X-linked chronic granulomatous disease

GENERAL INFORMATION

Description:

X-linked chronic granulomatous disease (X-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:

- X-CGD
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Classification:

- Defects of phagocyte function
  - Chronic granulomatous disease

Inheritance:

X-linked

OMIM:

- #306400 Granulomatous disease, chronic; CGD
- *300481 Cytochrome b(-245), beta subunit; CYBB

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for p22phox deficiency
- 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. CGD rarely appears initially in childhood, first presentation can occur in adults.

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 used widely 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: CYBB
Alias(es): CGD, GP91-PHOX, NOX2, cytochrome b-245, beta polypeptide, Cytochrome B-245 heavy chain , P22 phagocyte B-cytochrome, Neutrophil cytochrome B, 91 kDa polypeptide, CGD91-PHOX, Heme binding membrane glycoprotein GP91PHOX, Cytochrome B(558) beta chain, Superoxide-generating NADPH oxidase heavy chain subunit

Localization:

Reference sequences:

DNA: X05895 (EMBL) , **cDNA:** X04011 (EMBL) , **Protein:** P04839 (SWISSPROT) Other Sequences

Chromosomal Location:

Xp21.1

Maps:

CYBB (Map View)

Variations / Mutations:

- CYBBbase; Mutation registry for X-linked chronic granulomatous disease (XCGD)

Other gene-based resources:

Ensembl: ENSG00000165168, GENATLAS: CYBB, GeneCard: CYBB, UniGene: 292356, Entrez Gene: 1536, euGenes: 1536

PROTEIN INFORMATION

Description:

Protein function:

Critical component of the membrane-bound oxidase of phagocytes that generates superoxide. It is the terminal component of a respiratory chain that transfers single electrons from cytoplasmic NADPH across the plasma membrane to molecular oxygen on the exterior. Also functions as a voltage-gated proton channel that mediates the H+ currents of resting phagocytes. It participates in the regulation of cellular PH and is blocked by zinc.

Subunit:

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

Subcellular location:

Integral membrane protein

Post-translational modification:

Glycosylated

Cofactor:

FAD (probable)

Domains:

Cytoplasmic domain: 1-7

Extracellular domain: 29-47

Cytoplasmic domain: 69-101

Extracellular domain: 123-168

Cytoplasmic domain: 190-199

Extracellular domain: 221-260

Cytoplasmic domain: 282-569

Other features:

FAD nucleotide phosphate-binding region: 337-343

Heme binding site: 100

Heme binding site: 114

Heme binding site: 208

Heme binding site: 221

Other related resourses:

InterPro: IPR002916; Ferric_reduct, InterPro: IPR000778; GP91PhoX, Pfam: PF01794; Ferric_reduct

Expression pattern for human:

Tissue	Exp. (%)	Clones
subchondral bone	15.79	1:1332
kidney, pooled	11.37	4:7404
whole blood	8.60	1:2445
leukocyte	7.03	3:8982
tonsil, enriched for germinal center B-cells	5.76	10:36522
placenta human 8 week	5.21	1:4035
ovary (pool of 3)	4.80	1:4380
lymph	4.25	13:64395
germ cell, pooled	4.11	7:35870
pituitary	3.55	1:5926

Animal models:

Mouse:

MGD: ; Cybb

C. elegans:

euGenes: ; F53G12.3

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