Tumor necrosis factor receptor-associated periodic syndrome

GENERAL INFORMATION

Description:

Defects in TNFRSF1A are a cause of autosomal dominant familial hibernian fever. Familial hibernian fever is a disease characterized by recurrent fever, abdominal pain, localized tender skin lesions and myalgia.

Alternative names:

- FHF, TRAPS, FPF
- Familial hibernian fever
- TNFR associated periodic syndrome

Classification:

- Periodic fever syndromes

Inheritance:

Autosomal dominant

OMIM:

- #142680 Tumor necrosis factor receptor superfamily, member 1a; TNFRSF1A
- *191190 Periodic fever, familial, autosomal dominant

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for Familial Mediterranean Fever
- IDR factfile for Hyperimmunoglobulinemia D with periodic fever syndrome

Incidence:

Incidence is not known.

CLINICAL INFORMATION

Description:

Patients have recurrent fever with localized myalgia and painful erythema. The attacks can last one or two days or even weeks. Other symptoms include abdominal pain, diarrhea or constipation, nausea and vomiting, painful conjunctivitis, periorbital edema, chest pain, arthralgia and localized myalgia.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Syndrome TRAPS, ORPHANET

Genetic:

- IDdiagnostics

Therapeutic options:

- High doses of oral prednisone is effective. Etanercept was also effective and leads to remission that lasted for 6 month.
- Mediterranean fever, familial, eMedicine

Research programs, clinical trials:

- European Initiative for Primary Immunodeficiencies

GENE INFORMATION

Names:

HUGO name: TNFRSF1A
Alias(es): CD120a, FPF, MGC19588, TBP1, TNF-R, TNF-R-I, TNF-R55, TNFAR, TNFR1, TNFR55, TNFR60, P55, P55-R, P60, Tumor necrosis factor receptor 1 (55kD), Tumor necrosis factor receptor superfamily, member 1A, Tumor necrosis factor receptor superfamily member 1A precursor (p60)

Localization:

Reference sequences:

DNA: M75866 (EMBL) , **cDNA:** X55313 (EMBL) , **Protein:** P19438 (SWISSPROT) Other Sequences

Chromosomal Location:

12p13.2

Maps:

TNFRSF1A (Map View)

Other gene-based resources:

Ensembl: ENSG00000067182, GENATLAS: TNFRSF1A, GeneCard: TNFRSF1A, UniGene: 279594, Entrez Gene: 7132, euGenes: 7132, GDB: 125913, HomoloGene: 828

PROTEIN INFORMATION

Description:

Protein function:

Receptor for TNFSF2/TNF-alpha and homotrimeric TNFSF1/lymphotoxin-alpha. The adapter molecule fadd recruits caspase-8 to the activated receptor. The resulting death-inducing signaling complex (disc) performs caspase-8 proteolytic activation which initiates the subsequent cascade of caspases (aspartate-specific cysteine proteases) mediating apoptosis. Contributes to the induction of noncytocidal TNF effects including anti-viral state and activation of the acid sphingomyelinase.

Subunit:

Binding of TNF to the extracellular domain leads to homotrimerization. The aggregated death domains provide a novel molecular interface that interacts specifically with the death domain of tradd. Various tradd-interacting proteins such as trafs, rip and possibly fadd, are recruited to the complex by their association with tradd. This complex activates at least two distinct signaling cascades, apoptosis and NF-kappa-b signaling. Binds bag4. Constitutively associated with trpc4ap. Interacts with hcv core protein.

Subcellular location:

Type I membrane protein and secreted.

Post-translational modification:

The soluble form is produced from the membrane form by proteolytic processing.

Similarity:

Contains 1 death domain.

Structures (PDB):

1EXT Extracellular Domain Of The 55Kda Tumor Necrosis Factor Receptor. Crystallized At pH3.7 In P 21 21 21.
1FT4 Photochemically-Enhanced Binding Of Small Molecules To The Tumor Necrosis Factor Receptor-1
1ICH Solution Structure Of The Tumor Necrosis Factor Receptor-1 Death Domain
1NCF Crystallographic evidence for dimerization of unliganded tumor necrosis factor receptor.
1TNR Crystal structure of the soluble human 55 kd TNF receptor-human TNF complex: implications for TNF receptor activation.

Domains:

Death domain: 356-441

Other features:

Signal peptide: 1-21

Tumor necrosis factor receptor superfamily member 1a, membrane form: 22-455

Tumor necrosis factor binding protein 1: 41-291

N-linked (glcnac...) glycosylation sites: 54,145,151

Disulfide bonds: 44-58, 59-72, 62-81, 84-99, 102-117, 105-125, 127-143, 146-158, 149-166, 168-179, 182-195, 185-191

Other related resourses:

PIR: GQHUT1, InterPro: IPR000488; Death, InterPro: IPR011029; DEATH_like, InterPro: IPR001368; TNFR_c6, Pfam: PF00531; Death, Pfam: PF00020; TNFR_c6, PROSITE: PS50017; DEATH_DOMAIN, PROSITE: PS00652; TNFR_NGFR_1, PROSITE: PS50050; TNFR_NGFR_2

Expression pattern for human:

Tissue	Exp. (%)	Clones
colon mucosa	13.98	2:1345
coronary artery	7.97	10:11801
neuroblastoma	7.80	1:1205
amygdala	6.31	2:2979
corpus callosum	5.91	2:3185
embryonic stem	4.33	3:6512
caudate nucleus	3.69	1:2548
small intestine	3.42	2:5498
thymus	3.39	2:5542
embryonal kidney	3.14	1:2996

Animal models:

Mouse:

MGD: ; 4, NCBI Gene: ; 21937 (66.21 % aminoacid similarity to human)

Rat:

NCBI Gene: ; 25625 (66.22 % aminoacid similarity to human)

OTHER RESOURCES

Societies:

General:

- IPOPI, International Patient Organization for Primary Immunodeficiencies
- The Jeffrey Modell Foundation
- Immune Deficiency Foundation
- European Society for Immunodeficiencies

Disease specific:

- FMF community

Other information sources:

- Immunodeficiencies