Autoimmune lymphoproliferative syndrome type II

GENERAL INFORMATION

Description:

Defects in Caspase 10 are the cause of type II autoimmune lymphoproliferative syndrome (ALPS2). ALPS2 is characterized by abnormal lymphocyte and dendritic cell homeostasis and immune regulatory defects.

Alternative names:

- ALPS2
- Caspase 10 deficiency

Classification:

- Defects in lymphocyte apoptosis
  - Autoimmune lymphoproliferative syndrome

Inheritance:

Autosomal dominant

OMIM:

- #603909 Autoimmune lymphoproliferative syndrome, type II
- #601859 Autoimmune lymphoproliferative syndrome, type I
- *601762 Caspase 10, apoptosis-related cysteine protease; CASP10
- *134637 Tumor necrosis factor receptor superfamily, member 6; TNFRSF6
- #605027 non-Hodgkin lymphoma

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for Apoptosis mediator APO-1/Fas defects
- IDR factfile for APO-1 ligand/Fas ligand defects

Incidence:

Incidence is not known.

CLINICAL INFORMATION

Description:

The patients have a range of diverse autoimmune and inflammatory conditions with disturbed immune cell homeostasis. They can have consistently exhibited dramatic lymphoproliferation and a breakdown in tolerance to multiple self-antigens leading to severe autoimmune complications.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Autoimmune lymphoproliferative syndrome, ORPHANET

Therapeutic options:

- Lymphoproliferative disorders, eMedicine

Research programs, clinical trials:

- European Initiative for Primary Immunodeficiencies.
- APLSbase, National Human Genome Research Institute
- Pyrimethamine to Treat Autoimmune Lymphoproliferative Syndrome, ClinicalTrial.gov
- Study of Autoimmune Lymphoproliferative Syndrome (ALPS), ClinicalTrial.gov
- Genetic Analysis of Immune Disorders, ClinicalTrial.gov

GENE INFORMATION

Names:

HUGO name: CASP10
Alias(es): ALPS2, FLICE2, MCH4, FADD-like ICE2, Fas-associated death domain protein, ICE-like apoptotic protease 4, Apoptotic protease MCH-4, Caspase 10, apoptosis-related cysteine protease, Interleukin-1B-converting enzyme 2, Caspase-10 precursor, ICE-like apoptotic protease 4, Apoptotic protease MCH-4, Fas-associated death domain protein interleukin-1B-converting enzyme

Localization:

Reference sequences:

DNA: U60519 (EMBL) U86214 (EMBL) AF111344 (EMBL) AF111345 (EMBL) AB038978 (EMBL) AB038979 (EMBL) , **cDNA:** X58957 (EMBL) , **Protein:** Q92851 (SWISSPROT) Other Sequences

Chromosomal Location:

2q33-q34

Maps:

CASP10 (Map View)

Markers:

RH70685, RH68751, RH77986, PMC230316P3

Variations / Mutations:

- CASP10base; Mutation registry for autoimmune lymphoproliferative syndrome type II, (ALPS2)

Other gene-based resources:

Ensembl: ENSG00000003400, GENATLAS: CASP10, GeneCard: CASP10, UniGene: 5353, Entrez Gene: 843, euGenes: 843, GDB: 6053891, HomoloGene:

PROTEIN INFORMATION

Description:

Protein function:

Involved in the activation cascade of caspases responsible for apoptosis execution. Recruited to both FAS- and TNFR-1 receptors in a FADD dependent manner. May participate in the granzyme B apoptotic pathways. Cleaves and activates caspase-3, -4, -6, -7, -8, and -9. Hydrolyzes the small- molecule substrates, Tyr-Val-Ala-Asp-|-Amc and Asp-Glu-Val-Asp-|-Amc.

Subunit:

Heterodimer of a 23/17 kDa (p23/17) depending on the splicing events and a 12 kDa (p12) subunit.

Post-translational modification:

Cleavage by granzyme B and autocatalytic activity generate the two active subunits.

Tissue specificity:

Detectable in most tissues. Lowest expression is seen in brain, kidney, prostate, testis and colon.

Similarity:

Belongs to peptidase family C14.

Domains:

DED 1 domain: 19-97

DED 2 domain: 114-187

Other features:

Propeptide: 1-219

Caspase-10 subunit p23/17: 220-415

Caspase-10 subunit p12: 416-521

Other related resourses:

InterPro: IPR001875; DED, InterPro: IPR002138; ICE_p10, InterPro: IPR001309; ICE_p20, InterPro: IPR002398; Peptidase_C14, Pfam: PF01335; DED, Pfam: PF00656; Peptidase_C14, PROSITE: PS01122; CASPASE_CYS, PROSITE: PS01121; CASPASE_HIS, PROSITE: PS50207; CASPASE_P10, PROSITE: PS50208; CASPASE_P20, PROSITE: PS50168; DED

Expression pattern for human:

Tissue	Exp. (%)	Clones
uterus	25.68	1:1305
invasive adenocarcinoma	16.52	1:2028
leukopheresis	8.63	2:7769
cell line	8.52	1:3934
bone marrow	5.75	1:5829
liver	4.23	1:7919
dorsal root ganglia	4.16	1:8052
placenta	4.06	1:8261
colon tumor, RER+	4.01	1:8360
pooled human melanocyte, fetal heart, and pregnant uterus	3.09	3:32508
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Animal models:

Mouse:

MGD: ; alps2

OTHER RESOURCES

Societies:

General:

- International Patient Organization for Primary Immunodeficiencies
- Immune Deficiency Foundation
- March of Dimes Birth Defects Foundation
- NIH/National Institute of Allergy and Infectious Diseases
- European Society for Immunodeficiencies

Other information sources:

- Autoimmune lymphoproliferative syndromes: genetic defects of apoptosis pathways