p47^{phox} deficiency

GENERAL INFORMATION

Description:

Autosomal recessive chronic granulomatous disease (AR-CGD) 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 I
- Chronic granulomatous disease due to NCF1 deficiency
- Deficiency of neutrophil cytosol factor 1
- Deficiency of NCF1
- Deficiency of soluble oxidase component II
- Deficiency of SOC2
- p47-phox, deficiency of neutrophil cytosolic factor 1

Classification:

- Defects of phagocyte function
  - Chronic granulomatous disease

Inheritance:

Autosomal recessive

OMIM:

- #233700 Granulomatous disease, chronic, autosomal cytochrome-b-positive form I
- *608512 Neutrphil cytosolic factor 1; NCF1

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for X-linked chronic granulomatous disease
- IDR factfile for p22phox deficiency
- IDR factfile for p67phox 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: NCF1
Alias(es): p47phox, neutrophil cytosolic factor 1, Neutrophil cytosol factor 1 (NCF-1), Neutrophil NADPH oxidase factor 1, 47 kDa neutrophil oxidase factor, p47-phox, NCF-47K, 47 kDa autosomal chronic granulomatous disease protein

Localization:

Reference sequences:

DNA: U57833 (EMBL) , **cDNA:** M25665 (EMBL) , **Protein:** P14598 (SWISSPROT) Other Sequences

Chromosomal Location:

7q11.23

Maps:

NCF1 (Map View)

Variations / Mutations:

- NCF1base; Mutation registry for autosomal recessive p47 phox deficiency

Other gene-based resources:

Ensembl: ENSG00000158517, GENATLAS: NCF1, GeneCard: NCF1, UniGene: 458275, Entrez Gene: 4687, euGenes: 4687

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):

1GD5 Solution Structure Of The Px Domain From Human P47Phox Nadph Oxidase

Domains:

Px domain: 4-125

Asp/glu-rich (highly acidic) domain: 211-254

Arg/lys-rich (highly basic) domain: 292-390

SH3 1 domain: 156-215

SH3 2 domain: 226-285

Other features:

Other related resourses:

PIR: A39249, InterPro: IPR001655; P47PHOX, InterPro: IPR001683; PX, InterPro: IPR001452; SH3, Pfam: PF00018; SH3, Pfam: PF00787; PX, SMART: SM00312; PX, SMART: SM00326; SH3, PROSITE: PS50195; PX, PROSITE: PS50002; SH3

Expression pattern for human:

Tissue	Exp. (%)	Clones
B cells from Burkitt lymphoma	25.57	7:2143
blood, lymphocyte	12.44	18:11328
leukocyte	8.71	10:8982
blood, white cells	8.60	1:910
tonsil, enriched for germinal center B-cells	8.36	39:36522
colonic mucosa with ulcerative colitus	6.43	1:1218
B-cells	6.15	13:16533
lymph	5.71	47:64395
leukopheresis	3.44	2:4557
osteoarthritic cartilage	2.61	1:2999

Animal models:

Mouse:

MGD: ; Ncf1

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