C5 deficiency

GENERAL INFORMATION

Description:

C5 is part of late complement components C5-C9. Converting C5 to C5a and C5b marks the activation of the terminal components. C5 consists of alfa and beta polypeptide located on the chromosome 9. C5 is distantly related to C3, C4 and alfa 2 macroglobulin and is produced in liver, macrophages, lung, intestine and lymphocytes. Patients with C5 deficiency have decreased total hemolytic complement activity and very little C5 functional activity. The serum of patients with C5 deficiency is unable to generate any chemotactic or bactericidal activity.

Alternative names:

- C5 deficiency
- Complement component 5 deficiency

Classification:

- Defects of the classical complement cascade proteins

Inheritance:

OMIM:

- +120900 Complement component 5 deficiency

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for C6 deficiency
- IDR factfile for C7 deficiency
- IDR factfile for C8 alfa-polypeptide deficiency
- IDR factfile for C8 beta-polypeptide deficiency
- IDR factfile for C8 gamma-polypeptide deficiency
- IDR factfile for C9 deficiency

Incidence:

Incidence is not known.

CLINICAL INFORMATION

Description:

Patients with C5 deficiency have an increased susceptibility to neisserial infections. Recurrent meningococcal infections are very common, and also systemic gonococcal infections appear. Some patients develop systemic lupus erythematous (SLE) like syndrome.

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. Autoimmune disease is treated in the normal way.
- 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: C5
Alias(es): complement component 5, Complement C5 precursor

Localization:

Reference sequences:

DNA: AC006430 (EMBL) , **cDNA:** M57729 (EMBL) , **Protein:** P01031 (SWISSPROT) Other Sequences

Chromosomal Location:

9q32-q34

Maps:

C5 (Map View)

Variations / Mutations:

- C5base; Mutation registry for C5 deficiency.

Other gene-based resources:

Ensembl: ENSG00000106804, GENATLAS: C5, GeneCard: C5, UniGene: 494997, Entrez Gene: 727, euGenes: 727, GDB: 119734

PROTEIN INFORMATION

Description:

Protein function:

Activation of C5 by a C5 convertase initiates the spontaneous assembly of the late complement components, C5-C9, into the Membrane Attack Complex (MAC). C5b has a transient binding site for C6. The C5b-C6 complex is the foundation upon which the lytic complex is assembled.

Subunit:

C5 precursor is first processed by the removal of 4 basic residues, forming two chains, beta & alpha, linked by a disulfide bond. C5 convertase activates C5 by cleaving the alpha chain, releasing C5a anaphylatoxin & generating C5b (beta chain + alpha' chain).

Protein function:

Ref.3 sequence differs from that shown from position 855 onward due to the presence of an Alu repeat.

Structures (PDB):

1KJS	NMR Solution Structure Of C5A At pH 5.2, 303K, 20 Structures
1CFA	Solution Structure Of A Semi-Synthetic C5A Receptor Antagonist At pH 5.2, 303K, NMR, 20 Structures

Domains:

Anaphylatoxin-like domain: 698-732

Other features:

Signal peptide: 1-18

Complement c5 beta chain: 19-673

Propeptide: 674-677

Complement c5 alpha chain: 678-1676

Released active peptide C5a anaphylatoxin: 678-751

C5b (alpha'): 752-1676

Disulfide bonds: 698-724, 699-731, 711-732
N-linked (glcnac...) glycosylation sites: 741, 911, 1115, 1630
Other related resourses:

PIR: C5HU, InterPro: IPR002890; A2M_N, InterPro: IPR000020; Anaphylatoxin, InterPro: IPR001840; Anaphylatoxn, InterPro: IPR001599; MacroglobInA2, InterPro: IPR001134; Netrin_C, Pfam: PF00207; A2M, Pfam: PF01759; NTR, Pfam: PF01821; ANATO, Pfam: PF01835; A2M_N, SMART: SM00104; ANATO, PROSITE: PS00477; ALPHA_2_MACROGLOBULIN, PROSITE: PS01177; ANAPHYLATOXIN_1, PROSITE: PS01178; ANAPHYLATOXIN_2

Expression pattern for human:

Tissue	Exp. (%)	Clones
corresponding non cancerous liver tissue	27.80	16:13909
germ cell, yolk sac	21.40	1:1129
lung epithelial cells tissue nos 359-368	5.53	1:4366
bone marrow stroma	4.53	1:5331
human skeletal muscle	4.50	2:10746
liver	3.71	4:26031
hypothalamus	3.68	1:6565
hepatocellular carcinoma	3.40	2:14226
spleen	3.34	1:7229
kidney, pooled	3.26	1:7404

OTHER RESOURCES

Societies:

General:

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