RASA1 gene
RAS p21 protein activator 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.

Health Conditions Related to Genetic Changes
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.

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.
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.

Chromosomal Location

Cytogenetic Location: 5q14.3, which is the long (q) arm of chromosome 5 at position 14.3

Molecular Location: base pairs 87,267,845 to 87,391,926 on chromosome 5 (Homo sapiens Updated Annotation Release 109.20190607, GRCh38.p13) (NCBI)

Credit: Genome Decoration Page/NCBI

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

Additional Information & Resources

Educational Resources
• Madame Curie Bioscience Database: MAPK Signaling Pathway
  https://www.ncbi.nlm.nih.gov/books/NBK5964/#A40944

Clinical Information from GeneReviews
• RASA1-Related Disorders
  https://www.ncbi.nlm.nih.gov/books/NBK52764

Scientific Articles on PubMed
• PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28RASA1%5BTIAB%5D%29+OR+%28RAS+p21+protein+activator+++1%5BTIAB%5D%29%29+OR+%28%28p120GAP%5BTIAB%5D%29+OR+%28p120RASGAP%5BTIAB%5D%29+AND+%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM
• RAS p21 PROTEIN ACTIVATOR 1
  http://omim.org/entry/139150

Research Resources
• Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_RASA1.html
• ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=RASA1%5Bgene%5D
• HGNC Gene Symbol Report
• Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:5921
• NCBI Gene
• RASA1base
  http://structure.bmc.lu.se/idbase/RASA1base/
• UniProt
  https://www.uniprot.org/uniprot/P20936
Sources for This Summary


Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/gene/RASA1

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