Hyperimmunoglobulinemia D with periodic fever syndrome

GENERAL INFORMATION

Description:

Defects in mavalonate kinase (MVK) are the cause of mevalonicaciduria. It is an accumulation of mevalonic acid which cause a variety of symptoms such as psychomotor retardation, dysmorphic features, cataracts, hepatosplenomegaly, lymphadenopathy, anemia, hypotonia, myopathy, and ataxia.

Alternative names:

- HIGD with periodic fever syndrome
- Hyper-IgD syndrome
- Mevalonicaciduria
- Mevalonate kinase deficiency

Classification:

- Periodic fever syndromes

Inheritance:

Autosomal recessive

OMIM:

- #260920 Hyper-IgD syndrome; HIDS
- *251170 Mevalonate kinase; MVK

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for Familial Mediterranean Fever
- IDR factfile for Tumor necrosis factor receptor-associated periodic syndrome

Incidence:

Incidence is not known.

CLINICAL INFORMATION

Description:

Patients have recurrent febrile attacks that start before the end first of life. The attack is accompanied by chills, sharp rise in body temperature, cervical lymphadenopathy and abdominal pain with vomiting, diarrhea and last 4-6 days. Common symptoms include hepatosplenomegaly, headache, arthralgias, athritis of large joints, erythematous macules and papules, petechia and purpura, and an elevated serum IgD level (> 100 U/ml). After an attack, patients are free of symptoms, skin and joint symptoms dissapear slowly.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Hyperimmunoglobinemia D with recurrent fever, ORPHANET
- Mediterranean fever, familial, eMedicine

Genetic:

- IDdiagnostics

Therapeutic options:

- Colchicine has no preventive effect against febrile episodes. Simvastatin treatment and TNF (tumour necrosis factors) inhibitors have been recently tested with some success, for inflammatory attacks of the hyperimmunoglobulinemia D and periodic fever syndrome.
- Mediterranean fever, familial, eMedicine

Research programs, clinical trials:

- European Initiative for Primary Immunodeficiencies

GENE INFORMATION

Names:

HUGO name: MVK
Alias(es): LRBP, MVLK, Mevalonate kinase

Localization:

Reference sequences:

DNA: AF217535 (EMBL) , **cDNA:** M88468 (EMBL) , **Protein:** Q03426 (SWISSPROT) Other Sequences

Chromosomal Location:

12q24

Maps:

MVK (Map View)

Other gene-based resources:

Ensembl: ENSG00000110921, GENATLAS: MVK, GeneCard: MVK, UniGene: 130607, Entrez Gene: 4598, euGenes: 4598, GDB: 134189, HomoloGene: 372

PROTEIN INFORMATION

Description:

Protein function:

May be a regulatory site in cholesterol biosynthetic pathway.

Catalytic activity:

ATP + (r)-mevalonate = ADP + (r)-5-phosphomevalonate

Subunit:

Homodimer

Subcellular location:

Cytoplasmic and peroxisomal.

Enzyme regulation:

Farnesyl- and geranyl-pyrophosphates are competitive inhibitors.

Similarity:

Belongs to the ghmp kinase family. Mevalonate kinase subfamily.

Other features:

ATP nucleotide phosphate-binding region: 138-148

Other related resourses:

PIR: A42919, InterPro: IPR006204; GHMP_kinase, InterPro: IPR006203; GHMPknse_ATP, InterPro: IPR006205; Mev_gal_kin, InterPro: IPR006206; Mev_galkinase, Pfam: PF00288; GHMP_kinases, PRINTS: PR00959; MEVGALKINASE, PROSITE: PS00627; GHMP_KINASES_ATP

Expression pattern for human:

Tissue	Exp. (%)	Clones
larynx	31.85	1:838
adrenal gland	9.97	1:2677
spleen	6.88	4:15523
small intestine	4.86	1:5498
embryonic stem	4.10	1:6512
cervix	4.02	5:33205
human embryonic stem cells	3.70	1:7214
prostate	2.90	11:101396
other	2.47	41:442392
soft_tissue	2.32	1:11501

Animal models:

Mouse:

MGD: ; 4

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