RASA1 Gene

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RAS p21 protein activator 1

genes

1. Normal Function

The *RASA1* gene provides instructions for making a protein called p120-RasGAP. This protein helps regulate the RAS/MAPK signaling pathway, which transmits signals from outside the cell to the cell's nucleus. The RAS/MAPK signaling pathway helps direct several important cell functions, including the growth and division (proliferation) of cells, the process by which cells mature to carry out specific functions (differentiation), and cell movement. The p120-RasGAP protein is a negative regulator of the RAS/MAPK signaling pathway, which means it is involved in turning off these signals when they are not needed.

The exact role of p120-RasGAP is not fully understood. However, it appears to be essential for the normal development of the vascular system, which is the complex network of arteries, veins, and capillaries that carry blood to and from the heart.

2. Health Conditions Related to Genetic Changes

2.1. Capillary malformation-arteriovenous malformation syndrome

Several dozen mutations in the *RASA1* gene have been found to cause capillary malformation-arteriovenous malformation syndrome (CM-AVM), which is a condition characterized by abnormalities of the vascular system. Most of the mutations responsible for CM-AVM prevent the production of functional p120-RasGAP protein. As a result, this protein is unavailable to control RAS/MAPK signaling. It is unclear how changes in this tightly regulated signaling pathway lead to the specific vascular abnormalities seen in people with CM-AVM.

2.2. Parkes Weber syndrome

Several mutations in the *RASA1* gene have been identified in people with Parkes Weber syndrome. When the condition is caused by *RASA1* gene mutations, affected individuals usually have multiple vascular abnormalities known as capillary malformations. Parkes Weber syndrome is also characterized by other abnormalities of the vascular system and overgrowth of one limb, most commonly a leg.

Like the *RASA1* gene mutations that cause CM-AVM, the mutations responsible for Parkes Weber syndrome prevent the production of functional p120-RasGAP protein. A loss of this protein's activity disrupts the normal regulation of RAS/MAPK signaling. It is unclear how a lack of p120-RasGAP leads to the specific vascular abnormalities and limb overgrowth that occur in Parkes Weber syndrome.

2.3. Cancers

At least three mutations in the *RASA1* gene have been detected in a form of skin cancer called basal cell carcinoma. These mutations are described as somatic, which means they occur during a person's lifetime and are present only in the cells that become cancerous. Researchers suspect that the *RASA1* gene mutations lead to a loss of p120-RasGAP protein function, which may allow RAS/MAPK signaling to proceed in an uncontrolled way. This unchecked RAS/MAPK signaling could lead to unregulated cell proliferation and the formation of a cancerous tumor. *RASA1* gene mutations are found in only a small percentage of all basal cell carcinomas, and they are not thought to be a major cause of these cancers.

3. Other Names for This Gene

- DKFZp434N071
- GAP
- GTPase-activating protein
- p120
- p120GAP
- p120RASGAP
- ras GTPase-activating protein 1
- RAS p21 protein activator (GTPase activating protein) 1
- RASA
- RASA1_HUMAN
- RASGAP
- triphosphatase-activating protein

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