p22^{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-negative
- CGD due to deficiency of the alpha subunit of cytochrome-b
- CYBA deficiency cytochrome b(-245), alpha polypeptide

Classification:

- Defects of phagocyte function
  - Chronic granulomatous disease

Inheritance:

Autosomal recessive

OMIM:

- #233690 Granulomatous disease, chronic, autosomal cytochrome-b-negative form
- *608508 Cytochrome b(-245), alpha subunit; CYBA

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for X-linked chronic granulomatous disease
- IDR factfile for p47phox 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:

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

GENE INFORMATION

Names:

HUGO name: CYBA
Alias(es): cytochrome b-245, alpha polypeptide, Cytochrome b-245 light chain, p22 phagocyte B-cytochrome, Neutrophil cytochrome B, 22 kDa polypeptide, p22-phox, p22phox, Cytochrome B(558) alpha chain, Cytochrome b558 alpha-subunit, Superoxide- generating NADPH oxidase light chain subunit

Localization:

Reference sequences:

DNA: M61106 (GenBank) , **cDNA:** M21186 (EMBL) , **Protein:** P13498 (SWISSPROT) Other Sequences

Chromosomal Location:

16q24

Maps:

CYBA (Map View)

Variations / Mutations:

- CYBAbase; Mutation registry for p22 phox deficiency

Other gene-based resources:

Ensembl: ENSG00000051523, GENATLAS: CYBA, GeneCard: CYBA, UniGene: 513803, Entrez Gene: 1535, euGenes: 1535

PROTEIN INFORMATION

Description:

Protein function:

Critical component of the membrane-bound oxidase of phagocytes that generates superoxide.

Subunit:

Composed of a heavy chain (#) and a light chain (#).

Miscellaneous:

The heme prosthetic group could be coordinated with residues of the light chain, the heavy chain, or both, and it is possible that more than one heme is present per cytochrome B-245.

Other features:

Iron (heme axial ligand) binding site: 93

Other related resourses:

PIR: A28201

Expression pattern for human:

Tissue	Exp. (%)	Clones
brain, miningioma	17.86	1:709
blood, lymphocyte	11.18	10:11328
B-cells	6.89	9:16533
mixed	5.67	27:60341
leukocyte	5.64	4:8982
osteoarthritic cartilage	4.22	1:2999
tonsil, enriched for germinal center B-cells	4.16	12:36522
aorta	3.70	3:10275
colon	3.54	24:85835
human retina	3.14	1:4036

Animal models:

Mouse:

MGD: ; Cyba

Fly:

euGenes: ; CG1275

C. elegans:

euGenes: ; F55H2.5

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