Griscelli syndrome, type 1

GENERAL INFORMATION

Description:

Defects in MYO5A cause Griscelli syndrome (GS) type 1 (GS1), an autosomal recessive disorder. Mutations in MYO5A may also cause a form of Griscelli syndrome (GS3) with a phenotype restricted to hypopigmentation. GS1 correspond to the 'dilute' phenotype in the mouse, and GS2 correspond to the 'ashen' phenotype in mouse.

Alternative names:

- GS1
- Griscelli syndrome with neurologic impairment
- Partial albinism and primary neurologic disease without hemophagocytic syndrome
- Griscelli syndrome, cutaneous and neurologic type
- Elejalde syndrome

Classification:

- Defects of phagocyte function
  - Griscelli syndrome

Inheritance:

Autosomal recesseive

OMIM:

- #214450 Griscelli syndrome
- *160777 MYOSIN VA; MYO5A

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for Chediak-Higashi syndrome
- IDR factfile for Griscelli syndrome, type 2
- IDR factfile for Griscelli syndrome, type 3

Incidence:

Incidence is not known.

CLINICAL INFORMATION

Description:

Patients have partial pigmentary dilution or albinism with silvery gray hair, frequent infections, neurologic abnormalities. Neurologic symptoms consist of hypotonia, absence of coordinated voluntary movements and severe retarded psychomotor development. Central nervous system disorder is stable and never regresses with time. Hair shafts contain an accumulation of large pigment granules.
No immunological abnormalities have been observed. Patients never develop an accelerated phase. At computer tomograph (CT) scanning and magnetic resonance imaging (MRI) patients have isolated congenital cerebellar atrophy.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Griscelli disease, ORPHANET
- Griscelli Syndrome, eMedicine

Therapeutic options:

- Bone marrow transplantation. The severe neurological impairment and retarded psychomotor development do not improve with time. Recurrent infections can be improved with positional changes and antibiotic treatment.
- Griscelli Syndrome, eMedicine

Research programs, clinical trials:

- European Initiative for Primary Immunodeficiencies.
- Allogeneic Bone Marrow Transplantation in Patients With Primary Immunodeficiencies, Clinical.Trials.gov
- Study of Chediak-Higashi Syndrome, Clinical.Trials.gov
- Pilot Study of Unrelated Donor Hematopoietic Stem Cell Transplantation in Patients With Life Threatening Hemophagocytic Disorders, Clinical.Trials.gov
- Learning and Behavior Problems in Children with Chronic Granulomatous Disease and Related Disorders, Clinical.Trials.gov
- Detection and Characterization of Host Defense Defects, Clinical.Trials.gov

GENE INFORMATION

Names:

HUGO name: MYO5A
Alias(es): MYH12, myosin VA, heavy polypeptide 12, Myosin 5A, Dilute myosin heavy chain, non-muscle, Myosin heavy chain 12, Myoxin

Localization:

Reference sequences:

DNA: MYO5A_DNA (EMBL) , **cDNA:** U90942 (EMBL) Y07759 (EMBL) Y07759 (EMBL) Z22957 (EMBL) S74799 (EMBL) AF055459 (EMBL) , **Protein:** Q9Y4I1 (UniProt/Swiss-Prot)

Chromosomal Location:

15q21

Maps:

MYO5A (Map View)

Variations / Mutations:

- MYO5Abase; Mutation registry for Griscelli syndrome type I

Other gene-based resources:

Ensembl: ENSG00000197535, GENATLAS: MYO5A, GeneCard: MYO5A, UniGene: 21213, Entrez Gene: 4644, euGenes: 4644, GDB: 218824

PROTEIN INFORMATION

Description:

Protein function:

Processive actin-based motor that can move in large steps approximating the 36-nm pseudo-repeat of the actin filament. May be involved in melanosome transport, or alternatively, it may be required for some polarization process involved in dendrite formation.

Subunit:

May be a homodimer, which associates with multiple calmodulin or myosin light chains.

Protein function:

3 isoforms are produced by alternative splicing.

Other features:

Other related resourses:

InterPro: IPR002710; DIL, InterPro: IPR000048; IQ_region, InterPro: IPR001609; myosin_head, Pfam: PF00063; myosin_head, Pfam: PF00612; IQ, Pfam: PF01843; DIL, ProDom: PD000355; myosin_head, ProDom: PD003376; DIL, SMART: SM00015; IQ, SMART: SM00242; MYSc, PROSITE: PS50096; IQ

Expression pattern for human:

Tissue	Exp. (%)	Clones
eye, ciliary body	57.52	1:199
melanoma (mewo cell line)	14.32	2:1599
foreskin, melanocyte	6.79	8:13478
human skeletal muscle	4.26	4:10746
pool, melanocyte+heart +uterus	2.08	6:32944
human fetal eye	2.07	1:5520
human lung epithelial cell lines untreated lps 6hr to lps	1.82	1:6278
normal lung epithelial cells tissue nos 369-371 and 380-383	1.71	1:6713
breast	1.36	5:42231
rpe and choroid	1.08	1:10565

OTHER RESOURCES

Societies:

General:

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

Disease specific:

- European Hair Research Society