MAC inhibitor (CD59) deficiency

GENERAL INFORMATION

Description:

The CD59 is an 18- to 25-kD glycoprotein expressed on all human peripheral blood leukocytes, erythrocytes. CD59 prevent intravascular complement attack. Antigens encoded by both Ly6 and CD59 genes are important to T-cell and NK-cell function.

Alternative names:

- Antigen p18-20 deficiency
- Protectin deficiency

Classification:

- Defects of complement regulatory proteins

Inheritance:

Autosomal recessive

OMIM:

- +107271 CD59 antigen p18-20; CD59

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for Decay-accelerating factor (CD55) deficiency

Incidence:

Incidence is not known.

CLINICAL INFORMATION

Description:

Patients have recurrent hemolytic anemia, thrombosis and recurrent cerebral infarctions. Studies of four GPI-anchored proteins which are typically lost in paroxysmal nocturnal hemoglobinuria revealed normal levels of all except for CD59. CD59 was absent from the surface of his erythrocytes and fibroblasts. Erythrocytes are highly susceptible to complement-mediated lysis.

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: CD59
Alias(es): MIC11, MIN1, MIN2, MIN3, MSK21, CD59 antigen p18-20, CD59 glycoprotein precursor , Membrane attack complex inhibition facto, MACIF, MAC-inhibitory protein, MAC-IP, MEM43 antigen, Protectin, Membrane inhibitor of reactive lysis, MIRL

Localization:

Reference sequences:

DNA: M84345 (EMBL) M84349 (EMBL) Z14113 (EMBL) , **cDNA:** M27909 (EMBL) M95708 (EMBL) X16447 (EMBL) X17198 (EMBL) X15861 (EMBL) M34671 (EMBL) , **Protein:** P13987 (SWISSPROT) Other Sequences

Chromosomal Location:

11p13

Maps:

CD59 (Map View)

Other gene-based resources:

Ensembl: ENSG00000085063, GENATLAS: CD59, GeneCard: CD59, UniGene: 278573, Entrez Gene: 966, euGenes: 966, GDB: 119769

PROTEIN INFORMATION

Description:

Protein function:

Potent inhibitor of the complement Membrane Attack Complex (MAC) action. Acts by binding to the C8 and/or C9 complements of the assembling MAC, thereby preventing incorporation of the multiple copies of C9 required for complete formation of the osmolytic pore. This inhibitor appears to be species-specific. Involved in signal transduction for T-cell activation complexed to a protein tyrosine kinase. Interacts with T-cell surface antigen CD2.

Subcellular location:

Attached to the membrane by a GPI-anchor.

Post-translational modification:

N-and O-glycosylated. The N-gycosylation mainly consists of a family of bi-antennary complex-type structures with and without lactosamine extensions and outer arm fucose residues. The predomiant O-glycans are mono-sialylated forms of the disaccharide, GAL-beta-1, 3GALNAC, and their sites of attachment are probably on THR-76 and THR-77.

Structures (PDB):

1CDQ Structure of a soluble, glycosylated form of the human complement regulatory protein CD59.
1CDR Structure of a soluble, glycosylated form of the human complement regulatory protein CD59.
1CDS Structure of a soluble, glycosylated form of the human complement regulatory protein CD59.
1ERG Three-dimensional solution structure of the extracellular region of the complement regulatory protein CD59, a new cell-surface protein domain related to snake venom neurotoxins.
1ERH Three-dimensional solution structure of the extracellular region of the complement regulatory protein CD59, a new cell-surface protein domain related to snake venom neurotoxins.

Domains:

Upar/ly6 domain: 26-108

Other features:

Signal peptide: 1-25

Cd59 glycoprotein: 26-102

Propeptide Removed in mature form: 103-128

N-linked (glycation) glycosylation site: 66

N-linked (glycation) glycosylation site: 69

O-linked (glcnac...) glycosylation site: 76

O-linked (glcnac...) glycosylation site: 77

Glycosyl-phosphatidylinositol (GPI) group linked to the alpha-carboxyl group of the C-terminal residue of the mature form of a protein: 102

Disulfide bonds: 28-51, 31-38, 44-64, 70-88, 89-94

N-linked (glcnac...) glycosylation sites: 43

Other related resourses:

PIR: RWHU59, InterPro: IPR001526; LY6_UPAR, InterPro: IPR003632; Ly-6_CD59, Pfam: PF00021; UPAR_LY6, ProDom: PD003128; Ly-6_CD59, SMART: SM00134; LU, PROSITE: PS00983; LY6_UPAR

Expression pattern for human:

Tissue	Exp. (%)	Clones
lung, cell line	7.84	4:876
human choriocarcinoma	7.01	1:245
prostate, stroma	6.04	1:284
pituitary tumor	4.93	2:696
ovary, tumor tissue	4.58	3:1125
adipose, white adipose tissue	3.48	2:987
dorsal root ganglia	3.36	2:1021
normal gingiva (cell line from immortalized keratinocytes)	3.32	1:517
aorta, endothelium	2.82	5:3042
adult brain	2.52	1:682

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