RAB3GAP2 gene

RAB3 GTPase activating non-catalytic protein subunit 2

Normal Function

The *RAB3GAP2* gene provides instructions for making a protein that helps regulate the activity of specialized proteins called GTPases, which control a variety of functions in cells. To perform its function, the RAB3GAP2 protein interacts with another protein called RAB3GAP1 (produced from the *RAB3GAP1* gene) to form the RAB3GAP complex.

Often referred to as molecular switches, GTPases can be turned on and off. They are turned on (active) when they are attached (bound) to a molecule called GTP and are turned off (inactive) when they are bound to another molecule called GDP. The RAB3GAP complex turns on a GTPase known as RAB18 by exchanging GTP for the attached GDP. When active, RAB18 is involved in a process called vesicle trafficking, which moves proteins and other molecules within cells in sac-like structures called vesicles. RAB18 regulates the movement of substances between compartments in cells and the storage and release of fats (lipids) by structures called lipid droplets. The protein also appears to play a role in a process called autophagy, which helps clear unneeded materials from cells. RAB18 is important for the organization of a cell structure called the endoplasmic reticulum, which is involved in protein processing and transport.

The RAB3GAP complex is also thought to inactivate another GTPase known as RAB3 by stimulating a reaction that turns the attached GTP into GDP. RAB3 plays a role in the release of hormones and brain chemicals (neurotransmitters) from cells.

Health Conditions Related to Genetic Changes

RAB18 deficiency

At least 10 *RAB3GAP2* gene mutations have been found to cause RAB18 deficiency, resulting in conditions that affect the eyes, brain, and reproductive system. The two conditions caused by this deficiency are Warburg micro syndrome at the severe end of the spectrum and Martsolf syndrome at the mild end. *RAB3GAP2* gene mutations are the most common cause of Martsolf syndrome and can also cause Warburg micro syndrome.

Martsolf syndrome is caused by *RAB3GAP2* gene mutations that reduce the amount of functional RAB3GAP2 protein. Warburg micro syndrome occurs when the gene mutations prevent the production of any RAB3GAP2 protein or completely eliminate its function. Reduction or loss of this protein likely impairs the formation or function of the RAB3GAP complex, leading to a shortage (deficiency) of RAB18 activity. It is unclear why the loss of RAB18 function leads to eye problems, brain abnormalities, and other features of these two conditions.

Because Warburg micro syndrome and Martsolf syndrome can be caused by mutations in other genes that disrupt normal RAB18 activity, loss of control of this GTPase is thought to underlie the conditions. It is unclear if impaired regulation of RAB3 activity contributes to the features of Warburg micro syndrome or Martsolf syndrome.

Coloboma

MedlinePlus Genetics provides information about Coloboma

Other Names for This Gene

- DKFZP434D245
- KIAA0839
- p150
- RAB3 GTPase activating protein subunit 2 (non-catalytic)
- rab3 GTPase-activating protein 150 kDa subunit
- rab3 GTPase-activating protein non-catalytic subunit
- rab3-GAP p150
- rab3-GAP regulatory subunit
- RAB3-GAP150
- RAB3GAP150
- RGAP-iso
- SPG69
- WARBM2

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of RAB3GAP2 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=25782[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28RAB3GAP2%5BTIAB%5

D%29+OR+%28RAB3+GTPase+activating+non-catalytic+protein+subunit+2%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- RAB3 GTPase-ACTIVATING PROTEIN, NONCATALYTIC SUBUNIT; RAB3GAP2 (https://omim.org/entry/609275)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/25782)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=RAB3GAP2[gene])

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Genomic Location

The *RAB3GAP2* gene is found on chromosome 1 (https://medlineplus.gov/genetics/chromosome/1/).

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