

C1r deficiency

GENERAL INFORMATION

Description:

C1r deficiency is associated with early onset multiple autoimmune diseases. The genes for C1R and C1S 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:

- +216950 Complement component C1r deficiency

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for C1s deficiency

Incidence:

Incidence is not known.

CLINICAL INFORMATION

Description:

The most common clinical presentation of C1r/C1s deficiency is systemic lupus erythematosus (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
- Swegene Project

GENE INFORMATION

Names:

HUGO name: C1R

Alias(es): Complement component 1, r subcomponent, Complement C1r component precursor

Localization:**Reference sequences:**

DNA: AB083037 (GenBank) , **cDNA:** M14058 (EMBL) , **Protein:** P00736 (SWISSPROT)
Other Sequences

Chromosomal Location:

12p13

Maps:

C1R (Map View)

Other gene-based resources:

Ensembl: ENSG00000159403, GENATLAS: C1R, GeneCard: C1R, UniGene: 524224, Entrez Gene: 715, euGenes: 715

PROTEIN INFORMATION**Description:****Protein function:**

C1r 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.

Catalytic activity:

Activates C1s by proteolytic cleavage so that it can, in turn, activate C2 and C4.

Subunit:

C1 is a calcium-dependent trimolecular complex of C1q, r and s in the molar ration of 1:2:2. C1r is a dimer of identical chains, each of which is activated by cleavage into two chains, a and b, connected by disulfide bonds.

Structures (PDB):

1APQ Structure Of The Egf-Like Module Of Human C1R, NMR, 19 Structures

Domains:

Cub 1 domain: 18-141

Egf-like, calcium-binding domain: 142-190

Cub 2 domain: 193-305

Sushi 1 domain: 308-372

Sushi 2 domain: 375-448

Serine protease domain: 464-705

Other features:

Signal peptide: 1-17

Complement c1r heavy chain: 18-463

Complement c1r light chain: 464-705

Other related resources:

PIR: C1HURB, 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: 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
lymph node	17.52	1:125
thyroid gland	9.64	5:1136
skin, normal, 4 pooled samples	5.81	1:377
eye, cornea	4.86	1:451
mammary gland	4.56	3:1441
head/neck	4.20	1:522
gall bladder	3.60	4:2435
normal head/neck tissue	3.39	2:1292
subchondral bone	3.29	2:1332
brain, meningioma	3.09	1:709

Animal models:

Mouse:

MGD: ; C1r

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
- Lupus Home Page