Griscelli syndrome, type 2

GENERAL INFORMATION

Description:

Defects in RAB27A cause Griscelli syndrome type 2 (GS2). RAB27A regulates the cytotoxic granule exocytosis and affect T-lymphocyte and macrophage-activation. RABD27 encodes protein which is key effector of intracellular vesicular transport. Most patients also develop an uncontrolled T lymphocyte and macrophage activation syndrome, known as hemophagocytic syndrome, leading to death in the absence of bone marrow transplantation.

Alternative names:

- GS2
- Griscelli syndrome with hemophagocytic syndrome
- PAID
- Partial albinism with immunodeficiency

Classification:

- Defects of phagocyte function
  - Griscelli syndrome

Inheritance:

Autosomal recesseive

OMIM:

- #607624 Griscelli syndrome, type 2; GS2
- 604228 Partial albinism and immunodeficiency syndrome
- #214450 Griscelli syndrome, type 1; GS1
- *603868 Ras-associated protein rab27a; RAB27A

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for Chediak-Higashi syndrome
- IDR factfile for Griscelli syndrome, type 1
- 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, cellular immune deficiency, neurologic abnormalities and fatal outcome caused by an uncontrolled T lymphocyte and macrophage activation syndrome. GS2 is similar to Chediak-Higashi syndrome but is distinguished from it by the absence of giant granules. Silvery gray sheen to their hair is an expression of albinism. The patients's hair is generally lighter than their unaffected family members. Sometimes patients present a subtle pigmentary dilution of the skin and iris. Immunological and hematological manifestations include anemia, neutropenia and lack of natural killer cell function, with the development of an accelerated phase of the disease with fever, jaundice, hepatosplenomegaly, lymphadenopathy, pancytopenia and generalized lymphohistiocytic infiltrates of various organs including the central nervous system. Onset of accelerated phase is associated with a virus or bacterial infection. Neurological manifestations include hyperreflexia, seizures, signs of intracranial hypertension (vomiting, altered consciousness), regression of developmental milestones, hypertonia, nystagmus and ataxia. Psychomotor development is normal at onset and regression of the central nervous system signs can be observed during remission. Cranial computer tomograph (CT) and magnetic resonance imaging (MRI) reveal cerebellar hypodense areas, ventricular, or hyperdense areas compatible with inflammatory changes, white matter changes and periventricular calcifications.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Griscelli disease, ORPHANET
- Griscelli Syndrome, eMedicine

Therapeutic options:

- Bone marrow transplantation. Chemotherapy, antithymocyte globulins and cyclosporin have achieved remissions. Intrathecal methotrexate injections help in treatment of neurocerebral involvement.
- Griscelli Syndrome, eMedicine

Research programs, clinical trials:

- European Initiative for Primary Immunodeficiencies.

GENE INFORMATION

Names:

HUGO name: RAB27A
Alias(es): GS2, HsT18676, RAB27, RAM, GTP-binding protein Ram, RAB27A, member RAS oncogene family, RAB27A, member RAS oncogene family, Ras-related protein, GTP-binding protein Ram

Localization:

Reference sequences:

DNA: U38654 (EMBL) U57094 (EMBL) AF154840 (EMBL) AF125393 (EMBL) AF443871 (EMBL) AF498953 (EMBL) , **cDNA:** X58957 (EMBL) , **Protein:** P51159 (SWISSPROT) Other Sequences

Chromosomal Location:

15q21

Maps:

RAB27A (Map View)

Markers:

STS-H96653, RH93587, PMC307551P2

Variations / Mutations:

- RAB27Abase; Mutation registry for Griscelli syndrome, type 2
- ; Mutation Database Mutations of the Small Nucleotide-binding Protein 27a Gene (RAB27A)

Other gene-based resources:

Ensembl: ENSG00000069974, GENATLAS: RAB27A, GeneCard: RAB27A, UniGene: 298651, Entrez Gene: 5873, euGenes: 5873, GDB: 4642792, HomoloGene: 3069

PROTEIN INFORMATION

Description:

Subunit:

Binds SYT11, SYTl2, SLAC2b, MYRIP, SYTl3, SYTl4 and SYTl5. Binds MLPH.

Subcellular location:

Membrane-bound

Tissue specificity:

Found in all the examined tissues except in brain. Low expression was found in thymus, kidney, muscle and placenta. Detected in melanocytes, and in most tumor cell lines examined.

Similarity:

Belongs to the small GTPase superfamily. RAB family.

Domains:

Effector region domain: 38-46

Other features:

GTP nucleotide phosphate-binding region: 16-23

GTP nucleotide phosphate-binding region: 74-78

GTP nucleotide phosphate-binding region: 133-136

Other related resourses:

InterPro: IPR003579; GTPase_Rab, InterPro: IPR001806; Ras_trnsfrmng, InterPro: IPR005225; Small_GTP, Pfam: PF00071; ras

Expression pattern for human:

Tissue	Exp. (%)	Clones
follicular lymphoma	14.90	2:927
prostate	6.18	2:2237
olfactory epithelium	5.63	1:1227
malignant melanoma, metastatic to lymph node	5.36	2:2577
melanoma (MeWo cell line)	4.49	1:1539
melanotic melanoma, high MDR	4.29	4:6448
lung carcinoma	4.18	2:3303
mucoepidermoid carcinoma	4.15	4:6654
myeloid cells, 18 pooled CML cases, BCR/ABL rearrangement positive, includes both chronic phase and myeloid blast crisis	3.02	1:2287
melanotic melanoma, high MDR (cell line)	2.77	4:9990

Animal models:

Mouse:

MGD: ; Rab27a

OTHER RESOURCES

Societies:

General:

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

Other information sources:

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