

RAB27A gene

RAB27A, member RAS oncogene family

Normal Function

The *RAB27A* gene provides instructions for making a protein that is involved in a process called vesicle trafficking, which moves proteins and other molecules within cells in sac-like structures called vesicles. Although the Rab27a protein is found in cells and tissues throughout the body, it appears to be most critical in pigment-producing cells called melanocytes and in certain immune system cells.

In melanocytes, the Rab27a protein helps transport structures called melanosomes. These structures produce a pigment called melanin, which is the substance that gives skin, hair, and eyes their color (pigmentation). Rab27a interacts with proteins produced from the *MLPH* and *MYO5A* genes to form a complex that transports melanosomes to the outer edges of melanocytes. From there, the melanosomes are transferred to other types of cells, where they provide the pigment needed for normal hair, skin, and eye coloring.

The Rab27a protein also plays an important role in immune system cells called T-lymphocytes. These cells recognize and attack foreign invaders, such as viruses and bacteria, to prevent infection and illness. Specifically, Rab27a is involved in cytotoxic granule exocytosis, which is the process by which T-lymphocytes release cell-killing (cytotoxic) compounds to destroy foreign invaders.

Health Conditions Related to Genetic Changes

Griscelli syndrome

At least 24 mutations in the *RAB27A* gene have been found in people with Griscelli syndrome. These mutations cause a form of the condition designated type 2, which is characterized by unusually light (hypopigmented) skin, silvery-gray hair, and immune system abnormalities. The known mutations either prevent the production of any Rab27a protein or lead to the production of an abnormal or unstable protein that cannot form a complex with the proteins produced from the *MLPH* and *MYO5A* genes. A shortage of functional Rab27a protein impairs the normal transport of melanosomes to the edges of melanocytes. Instead, these structures clump near the center of melanocytes, trapping melanin within these cells and preventing normal pigmentation of skin and hair. A loss of Rab27a function in T-lymphocytes impairs cytotoxic granule

exocytosis, making people with Griscelli syndrome type 2 prone to recurrent infections.

Through mechanisms that are not well understood, a shortage of Rab27a in immune system cells also leads to a condition called hemophagocytic lymphohistiocytosis (HLH) in people with Griscelli syndrome type 2. This condition triggers the immune system to produce too many activated T-lymphocytes and other immune cells called macrophages (histiocytes). Overactivity of these cells can damage organs and tissues throughout the body, causing life-threatening complications if the condition is untreated.

Other Names for This Gene

- GS2
- GTP-binding protein Ram
- HsT18676
- rab-27
- RAB27
- RAM
- ras-related protein Rab-27A
- RB27A_HUMAN

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of RAB27A ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=5873\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=5873[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28RAB27A%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D>)

Catalog of Genes and Diseases from OMIM

- RAS-ASSOCIATED PROTEIN RAB27A; RAB27A (<https://omim.org/entry/603868>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/5873>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=RAB27A\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=RAB27A[gene]))

References

- Anikster Y, Huizing M, Anderson PD, Fitzpatrick DL, Klar A, Gross-Kieselstein E, Berkun Y, Shazberg G, Gahl WA, Hurvitz H. Evidence that Griscelli syndrome with neurological involvement is caused by mutations in RAB27A, not MYO5A. *Am J Hum Genet.* 2002 Aug;71(2):407-14. doi: 10.1086/341606. Epub 2002 Jun 7. Erratum In: *Am J Hum Genet* 2002 Oct;71(4):1007. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12058346>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC379173/>)
- Bahadoran P, Busca R, Chiaverini C, Westbroek W, Lambert J, Bille K, Valony G, Fukuda M, Naeyaert JM, Ortonne JP, Ballotti R. Characterization of the molecular defects in Rab27a, caused by RAB27A missense mutations found in patients with Griscelli syndrome. *J Biol Chem.* 2003 Mar 28;278(13):11386-92. doi:10.1074/jbc.M211996200. Epub 2003 Jan 16. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12531900>)
- Bizario JC, Feldmann J, Castro FA, Menasche G, Jacob CM, Cristofani L, Casella EB, Voltarelli JC, de Saint-Basile G, Espreafico EM. Griscelli syndrome: characterization of a new mutation and rescue of T-cytotoxic activity by retroviral transfer of RAB27A gene. *J Clin Immunol.* 2004 Jul;24(4):397-410. doi:10.1023/B:JOCI.0000029119.83799.cb. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15163896>)
- Durmaz A, Ozkinay F, Onay H, Tombuloglu M, Atay A, Gursel O, Peker E, Atmaca M, Genel F, Bozabali S, Akin H, Ozkinay C. Molecular analysis and clinical findings of Griscelli syndrome patients. *J Pediatr Hematol Oncol.* 2012 Oct;34(7):541-4. doi: 10.1097/MPH.0b013e31826781ad. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/22983416>)
- Menasche G, Pastural E, Feldmann J, Certain S, Ersoy F, Dupuis S, Wulffraat N, Bianchi D, Fischer A, Le Deist F, de Saint Basile G. Mutations in RAB27A cause Griscelli syndrome associated with haemophagocytic syndrome. *Nat Genet.* 2000 Jun;25(2):173-6. doi: 10.1038/76024. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/10835631>)
- Van Gele M, Dynodt P, Lambert J. Griscelli syndrome: a model system to study vesicular trafficking. *Pigment Cell Melanoma Res.* 2009 Jun;22(3):268-82. doi: 10.1111/j.1755-148X.2009.00558.x. Epub 2009 Feb 25. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/19243575>)

Genomic Location

The *RAB27A* gene is found on chromosome 15 (<https://medlineplus.gov/genetics/chromosome/15/>).

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