Hermansky-Pudlak syndrome 2

GENERAL INFORMATION

Description:

Defects in ADTB3A are the cause of Hermansky-Pudlak syndrome type 2 (HPS2). HPS is an autosomal recessive disorder characterized by oculocutaneous albinism, bleeding due to platelet storage pool deficiency, and lysosomal storage defects. This syndrome results from defects of diverse cytoplasmic organelles including melanosomes, platelet dense granules and lysosomes. Ceroid storage in the lungs is associated with pulmonary fibrosis, a common cause of premature death in individuals with HPS. HPS2 differs from the other forms of HPS in that it includes immunodeficiency in its phenotype and patients with HPS2 have an increased susceptibility to infections.

Alternative names:

- HPS2
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Classification:

- Defects of phagocyte function

Inheritance:

Autosomal recessive

OMIM:

- #608233 Hermansky-Pudlak syndrome 2; HPS2
- *603401 Adaptor-related protein complex 3, beta-1 subunit; AP3B1

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for Chediak-Higashi syndrome
- IDR factfile for Griscelli syndrome

Incidence:

Incidence is not known.

CLINICAL INFORMATION

Description:

Patients have oculocutaneous albinism, a bleeding diathesis, a platelet storage pool deficiency, other organ involvement, persistent neutropenia and an increased frequency of infections in childhood. Nearly all children with albinism of HPS have nystagmus at birth, wandering eye movements and lack of visual attention. Nystagmus is most noticeable when an individual is tired, angry or anxious. Iris colour may remain blue or change to a green/hazel or brown/tan colour. The hair colour ranges from white to brown, and can darken with age. The bleeding diathesis of HPS include variable bruising, epistaxis, gingival bleeding, postpartum hemorrhage, colonic bleeding, and prolonged bleeding during menstruation or after tooth extraction, or other surgeries. Pulmonary fibrosis, granulomatous colitis, cardiomyopathy, and renal failure are due to the lysosomal accumulation of ceroid lipofuscin.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Hermansky-Pudlak syndrome, eMedicine

Therapeutic options:

- Treatment involves minimizing the complications of bleeding; monitoring organ function, which ceroid deposits can impair; compensating for visual impairment; and evaluating skin that, because of albinism, can easily develop skin cancer.
- Hermansky-Pudlak syndrome, eMedicine

Research programs, clinical trials:

- European Initiative for Primary Immunodeficiencies 2001-2004

GENE INFORMATION

Names:

HUGO name: AP3B1
Alias(es): ADTB3, ADTB3A, Beta3A-adaptin, HPS, HPS2, PE, Beta3A-adaptin, AP-3 complex beta-3A subunit, Adaptor-related protein complex 3, beta 1 subunit, Adapter-related protein complex 3 beta 1 subunit

Localization:

Reference sequences:

DNA: U91931 (EMBL) U81504 (EMBL) BX538041 (EMBL) BC038444 (EMBL) AF247736 (EMBL) , **cDNA:** X58957 (EMBL) , **Protein:** O00203 (SWISSPROT)

Chromosomal Location:

Chr.5

Maps:

AP3B1 (Map View)

Markers:

1842, RH16414, A002S29

Variations / Mutations:

- AP3B1base; Mutation registry for Hermansky-Pudlak syndrome 2
- ; Mutation Database Mutations of the Adaptin b3a Gene (ADTB3A)

Other gene-based resources:

Ensembl: ENSG00000132842, GENATLAS: AP3B1, GeneCard: AP3B1, UniGene: 532091, Entrez Gene: 8546, euGenes: 8546, GDB: 9955590

PROTEIN INFORMATION

Description:

Protein function:

Subunit of non-clathrin- and clathrin-associated adaptor protein complex 3 that plays a role in protein sorting in the late-golgi/trans-golgi network (tgn) and/or endosomes. The ap complexes mediate both the recruitment of clathrin to membranes and the recognition of sorting signals within the cytosolic tails of transmembrane cargo molecules. Ap-3 appears to be involved in the sorting of a subset of transmembrane proteins targeted to lysosomes and lysosome-related organelles.

Subunit:

Adaptor protein complex 3 (ap-3) is an heterotetramer composed of two large adaptins (delta/ap3d1 and beta3a/ap3b2 or beta3b/ap3b1), a medium adaptin (mu3a/ap3m1 or mu3b/ap3m2) and a small adaptin (sigma3a/ap3s1 or sigma3b/ap3s2).

Subcellular location:

Component of the coat surrounding the cytoplasmic face of coated vesicles located at the golgi complex.

Post-translational modification:

Phosphorylated on serine residues.

Tissue specificity:

Ubiquitously expressed.

Similarity:

Belongs to the adaptor complexes large subunit family.

Domains:

Glu/Ser-rich domain: 677-802

Other features:

Other related resourses:

PIR: T50651, PIR: T50652, Pfam: PF01602; Adaptin_N

Expression pattern for human:

Tissue	Exp. (%)	Clones
bulk alveolar tumor	37.52	1:180
cell Line	3.43	2:3934
lymph	2.76	8:19564
large cell carcinoma, undifferentiated	2.57	2:5253
chondrosarcoma	2.47	6:16413
neuroblastoma cot 50-normalized	2.41	1:2799
multiple sclerosis lesions	2.40	3:8445
human chondrosarcoma cell line	2.04	1:3311
chondrosarcoma cell line 2	2.03	1:3330
pooled Wilms' tumors, one primary and one metastatic to brain	1.95	1:3469
bulk alveolar tumor	37.52	1:180
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Animal models:

Mouse:

MGD: ; Ap3b1, NCBI Gene: ; 11774 (88.86 % aminoacid similarity to human)

Rat:

NCBI Gene: ; 309969 (88.54 % aminoacid similarity to human)

OTHER RESOURCES

Societies:

General:

- International Patient Organization for Primary Immunodeficiencies (IPOPI)
- Immune Deficiency Foundation
- European Society for Immunodeficiencies

Disease specific:

- Neutropenia Support Association
- Severe Chronic Neutropenia International Registry
- Severe Chronic Neutropenia International Registry