RAB3GAP1 Gene

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Contributor: Karina Chen

RAB3 GTPase activating protein catalytic subunit 1

genes

1. Normal Function

The *RAB3GAP1* 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 RAB3GAP1 protein interacts with another protein called RAB3GAP2 (produced from the *RAB3GAP2* 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.

2. Health Conditions Related to Genetic Changes

2.1. RAB18 deficiency

More than 60 *RAB3GAP1* 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. *RAB3GAP1* gene mutations are the most common cause of Warburg micro syndrome and are rare in Martsolf syndrome.

Warburg micro syndrome is caused by *RAB3GAP1* gene mutations that prevent the production of any RAB3GAP1 protein or completely eliminate its function. Martsolf syndrome occurs when a small amount of functional RAB3GAP1 protein is produced from the mutated gene. 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.

3. Other Names for This Gene

- KIAA0066
- P130
- RAB3 GTPase activating protein subunit 1 (catalytic)
- RAB3 GTPase-activating protein 130 kDa subunit
- rab3 GTPase-activating protein catalytic subunit isoform 1
- rab3 GTPase-activating protein catalytic subunit isoform 2
- rab3-GAP p130
- RAB3GAP
- RAB3GAP130
- WARBM1

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