C3 deficiency

GENERAL INFORMATION

Description:

Complement component 3 occupies a central position in the complement pathway, mediating convertase activity, opsonization, anaphylotoxin production, B cell activation and immunoglobulin production, immune-complex clearance and adjuvant production. C3 gene is structurally related to C4 and alfa macroglobulin. It is produced in a wide variety of tissues and is an acute phase reactant. C3 deficiency is a rare autosomic recessive inherited disease, characterized by severe recurrent infections and immune-complex disorders.

Alternative names:

- Complement component 3 deficiency, autosomal recessive

Classification:

- Defects of the classical complement cascade proteins

Inheritance:

Autosomal recessive

OMIM:

- +120700 Complement component 3; C3

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for C2 deficiency

Incidence:

Incidence is not known.

CLINICAL INFORMATION

Description:

C3 deficiency is associated with severe pyogenic infections, glomerulonephritis, and systemic lupus erythematosus. Meningitis, osteomyelitis, sepsis, and pneumonia are all common. The typical organisms include encapsulated bacteria (Pneumococcus, H. influenzae, and Neisserial species). Patients tend to present early in life with recurrent severe infections. Aproximately 25% of patients also have renal disease and/or vasculitic rashes.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Complement deficiency, eMedicine

Therapeutic options:

- Fresh frozen plasma is used for emergent replacement of complements components. Supportive therapy is used for complement deficiencies. Prophylactic antibiotics for the infections.
- Complement deficiency, eMedicine
- Complement deficiency, eMedicine

Research programs, clinical trials:

- European Initiative for Primary Immunodeficiencies
- Molecular and Clinical Studies of Primary Immunodeficiency diseases, ClinicalTrials.gov
- Swegene Project

GENE INFORMATION

Names:

HUGO name: C3
Alias(es): Complement component 3, Complement C3 precursor

Localization:

Reference sequences:

DNA: C3_DNA (EMBL) , **cDNA:** K02765 (EMBL) , **Protein:** P01024 (SWISSPROT)

Chromosomal Location:

19p13.3-p13.2

Maps:

C3 (Map View)

Variations / Mutations:

- C3base; Mutation registry for C3 deficiency

Other gene-based resources:

Ensembl: ENSG00000125730, GENATLAS: C3, GeneCard: C3, UniGene: 529053, Entrez Gene: 718, euGenes: 718, GDB: 119044

PROTEIN INFORMATION

Description:

Protein function:

C3 plays a central role in the activation of the complement system. Its processing by C3 convertase is the central reaction in both classical and alternative complement pathways. After activation C3b can bind covalently, via its reactive thiolester, to cell surface carbohydrates or immune aggregates.

Subunit:

C3 precursor is first processed by the removal of 4 Arg residues, forming two chains, beta and alpha, linked by a disulfide bond. C3 convertase activates C3 by cleaving the alpha chain, releasing C3a anaphylatoxin and generating C3b (beta chain + alpha' chain). During pregnancy, C3dg exists as a complex (probably a 2:2:2 heterohexamer) with agt and the proform of prg2.

Miscellaneous:

C3b is rapidly split in two positions by Factor I and a cofactor to form IC3b (inactivated C3b) and C3f which is released.

Polymorphism:

There are two alleles: C3s (C3 slow), the most common allele in all races and C3f (C3 fast), relatively frequent in caucasoids, less common in black american, extremely rare in orientals.

Structures (PDB):

1C3D X-Ray Crystal Structure Of C3D: A C3 Fragment and Ligand For Complement Receptor 2

Domains:

Anaphylatoxin-like domain: 693-728

Properdin-binding domain: 1424-1456

Other features:

Signal peptide : 1-22

Complement C3: 23-1663

Complement C3, beta chain: 23-667

Complement C3, alpha chain: 672-1663

Released active peptide C3a anaphylatoxin: 672-748

C3b alpha' chain: 749-1663

Released active peptide C3c fragment: 749-954

Released active peptide C3dg fragment: 955-1303

Released active peptide C3g fragment: 955-1001

Released active peptide C3d fragment: 1002-1303

Released active peptide C3f fragment: 1304-1320

Disulfide bond interchain: 559-816

Disulfide bond : 627-662

Disulfide bond : 693-720

Disulfide bond : 694-727

Disulfide bond : 707-728

Disulfide bond : 873-1513

Disulfide bond : 1101-1158

Disulfide bond : 1358-1489

Disulfide bond : 1389-1458

Disulfide bond : 1506-1511

Disulfide bond : 1518-1590

Disulfide bond : 1537-1661

Disulfide bond : 1637-1646

N-linked (glcnac...) glycosylation sites: 85, 939, 1617

Other related resourses:

PIR: C3HU, InterPro: IPR000020; Anaphylatoxin, InterPro: IPR001840; Anaphylatoxn, InterPro: IPR001599; MacroglobInA2, InterPro: IPR001134; Netrin_C, Pfam: PF00207; A2M, Pfam:

Expression pattern for human:

Tissue	Exp. (%)	Clones
gall bladder	24.40	20:2445
adipose, white adipose	11.13	1:268
liver	6.58	81:36737
human spinal cord	6.01	1:496
nose, olfactory epithelium	5.33	2:1119
uterus, endometrium	4.98	3:1796
hepatocellular carcinoma	4.80	23:14298
corresponding non cancerous liver tissue	3.63	17:13955
testis, epididymus	3.16	1:945
adipose, white adipose tissue	3.01	1:990

OTHER RESOURCES

Societies:

General:

- International Patient Organization for Primary Immunodeficiencies
- Immune Deficiency Foundation
- European Society for Immunodeficiencies
- NIH/National Institute of Allergy and Infectious Diseases

Disease specific:

- Lupus Foundation of America
- Lupus Home Page