C2 deficiency

GENERAL INFORMATION

Description:

Complement component 2 (C2) is a serine protease and is highly homologous to factor B. C2 is produced by hepatocytes, macrophages, and fibroblasts. C2 deficiency is an autosomal recesive disease and has been the most widely reported of all the components in this pathway. Deficient individuals have an increased incidence of systemic lupus erythematosus SLE and SLE-like syndromes, glomerulonephritis, vasculitis and pyogenic infections. Type I C2 deficiency is characterized by complete loss of the protein while type II C2 deficiency is characterized by a selective block in C2 secretion.

Classification:

- Defects of the classical complement cascade proteins

Inheritance:

Autosomal recessive

OMIM:

- +217000 Complement component 2 deficiency

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for C1q alfa-polypeptide deficiency
- IDR factfile for C1q beta-polypeptide deficiency

Incidence:

1:10,000

CLINICAL INFORMATION

Description:

C2 deficiency is one of the most common inherited complement component deficiency. It may occur in asymptomatic individuals but it is frequently associated with autoimmune manifestations, particularly with discoid or systemic lupus erythematosus. Approximately 40% of the patients with C2 deficiency develop SLE or discoid lupus and aproximately 50% develop recurrent infections. Patients with C2 deficiency express many of the characteristic features of lupus, but severe nephritis, cerebritis, and aggressive arthritis are less common than in complement sufficient SLE patients. Cutaneous lesions are common in C2 deficiencient patients with lupus, and many have a characteristic annular photosensitive rash. C2 deficiency patients have also other reumathic disordes as glomerulonephritis, dermatomyositis, anaphylactoid purpura, and vasculitis. The bacterial infections are usually systemic infections (e.g. sepsis and meningitis) with encapsulated organisms (Pneumococcus and H.influenzae) and more common in childhood.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Complement deficiency, eMedicine

Genetic:

- Molecular diagnostics of C2 deficiency, ORPHANET

Therapeutic options:

- No specific treatment is available for C2 deficiency. Prevention and acute treatment of infections are essential; infusion of fresh frozen plasma can be used for emergency replacement of C2 component. Meningococcal, pneumococcal, and haemophilus vaccinations are recommended.
- Complement deficiency, eMedicine
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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: C2
Alias(es): Complement component 2, Complement C2 precursor(C3/C5 convertase)

Localization:

Reference sequences:

DNA: AF019413 (EMBL) , **cDNA:** X04481 (EMBL) , **Protein:** P06681 (SWISSPROT) Other Sequences

Chromosomal Location:

6p21.3

Maps:

C2 (Map View)

Variations / Mutations:

- C2base; Mutation registry for C2 deficiency

Other gene-based resources:

Ensembl: ENSG00000166278, GENATLAS: C2, GeneCard: C2, UniGene: 408903, Entrez Gene: 717, euGenes: 717, GDB: 119731

PROTEIN INFORMATION

Description:

Protein function:

Component C2 which is part of the classical pathway of the complement system is cleaved by activated factor C1 into two fragments: C2b and C2a. C2a, a serine protease, then combines with complement factor 4b to generate the C3 or C5 convertase.

Catalytic activity:

Cleaves C3 in the alpha-chain to yield C3a and C3b. Cleaves C5 in the alpha-chain to yield C5a and C5b. Both cleavages take place at the C-terminal of an Arginine residue.

Miscellaneous:

C2 is a Major Histocompatibility Complex Class-III protein.

Other features:

Other related resourses:

PIR: C2HU, InterPro: IPR001314; Chymotrypsin, InterPro: IPR001254; Ser_protease_Try, InterPro: IPR000436; Sushi_SCR_CCP, InterPro: IPR002035; VWF_A, Pfam: PF00084; sushi, Pfam: PF00089; trypsin, Pfam: PF00092; vwa, SMART: SM00032; CCP, SMART: SM00020; Tryp_SPc, SMART: SM00327; VWA, PROSITE: PS50240; TRYPSIN_DOM, PROSITE: PS00134; TRYPSIN_HIS, PROSITE: PS00135; TRYPSIN_SER, PROSITE: PS50234; VWFA

Expression pattern for human:

Tissue	Exp. (%)	Clones
eye, cornea	30.15	2:451
skin, melanocyte	13.07	1:520
blood, white cells	7.47	1:910
sympathetic trunk	7.45	1:913
dorsal root ganglia	6.66	1:1021
hepatocellular carcinoma	5.73	12:14226
lung with fibrosis	4.60	1:1479
uterus, endometrium	3.80	1:1790
uterus, pooled	2.19	5:15533
brain, pooled	2.15	1:3166

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

Disease specific:

- Lupus Foundation of America
- Lupus Home Page