C8 α-polypeptide deficiency

GENERAL INFORMATION

Description:

C8 is composed of three polypeptide chains (alfa, beta, and gamma). The three of the C8 genes are expressed in hepatocytes. Two types of C8 deficiency exist, and both result in loss of total hemolytic complement activity. C8beta deficiency is more common in Caucasians and C8alfa-gamma deficiency is more common in African-Americans.

Alternative names:

- C8 deficiency, type I
- C8 alpha-gamma deficiency
- C81 deficiency

Classification:

- Defects of the classical complement cascade proteins
  - C8 deficiency

Inheritance:

Autosomal recessive

OMIM:

- +120950 Complement component 8 deficiency, type I

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for C5 deficiency
- IDR factfile for C6 deficiency
- IDR factfile for C7 deficiency
- IDR factfile for C8 beta-polypeptide deficiency
- IDR factfile for C8 gamma-polypeptide deficiency

Incidence:

Incidence is not known.

CLINICAL INFORMATION

Description:

Patients have an inability to form membrane attack complex (MAC) and bactericidal activity is depressed. Patients are susceptible to recurrent pyogenic infections. Typically, they present with meningococcal meningitis and disseminated extragenital gonococcal infection. Two thirds of patients have at least 1 episode of meningococcal disease. Many patients experience recurrent infections.

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. Specific treatment of autoimmune disease is needed.
- 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: C8A
Alias(es): complement component 8, alpha polypeptide, Complement component C8 alpha chain precursor

Localization:

Reference sequences:

DNA: AL121998 (EMBL) , **cDNA:** M16974 (EMBL) , **Protein:** P07357 (SWISSPROT) Other Sequences

Chromosomal Location:

1p32

Maps:

C8A (Map View)

Other gene-based resources:

Ensembl: ENSG00000157131, GENATLAS: C8A, GeneCard: C8A, UniGene: 93210, Entrez Gene: 731, euGenes: 731, GDB: 119735

PROTEIN INFORMATION

Description:

Protein function:

C8 is a constituent of the membrane attack complex (MAC). C8 binds to the C5b-7 complex, forming the C5b-8 complex. C5-b8 binds C9 and acts as a catalyst in the polymerization of C9.

Subunit:

C8 is composed of three chains: alpha, beta and gamma. The alpha and gamma chains are disulfide bonded.

Subcellular location:

Secreted.

Domains:

Tsp type-1 1 domain: 38-93

Ldl-receptor class a domain: 94-132

Egf-like domain: 493-529

Tsp type-1 2 domain: 536-584

Other features:

Signal peptide: 1-20

Propeptide: 21-30

Complement component c8 alpha chain: 31-584

Disulfide bond interchain (with c8-gamma): 194

Disulfide bonds: 96-108, 102-121, 115-130, 375-399

Other related resourses:

PIR: C8HUA, InterPro: IPR002172; LDL_recept_A, InterPro: IPR001862; MAC_perforin, InterPro: IPR000884; TSP1, Pfam: PF00057; ldl_recept_a, Pfam: PF00090; tsp_1, Pfam: PF01823; MACPF, SMART: SM00192; LDLa, SMART: SM00457; MACPF, SMART: SM00209; TSP1, PROSITE: PS00022; EGF_1, PROSITE: PS01186; EGF_2, PROSITE: PS01209; LDLRA_1, PROSITE: PS50068; LDLRA_2, PROSITE: PS00279; MAC_PERFORIN, PROSITE: PS50092; TSP1

Expression pattern for human:

Tissue	Exp. (%)	Clones
gall bladder	52.46	3:2435
hepatocellular carcinoma	17.96	6:14226
liver	11.45	7:26031
corresponding non cancerous liver tissue	9.18	3:13909
spleen	5.89	1:7229
pool, liver+spleen	2.78	4:61327
lung	0.27	1:155782

Animal models:

Fly:

euGenes: ; CG18589

C. elegans:

euGenes: ; ZK337.1a

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