Decay-accelerating factor (CD55) deficiency

GENERAL INFORMATION

Description:

DAF, or CD55, is a control protein of the classical and alternative pathways. It is deficient in red blood cells from patients with paroxysmal nocturnal hemoglobinuria (PNH). DAF is a glycosyl phosphatidylinositol (GPI)-anchored membrane protein found on erythrocytes, lymphocytes, granulocytes, endothelium, and epithelium. The main function of DAF is to protect cells from complement-mediated cytolysis and it also plays a role in T cell activation. PNH is a rare condition, which causes increased sensitivity of red cells to lysis by complement due to absence of MIRL and DAF.

Alternative names:

- CD55 deficiency
- DAF deficiency

Classification:

- Defects of complement regulatory proteins

Inheritance:

Autosomal recessive

OMIM:

- *125240 Decay-accelerating factor for complement; DAF

Cross references:

Phenotype related immunodeficiencies:

- CD59 deficiency

Incidence:

Incidence is not known.

CLINICAL INFORMATION

Description:

DAF deficiency is associated with Inab phenotype (absence of all blood group antigens of the Cromer complex). Clinically, PNH (paroxysmal nocturnal hemoglobinuria) usually affects young adults and has a variable course of intravascular haemolysis, pancytopenia, and recurrent (usually venous) thromboses. It often arises in patients with aplastic anaemia, and may transform into acute myeloblastic leukaemia. Complications include iron deficiency (from chronic haemoglobinuria), progressive renal impairment (from haemoglobinuria), and the Budd Chiari syndrome (hepatic vein thrombosis).

Diagnosis:

Diagnostic laboratories:

Clinical:

- Complement deficiency, eMedicine
- Paroxysmal nocturnal hemoglobinuria, eMedicine

Therapeutic options:

- Treatment is primarily symptomatic (transfusion, erythropoietin, glucocorticoids, anticoagulation) or includes, in severe cases, bone marrow transplantation. Techniques for the suppression of complement activation with monoclonal antibodies are currently under development.
- Complement deficiency, eMedicine
- Complement deficiency, eMedicine
- Paroxysmal nocturnal hemoglobinuria, 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: CD55
Alias(es): DAF, CR, TC, decay accelerating factor for complement, Complement decay-accelerating factor precursor, CD55 antigen

Localization:

Reference sequences:

DNA: AB003312 (GenBank) , **cDNA:** M31516 (EMBL) , **Protein:** P08174 (SWISSPROT) Other Sequences

Chromosomal Location:

1q32

Maps:

DAF (Map View)

Other gene-based resources:

Ensembl: ENSG00000196352, GENATLAS: DAF, GeneCard: DAF, UniGene: 527653, Entrez Gene: 1604, euGenes: 1604, GDB: 119088

PROTEIN INFORMATION

Description:

Protein function:

This protein recognizes C4b and C3b fragments that condense with cell-surface hydroxyl or amino groups when nascent C4b and C3b are locally generated during C4 and C3 activation. Interaction of DAF with cell-associated C4b and C3b polypeptides interferes with their ability to catalyze the conversion of C2 and factor B to enzymatically active C2a and bb and thereby prevents the formation of C4b2a and C3bbb, the amplification convertases of the complement cascade.

Subunit:

Monomer (major form) and non-disulfide-linked, covalent homodimer (minor form).

Subcellular location:

Attached to the membrane by a GPI-anchor.

Post-translational modification:

The SER/THR-rich domain is heavily o-glycosylated.

Protein function:

2 isoforms; 1/DAF-1 and 2/DAF-2; are produced by alternative splicing.

Polymorphism:

DAF is responsible for the cromer blood group system. It consists of at least seven high-incidence (cr(a), tc(a), dr(a), es(a), wes(b), umc, and ifc) and low-incidence (tc(b), tc(c), and wes(a)) antigens that reside on DAF. In the cromer phenotypes dr(a-) and inab there is reduced or absent expression of DAF, respectively. In the case of the dr(a-) phenotype, a single nucleotide substitution within exon 5 accounts for two changes: a simple amino acid substitution that is the basis of the antigenic variation, and an alternative splicing event that underlies the decreased expression of daf in this phenotype.

Other features:

Other related resourses:

PIR: B26359, PIR: A26359, InterPro: IPR000436; Sushi_SCR_CCP, Pfam: PF00084; sushi, SMART: SM00032; CCP

Expression pattern for human:

Tissue	Exp. (%)	Clones
nose, olfactory epithelium	7.34	1:1116
muscle (skeletal)	6.85	8:9571
mammary gland	5.68	1:1441
cervix	5.50	17:25325
leukopheresis	5.39	3:4557
pancreas, exocrine	5.35	14:21418
bone marrow	4.95	12:19854
placenta	4.32	49:92983
lung	3.89	74:155782
gall bladder	3.36	1:2435

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