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.

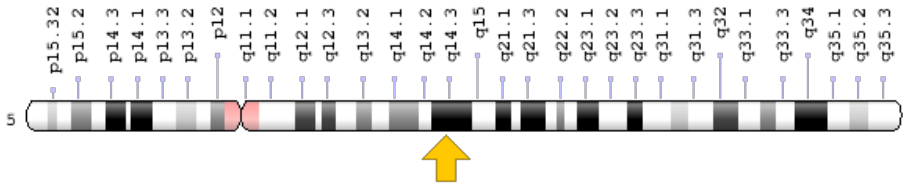
Cancers

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 Annotation Release 109, GRCh38.p12) (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

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%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

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 Family: C2 and RasGAP domain containing
  https://www.genenames.org/cgi-bin/genefamilies/set/830
- HGNC Gene Family: Pleckstrin homology domain containing
  https://www.genenames.org/cgi-bin/genefamilies/set/682
- HGNC Gene Family: SH2 domain containing
  https://www.genenames.org/cgi-bin/genefamilies/set/741
- HGNC Gene Symbol Report
  https://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=9871

- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/5921
- RASA1base
  http://structure.bmc.lu.se/idbase/RASA1base/
- UniProt
  http://www.uniprot.org/uniprot/P20936

Sources for This Summary

- Bayrak-Toydemir P, Stevenson D. RASA1-Related Disorders. 2011 Feb 22 [updated 2016 Oct 6]. In: Pagon RA, Adam MP, Ardinger HH, Wallace SE, Amemiya A, Bean LJH, Bird TD, Ledbetter N, Mefford HC, Smith RJH, Stephens K, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017. Available from http://www.ncbi.nlm.nih.gov/books/NBK52764/
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21348050
- Boon LM, Mulliken JB, Vikkula M. RASA1: variable phenotype with capillary and arteriovenous malformations. Curr Opin Genet Dev. 2005 Jun;15(3):265-9. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15917201
- Eerola I, Boon LM, Mulliken JB, Burrows PE, Dompmartin A, Watanabe S, Vanwijck R, Vikkula M. Capillary malformation-arteriovenous malformation, a new clinical and genetic disorder caused by RASA1 mutations. Am J Hum Genet. 2003 Dec;73(6):1240-9. Epub 2003 Nov 24.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/14639529
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1180390/
- Friedman E, Gejman PV, Martin GA, McCormick F. Nonsense mutations in the C-terminal SH2 region of the GTPase activating protein (GAP) gene in human tumours. Nat Genet. 1993 Nov;5(3): 242-7.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/8275088
- Kulkarni SV, Gish G, van der Geer P, Henkemeyer M, Pawson T. Role of p120 Ras-GAP in directed cell movement. J Cell Biol. 2000 Apr 17;149(2):457-70.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10769036
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2175152/
- Revencu N, Boon LM, Mulliken JB, Enjolras O, Cordisco MR, Burrows PE, Clapuyt P, Hammer F, Dubois J, Baselga E, Brancati F, Carder R, Quintal JM, Dallapiccola B, Fischer G, Frieden IJ, Garzon M, Harper J, Johnson-Patel J, Labrèze C, Martorell L, Paltiel HJ, Pohl A, Prendiville J, Quere I, Siegel DH, Valente EM, Van Hagen A, Van Hest L, Vaux KK, Vicente A, Weibel L, Chitayat D, Vikkula M. Parkes Weber syndrome, vein of Galen aneurysmal malformation, and other fast-flow vascular anomalies are caused by RASA1 mutations. Hum Mutat. 2008 Jul;29(7):959-65. doi: 10.1002/humu.20746.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18446851

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

Reviewed: August 2011
Published: June 12, 2018

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services