C4 binding protein α deficiency

GENERAL INFORMATION

Description:

Complement C4b-binding protein (C4BP) is a plasma protein synthesized in the liver and plays a regulatory role in the host defense complement system. C4BP binds to C4b and accelerates the decay of C4b2a. It is a cofactor for factor I inactivation of C4b. Mutations in C4BPA are associated with angioedema, cutaneous vasculitis, and arthritis.

Alternative names:

- Complement component 4-binding protein deficiency

Classification:

- Defects of complement regulatory proteins
  - C4-binding protein deficiency

Inheritance:

Autosomal recessive

OMIM:

- *120830 Complement component 4-binding protein, alpha; C4BPA

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for C4 binding protein β deficiency

Incidence:

Incidence is not known.

CLINICAL INFORMATION

Description:

Patients have angioedema, cutaneous vasculitis, and arthritis. Activation of the classical pathway increases C3 consumption with diminished inhibition of the C4b.2a enzyme. The increased production of C3a and C5a might have led to angioedema through increased vascular permeability.

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

Research programs, clinical trials:

- European Initiative for Primary Immunodeficiencies.
- Molecular and Clinical Studies of Primary Immunodeficiency diseases, ClinicalTrials.gov

GENE INFORMATION

Names:

HUGO name: C4BPA
Alias(es): C4BP, complement component 4 binding protein, alpha, complement component 4-binding protein, alpha, C4b-binding protein alpha chain precursor, Proline-rich protein, PRP

Localization:

Reference sequences:

DNA: AL445493 (GenBank) , **cDNA:** BC022312 (EMBL) , **Protein:** P04003 (SWISSPROT) Other Sequences

Chromosomal Location:

1q32

Maps:

C4BPA (Map View)

Other gene-based resources:

Ensembl: ENSG00000123838, GENATLAS: C4BPA, GeneCard: C4BPA, UniGene: 1012, Entrez Gene: 722, euGenes: 722

PROTEIN INFORMATION

Description:

Protein function:

C4BP controls the classical pathway of complement activation. It binds as a cofactor to C3b/C4b inactivator (C3bina), which then hydrolyzes the complement fragment C4b. It also accelerates the degradation of the C4bc2a complex (C3 convertase) by dissociating the complement fragment C2a. Alpha chain binds C4b. It interacts also with anticoagulant protein S and with serum amyloid P component.

Subunit:

Disulfide-linked complex of C4bp alpha and beta chains of 3 possible sorts: a 570 kda complex of 7 alpha chains and 1 beta chain, a 530 kda homoheptamer of alpha chains or a 500 kda complex of 6 alpha chains and 1 beta chain. The central body of the alpha chain homopolymer supports tentacles, each with the binding site for C4b at the end.

Protein function:

It is uncertain whether MET-1 or MET-17 is the initiator.

Domains:

Sushi 1 domain: 49-109

Sushi 2 domain: 112-171

Sushi 3 domain: 174-235

Sushi 4 domain: 238-295

Sushi 5 domain: 298-361

Sushi 6 domain: 364-423

Sushi 7 domain: 425-481

Sushi 8 domain: 483-539

Other features:

Signal peptide: 1-48

C4b-binding protein alpha chain: 49-597

Other related resourses:

PIR: NBHUC4, InterPro: IPR000436; Sushi_SCR_CCP, Pfam: PF00084; sushi, SMART: SM00032; CCP

Expression pattern for human:

Tissue	Exp. (%)	Clones
uterus, endometrium	29.36	2:1790
nose, olfactory epithelium	23.55	1:1116
corresponding non cancerous liver tissue	11.34	6:13909
liver	6.06	6:26031
hepatocellular carcinoma	5.54	3:14226
lung, 2 pooled	4.76	3:16549
neuroendocrine lung carcinoids		
pool, liver+spleen	4.29	10:61327
human lung epithelial cell lines untreated lps 6hr to lps	4.19	1:6278
lung metatastic chondrosarcoma	4.08	1:6448
human skeletal muscle	2.45	1:10746

Animal models:

Mouse:

MGD: ; C4bp

Fly:

euGenes: ; fw

C. elegans:

euGenes: ; T07H6.5

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