C4A deficiency

GENERAL INFORMATION

Description:

C4 is encoded by two genes C4A and C4B and is evolutionarily related to C3, C5, and alfa2 macroglobulin. The two isotypes are encoded by two distinct loci within the major histocompatibility complex (MHC) class III region on chromosome 6. Both genes are higly polymorphic.

Alternative names:

- Complement component 4A deficiency

Classification:

- Defects of the classical complement cascade proteins
  - C4 deficiency

Inheritance:

Autosomal recessive

OMIM:

- +120810 Complement component 4A; C4A

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for C4B deficiency

Incidence:

Incidence is not known.

CLINICAL INFORMATION

Description:

Most C4 deficient patients have discoid or systemic lupus erythematous, with or without associated glomerulonephritis. The disease onset is earlier than for systemic lupus erythematous (SLE) in complement-sufficient patients, and cutaneous features, as Raynaud's phenomenon and vasculitic ulcers are common. Bacterial infections are a common cause of morbidity and mortality. Systemic lupus erythematous (SLE) patients with C4A deficiency have a lower prevalence of anticardiolipin, anti-Ro, anti-dsDNA, and anti-Sm antibodies, less neurologic disease and renal disease, and more photosensitivity than other systemic lupus erythematous (SLE) patients.

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: C4A
Alias(es): C4S, C4A AND C4B, Complement component 4A, Complement C4 precursor

Localization:

Reference sequences:

DNA: AL929593 (GenBank) , **cDNA:** NM_007293 (GenBank) , **Protein:** P01028 (SWISSPROT) Other Sequences

Chromosomal Location:

6p21.3

Maps:

C4A (Map View)

Other gene-based resources:

Ensembl: ENSG00000182326, GENATLAS: C4A, GeneCard: C4A, UniGene: 534847, Entrez Gene: 720, euGenes: 720

PROTEIN INFORMATION

Description:

Protein function:

C4 plays a central role in the activation of the classical pathway of the complement system. It is processed by activated C1 which remove from the alpha chain the C4a anaphylatoxin.

Subunit:

This protein is synthesized as a single-chain precursor and, prior to secretion, is enzymatically cleaved to form a trimer of nonidentical chains (alpha, beta, and gamma).

Miscellaneous:

C4a allotypes react more rapidly with the amino group of peptide antigens while C4b allotypes react more rapidly with the hydroxyl group of carbohydrate antigens.

Polymorphism:

Human complement component C4 is polymorphic with at least two loci, C4a and C4b. 13 alleles of C4a and 22 alleles of C4b have been detected.

Domains:

Anaphylatoxin-like domain: 702-736

Other features:

Signal peptide: 1-19

Complement C4, beta chain: 20-675

Propeptide: 676-679

Complement C4, alpha chain: 680-1446

Propeptide: 1447-1453

Complement C4, gamma chain: 1454-1744

Released active peptide C4a anaphylatoxin: 680-756

Disulfide bonds: 702-728, 703-735, 716-736

Other related resourses:

PIR: C4HU, PIR: B20807, InterPro: IPR002890; A2M_N, InterPro: IPR000020; Anaphylatoxin, InterPro: IPR001599; MacroglobInA2, InterPro: IPR001134; Netrin_C, Pfam: PF00207; A2M, Pfam: PF01759; NTR, Pfam: PF01821; ANATO, Pfam: PF01835; A2M_N, SMART: SM00104; ANATO, PROSITE: PS00477; ALPHA_2_MACROGLOBULIN, PROSITE: PS01177; ANAPHYLATOXIN_1, PROSITE: PS01178; ANAPHYLATOXIN_2

Expression pattern for human:

Tissue	Exp. (%)	Clones
liver	50.53	8:26031
human optic nerve	37.32	1:4406
hepatocellular carcinoma	11.56	1:14226
brain	0.60	1:274929

Animal models:

Mouse:

MGD: ; Slp

Fly:

euGenes: ; Tepl

C. elegans:

euGenes: ; ZK337.1b

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