Factor H1 deficiency

GENERAL INFORMATION

Description:

Factor H, also known as beta-1H, is a serum glycoprotein that controls the function of the alternative complement pathway and acts as a cofactor with factor I. It regulates the activity of the C3 convertases such as C4b2a. Factor H is synthesized in hepatocytes, macrophages, B cells, endothelial cells, and platelets. Deficiency of factor H leads to uncontrolled activation of the alternative pathway and C3 consumption. Levels of C3 are reduced, and total hemolytic complement activity and alternative pathway complement activity are usually reduced.

Alternative names:

- Complement factor H deficiency

Classification:

- Defects of the alternative complement pathway

Inheritance:

Autosomal recessive

OMIM:

- +134370 H factor 1; HF1

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for C4 binding protein α deficiency

Incidence:

Incidence is not known.

CLINICAL INFORMATION

Description:

The most common finding in patients with factor H deficiency is renal disease. Glomerulonephritis, IgA nephropathy, and hemolytic uremic syndrome have been described in some patients. Infections with neisserial species and encapsulated organisms are also common. Some patients with factor H deficiency are asymptomatic.

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: CFH
Alias(es): HF1, HF, HUS, H factor 1 complement, Complement factor H precursor, H factor 1

Localization:

Reference sequences:

DNA: AL049744 (EMBL) , **cDNA:** Y00716 (EMBL) , **Protein:** P08603 (SWISSPROT) Other Sequences

Chromosomal Location:

1q32

Maps:

HF1 (Map View)

Variations / Mutations:

- CFHbase; Mutation registry for Factor H deficiency

Other gene-based resources:

Ensembl: ENSG00000000971, GENATLAS: CFH, GeneCard: CFH, UniGene: 363396, Entrez Gene: 3075, euGenes: 3075, GDB: 120041

PROTEIN INFORMATION

Description:

Protein function:

Factor H functions as a cofactor in the inactivation of C3b by factor I and also increases the rate of dissociation of the C3bbb complex (C3 convertase) and the (C3b)nbb complex (C5 convertase) in the alternative complement pathway.

Protein function:

2 isoforms; 1 and 2; are produced by alternative splicing.

Structures (PDB):

1HCC	Three-dimensional structure of a complement control protein module in solution.
1HFH	Solution structure of a pair of complement modules by nuclear magnetic resonance.
1HFI	Solution structure of a pair of complement modules by nuclear magnetic resonance.

Domains:

Sushi 1 domain: 20-81

Sushi 2 domain: 84-142

Sushi 3 domain: 145-206

Sushi 4 domain: 209-263

Sushi 5 domain: 266-321

Sushi 6 domain: 324-386

Sushi 7 domain: 388-443

Sushi 8 domain: 447-506

Sushi 9 domain: 508-565

Sushi 10 domain: 568-624

Sushi 11 domain: 629-685

Sushi 12 domain: 690-745

Sushi 13 domain: 752-804

Sushi 14 domain: 810-865

Sushi 15 domain: 869-927

Sushi 16 domain: 930-985

Sushi 17 domain: 988-1044

Sushi 18 domain: 1047-1103

Sushi 19 domain: 1108-1164

Sushi 20 domain: 1166-1229

Other features:

Signal peptide: 1-18

Complement factor h: 19-1231

Disulfide bonds: 21-66, 52-80, 85-129, 114-141, 146-192, 178-205, 210-251, 237-262, 267-309, 294-320, 325-374, 357-385, 389-431, 416-442, 448-494, 477-505, 509-553, 536-564, 569-611, 597-623, 630-673, 659-684, 691-733, 719-744, 753-792, 781-803, 811-853, 839-864, 870-915, 901-926, 931-973, 959-984, 989-1032, 1018-1043, 1048-1091, 1077-1102, 1109-1152, 1138-1163, 1167-1218, 1201-1228

N-linked (glcnac...) glycosylation sites: 529, 718, 802, 822, 882, 911, 1029, 1095

Other related resourses:

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

Expression pattern for human:

Tissue	Exp. (%)	Clones
corresponding non cancerous liver tissue	15.23	19:13909
whole embryo, mainly head	12.95	4:3442
subchondral bone	8.37	1:1332
mammary gland	7.74	1:1441
muscle, striated	6.46	2:3451
liver	6.00	14:26031
hepatocellular carcinoma	4.70	6:14226
bladder	4.36	7:17890
grade-2-chondrosarcoma	4.22	1:2639
osteoarthritic cartilage	3.72	1:2999

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