



## Retinal arterial macroaneurysm with supravulvular pulmonic stenosis

Retinal arterial macroaneurysm with supravulvular pulmonic stenosis (RAMSVPS) is a disorder that affects blood vessels in the eyes and heart. The condition generally becomes apparent in infancy or childhood.

RAMSVPS damages the arteries in the light-sensitive tissue at the back of the eye (the retina). These arteries gradually develop multiple small bulges called beading. Eventually, larger bulges in the blood vessel walls (macroaneurysms) occur. These macroaneurysms can tear (rupture), leading to bleeding that can spread into other areas of the eye and cause vision loss.

People with RAMSVPS also have a heart condition called supravulvular pulmonic stenosis. Pulmonic stenosis is a narrowing that affects the pulmonic valve between the heart and the lungs. The term "supravulvular" means that the narrowing occurs just above the valve, in a blood vessel called the pulmonary artery. Supravulvular pulmonic stenosis impairs blood flow into the lungs, where blood normally picks up oxygen for distribution to cells and tissues throughout the body. As a result, less oxygen is carried through the bloodstream, leading to signs and symptoms that include shortness of breath; a rapid heartbeat; fatigue; and swelling in the face, feet, or abdomen.

### Frequency

RAMSVPS is a rare disorder. Only a small number of affected individuals and families, all from Saudi Arabia, have been described in the medical literature.

### Causes

RAMSVPS is caused by a mutation in the *IGFBP7* gene. This gene provides instructions for making a protein called insulin-like growth factor-binding protein 7 (IGFBP7). The IGFBP7 protein is active in the lining of blood vessels (the vascular endothelium). It is thought to help stop a pathway called BRAF signaling, which is involved in directing cell growth.

The *IGFBP7* gene mutation that causes RAMSVPS results in an abnormally short IGFBP7 protein that does not function properly. Without normally functioning IGFBP7 protein to control BRAF signaling, this signaling is increased. It is unknown how this increase is related to the specific blood vessel abnormalities that occur in RAMSVPS, or why these abnormalities are confined to the eyes and the pulmonary artery. Researchers suggest that differences in normal levels of IGFBP7 protein in various parts of the body or the presence of other proteins with a similar function in different tissues may account for the specific signs and symptoms of this disorder.

## **Inheritance Pattern**

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

## **Other Names for This Condition**

- familial retinal arterial macroaneurysm
- FRAM
- RAMSVPS

## **Diagnosis & Management**

### Genetic Testing Information

- What is genetic testing?  
[/primer/testing/geneticTesting](#)
- Genetic Testing Registry: Retinal arterial macroaneurysm with supravulvular pulmonic stenosis  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C3280205/>

### Other Diagnosis and Management Resources

- Calgary Retina Consultants: Retinal Arterial Macroaneurysm  
<https://www.calgaryretina.ca/retinal-conditions/retinal-arterial-macroaneurysm/>
- MedlinePlus Encyclopedia: Fluorescein Angiography  
<https://medlineplus.gov/ency/article/003846.htm>
- University of Rochester Medical Center: Pulmonary Stenosis  
<https://www.urmc.rochester.edu/encyclopedia/content.aspx?ContentTypeID=90&ContentID=P01815>

## **Additional Information & Resources**

### Health Information from MedlinePlus

- Encyclopedia: Fluorescein Angiography  
<https://medlineplus.gov/ency/article/003846.htm>
- Encyclopedia: Pulmonary Valve Stenosis  
<https://medlineplus.gov/ency/article/001096.htm>
- Health Topic: Retinal Disorders  
<https://medlineplus.gov/retinaldisorders.html>

### Genetic and Rare Diseases Information Center

- Retinal arterial macroaneurysm with supra-avalvular pulmonic stenosis  
<https://rarediseases.info.nih.gov/diseases/12779/retinal-arterial-macroaneurysm-with-supra-avalvular-pulmonic-stenosis>

### Educational Resources

- MalaCards: retinal arterial macroaneurysm with supra-avalvular pulmonic stenosis  
[https://www.malacards.org/card/retinal\\_arterial\\_macroaneurysm\\_with\\_supra\\_avalvular\\_pulmonic\\_stenosis](https://www.malacards.org/card/retinal_arterial_macroaneurysm_with_supra_avalvular_pulmonic_stenosis)
- Orphanet: Familial retinal arterial macroaneurysm  
[https://www.orpha.net/consor/cgi-bin/OC\\_Exp.php?Lng=EN&Expert=284247](https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=284247)
- Orphanet: Supra-avalvular pulmonary stenosis  
[https://www.orpha.net/consor/cgi-bin/OC\\_Exp.php?Lng=EN&Expert=3192](https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=3192)

### Patient Support and Advocacy Resources

- American Heart Association  
<https://www.heart.org/en/health-topics/congenital-heart-defects>
- Foundation Fighting Blindness  
<https://www.fightingblindness.org/>
- Retina International  
<http://www.retina-international.org/>

### Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28retinal+arterial+macroaneurysm%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

### Catalog of Genes and Diseases from OMIM

- RETINAL ARTERIAL MACROANEURYSM WITH SUPRAVALVULAR PULMONIC STENOSIS  
<http://omim.org/entry/614224>

## Sources for This Summary

- Abu-Safieh L, Abboud EB, Alkuraya H, Shamseldin H, Al-Enzi S, Al-Abdi L, Hashem M, Colak D, Jarallah A, Ahmad H, Bobis S, Nemer G, Bitar F, Alkuraya FS. Mutation of IGFBP7 causes upregulation of BRAF/MEK/ERK pathway and familial retinal arterial macroaneurysms. *Am J Hum Genet.* 2011 Aug 12;89(2):313-9. doi: 10.1016/j.ajhg.2011.07.010.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/21835307>  
*Free article on PubMed Central:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3155176/>
  - Dhindsa HS, Abboud EB. Familial retinal arterial macroaneurysms. *Retina.* 2002 Oct;22(5):607-15.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/12441727>
  - Hooper AT, Shmelkov SV, Gupta S, Milde T, Bambino K, Gillen K, Goetz M, Chavala S, Baljevic M, Murphy AJ, Valenzuela DM, Gale NW, Thurston G, Yancopoulos GD, Vahdat L, Evans T, Rafii S. Angiomodulin is a specific marker of vasculature and regulates vascular endothelial growth factor-A-dependent neoangiogenesis. *Circ Res.* 2009 Jul 17;105(2):201-8. doi: 10.1161/CIRCRESAHA.109.196790. Epub 2009 Jun 18.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/19542015>  
*Free article on PubMed Central:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2936249/>
- 

Reprinted from Genetics Home Reference:

<https://ghr.nlm.nih.gov/condition/retinal-arterial-macroaneurysm-with-supravalvular-pulmonic-stenosis>

Reviewed: August 2015

Published: September 10, 2019

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