Osteopetrosis, AR

GENERAL INFORMATION

Description:

Defects in TCIRG1 are a cause of autosomal recessive osteopetrosis. Osteopetrosis is a rare genetic disease characterized by abnormally dense bone, due to defective resorption of immature bone. The defect is an heterogeneous disorder of bone metabolism, which, if untreated, has a fatal outcome. It occurs in two forms: a severe autosomal recessive form, occurring in utero, infancy, or childhood, and a benign autosomal dominant form, occurring in adolescence or adulthood. Mild and atypical forms have also been reported.

Alternative names:

- OPTB1
- Autosomal recessive Albers-Schonberg disease
- Autosomal recessive marble bones

Classification:

- Other well-defined immunodeficiency syndromes

Inheritance:

Autosomal recessive

ICD code:

ICD Q78.2

OMIM:

- *604592 T cell immune regulator 1; TCIRG1
- #259700 Autosomal recessive osteopetrosis

Cross references:

Incidence:

Incidence is not known yet.

CLINICAL INFORMATION

Description:

The features of OPTB1 are macrocephaly, progressive deafness and blindness, hepatosplenomegaly, and severe anemia beginning in early infancy or in fetal life. Deafness and blindness are generally thought to represent effects of pressure on nerves.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Osteopetrosis, eMedicine

Genetic:

- IDdiagnostics, TCIRG1

Therapeutic options:

- Bone marrow transplant can alleviate many features of the disease but needs to be performed early to minimise optic nerve encroachment. The prognosis is variable but improves if bone marrow transplant is performed early.
- Osteopetrosis, eMedicine

Research programs, clinical trials:

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GENE INFORMATION

Names:

HUGO name: TCIRG1

Localization:

Reference sequences:

DNA: D0101 (IDRefSeq) , **cDNA:** U45285 (EMBL) , **Protein:** Q13488 (SWISSPROT) Other Sequences

Chromosomal Location:

11q13.4-q13.5

Maps:

TCIRG1 (Map View)

Variations / Mutations:

- TCIRG1base; Mutation registry for AR Osteopetrosis

Other gene-based resources:

Ensembl: ENSG00000110719, GENATLAS: TCIRG1, GeneCard: TCIRG1, UniGene: 495985, Entrez Gene: 10312, euGenes: 10312, GDB: 9956269, HomoloGene: 4392

PROTEIN INFORMATION

Description:

Protein function:

Part of the proton channel of V-ATPases (by similarity). Seems to be directly involved in T-cell activation.

Subunit:

The V-ATPase is an heteromultimeric enzyme composed of at least thirteen different subunits. It has a membrane peripheral V1 sector for ATP hydrolysis and an integral V0 for proton translocation. The V1 sector comprises subunits A-H, whereas V0 includes subunits A, D, C, C', and C''.

Subcellular location:

Membrane; multi-pass membrane protein (by similarity).

Protein function:

Event=alternative splicing; named isoforms=2; name=long; isoid=q13488-1; sequence=displayed; name=short; isoid=q13488-2; sequence=vsp_000345; note=no experimental confirmation available;

Tissue specificity:

The long isoform is highly expressed in osteoclastomas. The short isoform is highly expressed in thymus.

Similarity:

Belongs to the V-ATPase 116 kda subunit family.

Other features:

Vacuolar proton translocating atpase 116 kda subunit a isoform 3: 1-830

N-linked (glcnac...) glycosylation sites: 41,483,503

Other related resourses:

InterPro: IPR002490; ATPase_V0/A0_116,
Pfam: PF01496; V_ATPase_I

Expression pattern for human:

Tissue	Exp. (%)	Clones
bone_marrow	11.81	9:41353
nerve_tissue	8.54	4:25421
lymph_node	6.53	10:83039
colon	5.92	11:100892
uncharacterized_tissue	5.79	23:215582
spleen	5.73	5:47318
ovary	4.67	7:81370
unclassified	4.61	8:94133
stomach	4.43	6:73494
bone	3.85	5:70388

Animal models:

Mouse:

MGD: ; Tcirg1

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:

- AR Osteopetrosis OR TCIRG1