# TAP1 deficiency

## GENERAL INFORMATION

### Description:

The transporter associated with antigen processing (TAP), which is composed of two subunits (TAP1 and TAP2) that have different biochemical and functional properties, plays a key role in peptide loading and the cell surface expression of HLA class I molecules. The TAP1 defect leads to unstable HLA class I molecules and their retention in the endoplasmic reticulum. The absence of TAP1 is compatible with life and do not result in higher susceptibility to viral infections than TAP2 deficiency.

### Alternative names:

- TAP1D
- Major histocompatibility complex class I deficiency
- Bare Lymphocyte Syndrome type 1

### Classification:

- Combined B and T cell immunodeficiencies
  - Major histocompatibility complex class I deficiency

### Inheritance:

Autosomal recessive

### OMIM:

- #604571 Bare lymphocyte syndrome, type I
- *170260 Transporter, atp-binding cassette, major histocompatibility complex,

### Cross references:

**Phenotype related immunodeficiencies:**

- IDR factfile for TAP2 deficiency

### Incidence:

Incidence is not known.

## CLINICAL INFORMATION

### Description:

Patients developed chronic inflammation of the respiratory tract in late childhood and skin lesions at different ages. In one patient the skin lesions were first observed at the age of 8, whereas in the second patient they developed at the age of 21 . TAP1 deficiency is compatible with life. The syndromes associated with TAP1 and TAP2 deficiency are similar and characterized by the development of chronic inflammation of the respiratory tract in late childhood and vasculitis at variable ages. Medical observations suggest that the different biochemical properties of the TAP1 and TAP2 subunits do not result in major differences in the health status of the patients.

### Diagnosis:

### Diagnostic laboratories:

**Clinical:**

- Defective expression of HLA class 1, ORPHANET

### Therapeutic options:

- Bone marrow transplantation is the only treatment of SCID. Other recommendations include intravenous gamma-globulin infusion, irradiation of all blood products, antibiotherapy.
- Bone marrow transplant, UCSF Medical Center
- Stem Cell Transplant, National Marrow Donor Program (NMDP)

## Research programs, clinical trials:

- Pilot Study of Allogeneic Bone Marrow Transplantation Plus Cyclosporine and Mycophenolate Mofetil to Induce Mixed Hematopoietic Chimerism in Patients With Primary T-Cell Immunodeficiency Disorders, ClinicalTrial.gov
- European Initiative for Primary Immunodeficiencies

# GENE INFORMATION

## Names:

**HUGO name:** TAP1
**Alias(es):** ABC17, ABCB2, APT1, D6S114E, PSF1, RING4, Y3, ABC transporter, MHC 1, ATP-binding cassette, sub-family B (MDR/TAP), member 2, ATP-binding cassette, sub-family B, member 2, Antigen peptide transporter 1, Peptide supply factor 1, Transporter 1, ABC (ATP binding cassette), Transporter 1, ATP-binding cassette, sub-family B (MDR/TAP), Transporter, ATP-binding cassette, major histocompatibility complex, 1, Antigen peptide transporter 1 (APT1), Peptide transporter TAP1, Peptide transporter PSF1, Peptide supply factor 1) (PSF-1), Peptide transporter involved in antigen processing 1

## Localization:

**Reference sequences:**

**DNA:** X66401 (EMBL) X57521 (EMBL) X57522 (EMBL) L21204 (EMBL) L21205 (EMBL) L21206 (EMBL) L21207 (EMBL) L21208 (EMBL) X87344 (EMBL) S70274 (EMBL) , **cDNA:** X58957 (EMBL) , **Protein:** Q03518 (SWISSPROT)

**Chromosomal Location:**

6p21.3

**Maps:**

TAP1 (Map View)

**Markers:**

RH70842, D6S2042, GDB:365643, PMC115886P1

## Variations / Mutations:

- TAP1base; Mutation registry for TAP1 deficiency

## Other gene-based resources:

Ensembl: ENSG00000168394, GENATLAS: TAP1, GeneCard: TAP1, UniGene: 352018, Entrez Gene: 6890, euGenes: 6890, GDB: 132668, HomoloGene: 495

# PROTEIN INFORMATION

## Description:

**Protein function:**

Involved in the transport of antigens from the cytoplasm to the endoplasmic reticulum for association with MHC class I molecules. Also acts as a molecular scaffold for the final stage of MHC class I folding, namely the binding of peptide. Nascent MHC class I molecules associate with TAP via Tapasin. Inhibited by the covalent attachment of herpes simplex virus ICP47 protein, which blocks the peptide-binding site of TAP. Inhibited by human cytomegalovirus US6 glycoprotein, which binds to the lumenal side of the TAP complex and inhibits peptide translocation by specifically blocking ATP-binding to TAP1 and prevents the conformational rearrangement of TAP induced by peptide binding. Inhibited by human adenovirus e3-19k glycoprotein, which binds the TAP complex and acts as a tapasin inhibitor, preventing MHC class I/ TAP association. Expression of TAP1 is down-regulated by human Epstein-Barr virus vil-10 protein, thereby affecting the transport of peptides into the endoplasmic reticulum and subsequent peptide loading by MHC class I molecules.

**Subunit:**

Heterodimer of TAP1 and TAP2

**Subcellular location:**

Integral membrane protein. Endoplasmic reticulum. The transmembrane segments seem to form a pore in the membrane.

**Induction:**

By interferon gamma

**Polymorphism:**

There are five common alleles; TAP1*0101 (psf1a), TAP1*0201 (psf1b), TAP1*0301 (psf1c), TAP1*0104 and TAP1*x.

**Similarity:**

Belongs to the abc transporter family. Mdr subfamily

## Structures (PDB):

1JJ7 Crystal Structure Of The C-Terminal ATPase Domain Of Human Tap1

## Domains:

**Cytoplasmic domain: 1-15**

**Lumenal domain: 37-53**

**Cytoplasmic domain: 77-92**

**Lumenal domain: 114-133**

**Cytoplasmic domain: 155-186**

**Lumenal domain: 208-227**

**Cytoplasmic domain: 249-298**

**Lumenal domain: 320-328**

**Cytoplasmic domain: 350-418**

**Lumenal domain: 440-443**

**Cytoplasmic domain: 465-748**

**Involved in peptide-binding site domain: 375-420**

**Involved in peptide-binding site domain: 453-487**

**ABC transporter domain: 503-748**

## Other features:

**ATP nucleotide phosphate-binding region: 538-545**

**Other related resourses:**

InterPro: IPR003593; AAA_ATPase, InterPro: IPR001140; ABC_TM_transpt, InterPro: IPR003439; ABC_transporter, InterPro: IPR005293; Ag_transporter2, Pfam: PF00664; ABC_membrane, Pfam: PF00005; ABC_tran, SMART: SM00382; AAA, PROSITE: PS50929; ABC_TM1F, PROSITE: PS00211; ABC_TRANSPORTER_1, PROSITE: PS50893; ABC_TRANSPORTER_2

## Expression pattern for human:

| Tissue | Exp. (%) | Clones |
|---|---|---|
| colon tumor | 7.41 | 5:2311 |
| larynx | 4.44 | 1:771 |
| natural killer cells, cell line | 4.38 | 7:5480 |
| breast tumor | 4.23 | 1:809 |
| invasive prostate tumor | 4.09 | 1:838 |
| colonic mucosa from 3 patients with Crohn's disease | 3.69 | 3:2785 |
| amelanotic melanoma, cell line | 3.65 | 15:14069 |
| glioblastoma with probably TP53 mutation and without EGFR amplification | 3.53 | 1:970 |
| juvenile granulosa tumor | 3.17 | 2:2159 |
| thyroid gland | 3.00 | 1:1141 |
| colon tumor | 7.41 | 5:2311 |
| larynx | 4.44 | 1:771 |
| natural killer cells, cell line | 4.38 | 7:5480 |
| breast tumor | 4.23 | 1:809 |
| invasive prostate tumor | 4.09 | 1:838 |
| colonic mucosa from 3 patients with Crohn's disease | 3.69 | 3:2785 |
| amelanotic melanoma, cell line | 3.65 | 15:14069 |
| glioblastoma with probably TP53 mutation and without EGFR amplification | 3.53 | 1:970 |
| juvenile granulosa tumor | 3.17 | 2:2159 |
| thyroid gland | 3.00 | 1:1141 |

## Animal models:

**Mouse:**

MGD: ; Tap1, NCBI Gene: ; 21354 (73.06 % aminoacid similarity to human)

**Rat:**

NCBI Gene: ; 24811 (72.60 % aminoacid similarity to human)

# 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