C8 β-polypeptide deficiency

GENERAL INFORMATION

Description:

C8 is composed of three polypeptide chains (alfa, beta, and gamma), each encoded by distinct genes. The three 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 II
- C8 beta deficiency
- Complement component 8, beta subunit deficiency

Classification:

- Defects of the classical complement cascade proteins
  - C8 deficiency

Inheritance:

Autosomal recessive

OMIM:

- +120960 Complement component 8 deficiency, type II

Cross references:

Phenotype related immunodeficiencies:

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

Incidence:

Incidence is not known.

CLINICAL INFORMATION

Description:

Patients have 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 as one half of 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: C8B
Alias(es): Complement component 8, beta polypeptide, Complement component C8 beta chain precursor

Localization:

Reference sequences:

DNA: AL121998 (EMBL) , **cDNA:** M16973 (EMBL) , **Protein:** P07358 (SWISSPROT) Other Sequences

Chromosomal Location:

1p32

Maps:

C8B (Map View)

Variations / Mutations:

- C8Bbase; Mutation registry for C(B deficiency.

Other gene-based resources:

Ensembl: ENSG00000021852, GENATLAS: C8B, GeneCard: C8B, UniGene: 391835, Entrez Gene: 732, euGenes: 732, GDB: 119736

PROTEIN INFORMATION

Description:

Protein function:

C8 is a constituent of the membrane attack complex. 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 beta chain binds to the C8 alpha chain and to the C5b-C7 complex, presumably to C5b. It is essential to the incorporation of C8 into the C5b-C8 complex.

Subcellular location:

Secreted

Post-translational modification:

Composition indicates one or two n-linked oligosaccharide chains and no o-glycosylation.

Polymorphism:

The sequence shown is that of allotype C8b.

Domains:

Tsp type-1 1 domain: 64-119

Ldl-receptor class a domain: 120-157

Egf-like domain: 499-535

Tsp type-1 2 domain: 542-591

Other features:

Signal peptide: 1-32

Propeptide: 33-54

Complement component c8 beta chain: 55-591

Disulfide bonds: 122-133, 127-146, 140-155, 378-403

Other related resourses:

PIR: C8HUB, 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
hepatocellular carcinoma	60.39	12:14226
corresponding non cancerous liver tissue	20.59	4:13909
pool, liver+spleen	10.51	9:61327
liver	8.25	3:26031
brain	0.26	1:274929

Animal models:

Mouse:

MGD: ; C8b

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