-based resources:

Ensembl: ENSG00000116701, GENATLAS: NCF2, GeneCard: NCF2, UniGene: 518604, Entrez Gene: 4688, euGenes: 4688

PROTEIN INFORMATION

Description:

Protein function:

NCF2, NCF1, and a membrane bound cytochrome B558 are required for activation of the latent NADPH oxidase (necessary for superoxide production).

Subcellular location:

Cytoplasmic

Structures (PDB):

1E96 Structure Of The Rac/P67Phox Complex

Domains:

SH3 1 domain: 240-299

SH3 2 domain: 457-516

Other features:

Other related resourses:

PIR: A34855, InterPro: IPR000108; Neu_cyt_fact_2, InterPro: IPR001452; SH3, InterPro: IPR001440; TPR, Pfam: PF00018; SH3, Pfam: PF00515; TPR, SMART: SM00326; SH3, SMART: SM00028; TPR, PROSITE: PS50002; SH3

Expression pattern for human:

Tissue	Exp. (%)	Clones
blood, white cells	22.96	1:910
whole blood	17.09	2:2445
mammary gland	14.50	1:1441
lung metatastic chondrosarcoma	12.96	4:6448
lung epithelial cells tissue nos 359-368	4.79	1:4366
human optic nerve	4.74	1:4406
blood	3.30	2:12646
normal lung epithelial cells tissue nos 369-371 and 380-383	3.11	1:6713
human fetal eyes	3.02	2:13838
germ cell	2.08	2:20077

Animal models:

Mouse:

MGD: ; Ncf2

Fly:

euGenes: ; Cbp20

C. elegans:

euGenes: ; F26A3.2

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

Disease specific:

- The Chronic Granulomatous Disease Association
- CGD cafe, a CGD community