TNFRSF13B deficiency

GENERAL INFORMATION

Description:

Defects in TNFRSF13B are a cause of common variable immunodeficiency and selective deficiency of immunoglobulin A (IgA). TNFRSF13B encodes the transmembrane activator and CAML interactor (TACI).
CVID is characterized by a deficiency in all immunoglobulin (Ig) isotypes. There is evidence for a global isotype switching defect in some individuals with CVID. CVID is a complex and heterogeneous disease in which defects in B-cell survival, number of circulating Cd27+ memory B-cells, B-cell activation after antigen receptor cross-linking, T-cell signaling and cytokine expression have been observed. Individuals with symptomatic IgAD and individuals with CVID suffer from recurrent sinopulmonary and gastrointestinal infections and have an increased incidence of autoimmune disorders and of lymphoid and nonlymphoid malignancies. IgAD and CVID can coexist in families, and some individuals initially present with IgAD and then develop CVID.

Alternative names:

- TACID
- TACI deficiency, TACI-associated immunodeficiency

Classification:

- Deficiencies predominantly affecting antibody production
  - Common variable immunodeficiency

Inheritance:

OMIM:

- *604907 Tumor necrosis factor receptor superfamily, member 13b; TNFRSF13B
- #240500 Common variable immunodeficiency; CVID
- #609529 Immunoglobulin A deficiency 2; IGAD2

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for Common variable immunodeficiency of unknown origin
- IDR factfile for IgA deficiency

Incidence:

Incidence is not known yet.

CLINICAL INFORMATION

Description:

Individuals with CVID suffer from recurrent sinopulmonary and gastrointestinal infections and have an increased incidence of autoimmune disorders and of lymphoid and non-lymphoid malignancies.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Common Variable Immune Deficiency-workup, eMedicine

Genetic:

- TNFRSF13B, IDdiagnostics
- CVID, GeneTest

Therapeutic options:

- (Intravenous) immunoglobulins and antibiotic therapy together with physiotherapy and postural drainage in case of lung damage. Oral poliovaccine should not be given because there is risk of paralytic disease.
- Common Variable Immunodeficiency (CVID), eMedicine
- Hypogammaglobulinemia, eMedicine

Research programs, clinical trials:

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GENE INFORMATION

Names:

HUGO name: TNFRSF13B
Alias(es): TACI, CD267 , CVID, FLJ39942

Localization:

Reference sequences:

DNA: D0105 (IDRefSeq) , **cDNA:** AF023614 (EMBL) , **Protein:** O14836 (SWISSPROT) Other Sequences

Chromosomal Location:

17p11.2

Maps:

TNFRSF13B (Map View)

Variations / Mutations:

- TNFRSF13Bbase; Mutation registry for TACI deficiency

Other gene-based resources:

Ensembl: ENSG00000108516, GENATLAS: TNFRSF13B, GeneCard: TNFRSF13B, UniGene: 158341, Entrez Gene: 23495, euGenes: 23495, GDB: 9834791, HomoloGene: 49320

PROTEIN INFORMATION

Description:

Protein function:

Receptor for TNFSF13/APRIL and TNFSF13b/ TAll1/BAFF/BLYS that binds both ligands with similar high affinity. Mediates calcineurin-dependent activation of NF-AT, as well as activation of NF-kappa-b and AP-1. Involved in the stimulation of B- and T-cell function and the regulation of humoral immunity.

Subunit:

Binds Traf2, Traf5 and Traf6. Binds the Nh2-terminal domain of Camlg with its C-terminus.

Subcellular location:

Membrane; single-pass type iii membrane protein

Protein function:

Event=alternative splicing; named isoforms=2; name=1; isoid=o14836-1; sequence=displayed; name=2; isoid=o14836-2; sequence=vsp_013798;

Tissue specificity:

Highly expressed in spleen, thymus, small intestine and peripheral blood leukocytes. Expressed in resting B-cells and activated T-cells, but not in resting T-cells.

Similarity:

Contains 2 Tnfr-cys repeats.

Structures (PDB):

1XU1 .
1XUT .

Other features:

Tumor necrosis factor receptor superfamily member 13b: 1-293

Disulfide bonds: 34-47, 50-62, 54-66, 71-86, 89-100, 93-104
N-linked (glcnac...) glycosylation sites: 128
Other related resourses:

InterPro: IPR001368; TNFR_c6, PROSITE: PS00652; TNFR_NGFR_1, PROSITE: PS50050; TNFR_NGFR_2

Expression pattern for human:

Tissue	Exp. (%)	Clones
lymph	31.36	3:43667
spleen	28.94	3:47318
small_intestine	21.31	2:42840
trachea	9.84	1:46384
unclassified	4.85	1:94133
uncharacterized_tissue	2.12	1:215582
mixed	1.58	1:288723

Animal models:

Mouse:

MGD: ; Tnfrsf13b

OTHER RESOURCES

Societies:

General:

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

Other information sources:

- TACI deficiency