Hereditary angioedema type III

GENERAL INFORMATION

Description:

Defects in F12 are the cause of factor 12 deficiency (F12 deficiency) [mim:234000]; also known as Hageman factor deficiency. This trait is an asymptomatic anomaly of in vitro blood coagulation. Its diagnosis is based on finding a low plasma activity of the factor in coagulating assays. It is usually only accidentally discovered through pre-operative blood tests. F12 deficiency is divided into two categories, a cross-reacting material (crm)-negative group (negative f12 antigen detection) and a crm-positive group (positive f12 antigen detection). Hereditary angioedema is episodic and asymptomatic in most patients. There are 3 types of the disorder. In type I, representing 85% of patients, serum levels of C1NH are less than 35%. In type II, the levels are normal or elevated, but the protein is nonfunctional. The two types are clinically similar. In HAE type III patients have normal C1-inhibitor concentration and function and a missense mutation in F12. Patients are exclusively women and their episodes of angioedema are precipitated or worsened by high estrogen levels.

Alternative names:

- HAE type III
- Estrogen-related HAE
- Estrogen-sensitive HAE
- Angioneurotic edema, hereditary, with normal C1 inhibitor concentration and function
- HAE with normal C1 inhibitor concentration and function
- Hereditary angioedema with normal C1 inhibitor activity

Classification:

- Defects of complement regulatory proteins
  - Hereditary angioedema type III

Inheritance:

Autosomal dominant

OMIM:

- #610618 Angioedema, hereditary, type III; HAE III
- #106100 Angioedema, hereditary, type III; HAE III

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for Hereditary angioedema type I and type II

Incidence:

Incidence is not known.

CLINICAL INFORMATION

Description:

Patients can develop rapid swelling of the hands, feet, limbs, face, intestinal tract, or airway (larynx or trachea). HANE is characterized by recurrent episodes of angioedema involving any part of the body. Laryngeal edema is common, and it is the major cause of death. Angioedema of the gastrointestinal tract may frequently mimic an acute abdomen.

Diagnosis:

Diagnostic laboratories:

Clinical:

- GeneTest
- ORPHANET
- eMedicine

Genetic:

- IDdiagnostics

Therapeutic options:

- C1 inhibitor concentrate is preferred for acute treatment. Androgens such as winstrol, danazol, and oxandrolone for possible prevention of episodes. Hypotension accompanies abdominal attacks in some patients and fluid replacement therapy is required. A combination of Demerol and Compazine suppositories, and possibly Dicyclomine is useful to relieve abdominal pain and vomiting.
- Angioedema, Hereditary, eMedicine

Research programs, clinical trials:

- European Initiative for Primary Immunodeficiencies.
- Study of Heparin Prophylaxis of Hereditary Angioedema Exacerbations, ClinicalTrials.gov

GENE INFORMATION

Names:

HUGO name: F12

Localization:

Reference sequences:

DNA: D0119 (IDRefSeq) , **cDNA:** M31315 (EMBL) , **Protein:** P00748 (SWISSPROT) Other Sequences

Chromosomal Location:

Maps:

F12 (Map View)

Variations / Mutations:

- F12base; Mutation registry for HAE type III

Other gene-based resources:

Ensembl: ENSG00000131187, GENATLAS: F12, GeneCard: F12, UniGene: 2161, Entrez Gene: 2161, euGenes: 2161, GDB: 2161, HomoloGene: 425

PROTEIN INFORMATION

Description:

Protein function:

Factor XII is a serum glycoprotein that participates in the initiation of blood coagulation, fibrinolysis, and the generation of bradykinin and angiotensin. Prekallikrein is cleaved by Factor XII to form kallikrein, which then cleaves Factor XII first to alpha-factor XIIa and then to beta-factor XIIa. Alpha-factor XIIa activates factor XI to factor XIa

Catalytic activity:

Selective cleavage of Arg-|-ile bonds in factor VII to form factor VIIa and factor XI to form factor XIa

Subcellular location:

Secreted

Post-translational modification:

O- and n-glycosylated. The o-linked polysaccharides were not identified, but are probably the mucin type linked to galnac

Similarity:

Belongs to the peptidase S1 family

Domains:

Fibronectin type-II domain: 42-90

EGF-like 1 domain: 94-131

Fibronectin type-I domain: 133-173

EGF-like 2 domain: 174-210

Kringle domain: 217-295

Peptidase S1 domain: 373-614

Other features:

Signal peptide: 1-19

Coagulation factor XIIa heavy chain: 20-372

Beta-factor XIIa part 1: 354-362

Beta-factor XIIa part 2: 373-615

Coagulation factor XIIa light chain: 373-615

O-linked (fuc) and N-linked (glcnac...) and O-linked (galnac...) glycosylation sitess: 109,249,299,305,308,328,329,337,433

Disulfide bonds: 47-73, 61-88, 98-110, 104-119, 121-130, 135-163, 161-170, 178-189, 183-198, 200-209, 217-295, 238-277, 266-290, 359-486, 397-413, 405-475, 436-439, 500-569, 532-548, 559-590

Other related resourses:

PIR: KFHU12, InterPro: IPR006210; EGF, InterPro: IPR000742; EGF_3, InterPro: IPR006209; EGF_like, InterPro: IPR013032; EGF_like_reg, InterPro: IPR014394; Factor_XII_HGFA, InterPro: IPR000083; Fibrnctn1, InterPro: IPR000562; FN_type2_col_bd, InterPro: IPR000001; Kringle, InterPro: IPR001254; Peptidase_S1_S6, InterPro: IPR001314; Peptidase_S1A, Pfam: PF00008; EGF, Pfam: PF00039; fn1, Pfam: PF00040; fn2, Pfam: PF00051; Kringle, Pfam: PF00089; Trypsin, PRINTS: PR00722; CHYMOTRYPSIN, PRINTS: PR00013; FNTYPEII, PRINTS: PR00018; KRINGLE, ProDom: PD000995; FN_Type_II, ProDom: PD000395; Kringle, SMART: SM00181; EGF, SMART: SM00058; FN1, SMART: SM00059; FN2, SMART: SM00130; KR, SMART: SM00020; Tryp_SPc, PROSITE: PS00022; EGF_1, PROSITE: PS01186; EGF_2, PROSITE: PS50026; EGF_3, PROSITE: PS01253; FN1_1, PROSITE: PS51091; FN1_2, PROSITE: PS00023; FN2_1, PROSITE: PS51092; FN2_2, PROSITE: PS00021; KRINGLE_1, PROSITE: PS50070; KRINGLE_2, PROSITE: PS50240; TRYPSIN_DOM, PROSITE: PS00134; TRYPSIN_HIS, PROSITE: PS00135; TRYPSIN_SER

Expression pattern for human:

Tissue	Exp. (%)	Clones
ascites	38.94	9:47004
stomach	16.59	6:73538
whole_body	7.49	1:27167
liver	6.42	5:158276
mixed	4.95	7:287479
uncharacterized_tissue	4.74	5:214464
colon	4.06	2:100063
lung	3.55	5:286589
prostate	3.45	2:117863
uterus	3.19	3:191472

Animal models:

Mouse:

MGD: ; 4

OTHER RESOURCES

Societies:

General:

- International Patient Organization for Primary Immunodeficiencies (IPOPI)
- Immune Deficiency Foundation
- NIH/National Institute of Allergy and Infectious Diseases
- European Society for Immunodeficiencies

Disease specific:

- International Patient Organisation for C1 Inhibitor Deficiencies
- United States Hereditary Angioedema Association
- Italian Hereditary Angioedema Association
- Argentinian Hereditary Angioedema Association
- Canadian Hereditary Angioedema Society
- Danish Hereditary Angioedema Association
- French Hereditary Angioedema Association
- German Hereditary Angioedema Association
- Netherlands Hereditary Angioedema Association
- Spanish Association Hereditary Angioedema

Other information sources:

- Immunodeficiencies