C1s deficiency

GENERAL INFORMATION

Description:

C1s deficiency is associated with early onset multiple autoimmune diseases. The genes for C1R and CIS are highly homologous and lie closely linked to chromosome 12p13 and are produced primarily in liver and macrophages.

Classification:

- Defects of the classical complement cascade proteins
  - C1r and C1s deficiency

Inheritance:

Autosomal recessive

OMIM:

- +120580 Complement component 1, s subcomponent; C1S

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for C1r deficiency

Incidence:

Incidence unknown.

CLINICAL INFORMATION

Description:

The most common clinical presentation of C1r/ C1s deficiency is systemic lupus eritematous (SLE), although bacterial infections and glomerulonephritis are also common in this patient population.

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

GENE INFORMATION

Names:

HUGO name: C1S
Alias(es): Complement component 1, s subcomponent, Complement C1s component precursor (C1 esterase)

Localization:

Reference sequences:

DNA: C1S_DNA (C1Sbase) , **cDNA:** J04080 (EMBL) , **Protein:** P09871 (SWISSPROT) Other Sequences

Chromosomal Location:

12p13

Maps:

C1S (Map View)

Variations / Mutations:

- C1Sbase; Mutation registry for C1s deficiency.

Other gene-based resources:

Ensembl: ENSG00000182326, GENATLAS: C1S, GeneCard: C1S, UniGene: 458355, Entrez Gene: 716, euGenes: 716

PROTEIN INFORMATION

Description:

Protein function:

C1s b chain is a serine protease that combines with C1q and C1s to form C1, the first component of the classical pathway of the complement system. C1r activates C1s so that it can, in turn, activate C2 and C4.

Catalytic activity:

Cleaves component C4 to C4a and C4b, and component C2 to C2a and C2b.

Subunit:

C1 is a calcium-dependent trimolecular complex of C1q, r and s in the molar ration of 1:2:2. Activated C1s is an disulfide-linked heterodimer of an heavy chain and a light chain.

Domains:

Cub 1 domain: 16-130

Egf-like, calcium-binding domain: 131-172

Cub 2 domain: 175-290

Sushi 1 domain: 293-355

Sushi 2 domain: 358-422

Serine protease domain: 438-688

Other features:

Signal peptide: 1-15

Complement c1s heavy chain: 16-437

Complement c1s light chain: 438-688

Other related resourses:

PIR: C1HUS, InterPro: IPR000152; Asx_hydroxyl, InterPro: IPR000859; CUB_domain, InterPro: IPR001314; Chymotrypsin, InterPro: IPR006210; EGF-like, InterPro: IPR001881; EGF_Ca, InterPro: IPR001254; Ser_protease_Try, InterPro: IPR000436; Sushi_SCR_CCP, Pfam: PF00008; EGF, Pfam: PF00084; sushi, Pfam: PF00089; trypsin, Pfam: PF00431; CUB, SMART: SM00032; CCP, SMART: SM00042; CUB, SMART: SM00179; EGF_CA, SMART: SM00020; Tryp_SPc, PROSITE: PS00010; ASX_HYDROXYL, PROSITE: PS01180; CUB, PROSITE: PS00022; EGF_1, PROSITE: PS01186; EGF_2, PROSITE: PS01187; EGF_CA, PROSITE: PS50240; TRYPSIN_DOM, PROSITE: PS00134; TRYPSIN_HIS, PROSITE: PS00135; TRYPSIN_SER

Expression pattern for human:

Tissue	Exp. (%)	Clones
connective tissue	9.43	3:1301
thyroid gland	7.20	2:1136
nasopharynx	6.33	1:646
subchondral bone	6.14	2:1332
brain, meningioma	5.77	1:709
adipose	4.82	1:849
pancreas, exocrine	4.39	23:21418
mammary gland	2.84	1:1441
esophagus	2.77	2:2949
lung with fibrosis	2.77	1:1479

Animal models:

Fly:

euGenes: ; CG6807

C. elegans:

euGenes: ; Y48G9A.4

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:

- Lupus Foundation of America