Mannan-binding lectin - associated serine protease 2 deficiency

GENERAL INFORMATION

Description:

Mannan-binding lectin associated serine protease (MASP-2) is homologous to MASP-1 and the two C1q-associated serine proteases C1r and C1s. When mannan-binding lectin binds to carbohydrate structures on microorganisms, the manan-binding lectin pathway of the complement system is activated. By autoactivating MASP2 cleaves complement factors C4 and C2, generating the C3 convertase C4bC2b. Activation of C3 initiates the alternative pathway and the formation of the membrane-attack complex. Phagocytosis and inflammatory reactions are facilitated by complement fragments deposited on microorganisms. The MASP-2 deficiency is associated with susceptibility to infections and with the development of immunologic disease.

Alternative names:

- Inherited deficiency of mannan-binding lectin-associated serin protease 2
- MASP-2 deficiency

Classification:

- Complement regulatory proteins
  - Mannose-binding lectin deficiency

Inheritance:

Autosomal recessive

OMIM:

- *605102 Mannan-binding lectin serine protease 2; MASP2

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for Manose-binding lectin (protein) deficiency

Incidence:

Incidence is not known.

CLINICAL INFORMATION

Description:

Patients have frequent infections (pneumococcal pneumonia) and chronic inflammatory disease, including pulmonary fibrosis. Hypocomplementemia contributes also to an impaired immune defense.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Complement deficiency, eMedicine

Therapeutic options:

- Fresh frozen plasma is used for emergent replacement of complement components. Prophylactic antibiotics for the infections. Acute infections are treated with appropriate antibiotics and prevented also with vaccination (meningococcal, pneumococcal, and haemophilus).
- 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, South Westernn

GENE INFORMATION

Names:

HUGO name: MASP2
Alias(es): MAP19, SMAP, MBL-associated plasma protein of 19 kD, Mannan-binding lectin serine protease 2, Mannose-binding protein-associated 2, Small MBL-associated protein, Mannan-binding lectin serine protease 2 precursor

Localization:

Reference sequences:

DNA: Y09926 (EMBL) X98400 (EMBL) Y18281 (EMBL) Y18283 (EMBL) Y18284 (EMBL) Y18286 (EMBL) Y18286 (EMBL) Y18287 (EMBL) Y18287 (EMBL) AB008047 (EMBL) AB033742 (EMBL) AF321562 (EMBL) AF321558 (EMBL) , **cDNA:** X58957 (EMBL) , **Protein:** O00187 (SWISSPROT) Other Sequences

Chromosomal Location:

1p36.3-p36.2

Maps:

MASP2 (Map View)

Variations / Mutations:

- MASP2base; Mutation registry for MASP-2 deficiency

Other gene-based resources:

Ensembl: ENSG00000009724, GENATLAS: MASP2, GeneCard: MASP2, UniGene: 119983, Entrez Gene: 10747, euGenes: 10747, GDB: 6071500, HomoloGene: 4819

PROTEIN INFORMATION

Description:

Protein function:

Trypsin protease that presumably plays an important role in the initiation of the mannose-binding lectin (MBL) complement activation pathway. After activation it cleaves C4 generating C4a and C4b.

Subunit:

Isoform 2 binds to MASP-1.

Similarity:

Belongs to peptidase family S1.

Domains:

CUB 1 domain: 16-137

EGF-like, calcium-binding domain: 138-181

CUB 2 domain: 184-296

Sushi 1 domain: 298-363

Sushi 2 domain: 364-432

Serine protease domain: 445-686

Other features:

Signal peptide: 1-15

Mannan-binding lectin serine protease 2: 16-686

Mannan-binding lectin serine protease 2 a chain: 16-444

Mannan-binding lectin serine protease 2 b chain: 445-686

Disulfide bond interchain: 434-552

Disulfide bonds: 72-90, 142-156, 152-165, 167-180, 184-211, 241-259, 300-348, 328-361, 366-412, 396-430, 598-618, 629-660

Other related resourses:

PIR: A59271, InterPro: IPR000152; Asx_hydroxyl_S, InterPro: IPR000859; CUB, InterPro: IPR009003; Cys_Ser_trypsin, InterPro: IPR001881; EGF_Ca, InterPro: IPR006209; EGF_like, InterPro: IPR001254; Peptidase_S1, InterPro: IPR001314; Peptidase_S1A, InterPro: IPR000436; Sushi_SCR_CCP, Pfam: PF00431; CUB, Pfam: PF00084; sushi, Pfam: PF00089; trypsin, SMART: SM00032; CCP, SMART: SM00042; CUB, SMART: SM00179; EGF_CA, SMART: SM00020; Tryp_SPc, PROSITE: PS00010; ASX_HYDROXYL, PROSITE: PS01180; CUB, PROSITE: PS01186; EGF_2, PROSITE: PS01187; EGF_CA, PROSITE: PS50923; SUSHI, PROSITE: PS50240; TRYPSIN_DOM, PROSITE: PS00134; TRYPSIN_HIS, PROSITE: PS00135; TRYPSIN_SER

Expression pattern for human:

Tissue	Exp. (%)	Clones
fetal pancreas	98.82	1:2
hepatic adenoma	0.87	1:228
hepatocellular carcinoma, cell line	0.12	8:13099
optic nerve	0.04	1:4780
embryonic stem cells	0.04	1:4803
subchondral bone	0.03	1:5896
carcinoid	0.02	5:48801
primary lung epithelial cells	0.02	1:11269
human lung epithelial cells	0.01	1:13464
pooled human melanocyte, fetal heart, and pregnant uterus	0.01	1:32508

Animal models:

Mouse:

MGD: ; Masp2

OTHER RESOURCES

Societies:

General:

- International Patient Organization for Primary Immunodeficiencies
- Immune Deficiency Foundation
- European Society for Immunodeficiencies