SAMD9L gene
sterile alpha motif domain containing 9 like

Normal Function
The SAMD9L gene provides instructions for making a protein that is active in cells throughout the body. The protein is involved in regulating the growth and division (proliferation) and maturation (differentiation) of cells, particularly cells in the bone marrow that give rise to blood cells. Studies suggest that the SAMD9L protein acts as a tumor suppressor, keeping cells from growing and dividing too rapidly or in an uncontrolled way. The SAMD9L protein also appears to play an important role in the brain, particularly the part of the brain that coordinates movement (the cerebellum), although less is known about the protein’s function there.

Health Conditions Related to Genetic Changes
Ataxia-pancytopenia syndrome
At least four inherited mutations in the SAMD9L gene have been found to cause ataxia-pancytopenia syndrome, a rare condition that affects the cerebellum and blood-forming cells in the bone marrow. This condition causes neurological problems such as ataxia, which is difficulty with balance and coordination. It is also associated with pancytopenia, which is a reduced number of blood cells, including red blood cells, white blood cells, and platelets. People with ataxia-pancytopenia syndrome have an increased risk of certain cancerous conditions of the blood, particularly myelodysplastic syndrome and acute myeloid leukemia.

The mutations that cause ataxia-pancytopenia syndrome are present in essentially all of the body’s cells. They are described as "gain-of-function." They increase the SAMD9L protein’s ability to block cell growth and division. In the bone marrow, the resulting reduction in cell proliferation leads to a shortage of blood cells. It is unclear how the effects of these mutations are related to ataxia and the other neurological problems associated with ataxia-pancytopenia syndrome.

It seems paradoxical that gain-of-function mutations in the SAMD9L gene, which enhance the protein’s tumor suppressor function, could increase the risk of developing cancerous conditions such as myelodysplastic syndrome and acute myeloid leukemia. It appears that certain cells in the bone marrow with an inherited gain-of-function SAMD9L gene mutation can develop additional genetic changes that are associated with milder pancytopenia but an increased cancer risk. These changes include mutations that disable the SAMD9L gene ("loss-of-function" mutations) or a deletion of part of the long (q) arm of chromosome 7 that contains the SAMD9L gene. These additional changes compensate for the effects of the gain-
of-function mutation in bone marrow cells. They prevent an overactive SAMD9L protein from excessively restricting cell proliferation, which reduces the severity of pancytopenia in affected individuals. However, a loss of the SAMD9L gene and other genes on the long arm of chromosome 7 may allow cells to grow and divide uncontrollably, leading to cancer. A deletion of the long arm of chromosome 7 is a well-known risk factor for myelodysplastic syndrome and leukemia.

Cancers

Mutations in the SAMD9L gene have been found in a form of liver cancer called hepatocellular carcinoma. Unlike the mutations that cause ataxia-pancytopenia syndrome (described above), these genetic changes are somatic, which means they are acquired during a person's lifetime and are present only in cells that give rise to the tumor. The mutations are described as "loss-of-function." They disable the SAMD9L gene, which prevents the SAMD9L protein from regulating cell proliferation effectively. As a result, cells in the liver can grow and divide without control or order, leading to cancer.

Chromosomal Location

Cytogenetic Location: 7q21.2, which is the long (q) arm of chromosome 7 at position 21.2

Molecular Location: base pairs 93,130,056 to 93,148,385 on chromosome 7 (Homo sapiens Updated Annotation Release 109.20200228, GRCh38.p13) (NCBI)

Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- ATXPC
- C7orf6
- DRIF2
- FLJ39885
- KIAA2005
- SAM domain-containing protein 9-like
• sterile alpha motif domain-containing protein 9-like
• UEF1

Additional Information & Resources

Educational Resources
• Molecular Cell Biology (fourth edition, 2000): Proto-Oncogenes and Tumor-Suppressor Genes
  https://www.ncbi.nlm.nih.gov/books/NBK21662/

Clinical Information from GeneReviews
• SAMD9L-Related Ataxia-Pancytopenia Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK435692

Scientific Articles on PubMed
• PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28SAMD9L%5BTIAB%5D%29+OR+%28sterile+alpha+motif+domain+containing+9+like%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D

Catalog of Genes and Diseases from OMIM
• STERILE ALPHA MOTIF DOMAIN-CONTAINING PROTEIN 9-LIKE
  http://omim.org/entry/611170

Research Resources
• Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_SAMD9L.html
• ClinVar
• HGNC Gene Symbol Report
• Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:219285
• NCBI Gene
• UniProt
  https://www.uniprot.org/uniprot/Q8IVG5
Sources for This Summary

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/27259050 
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4908176/

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/28428236

- OMIM: STERILE ALPHA MOTIF DOMAIN-CONTAINING PROTEIN 9-LIKE  
  http://omim.org/entry/611170

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/28202457 
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5399482/

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Reprinted from Genetics Home Reference:  

Reviewed: September 2017  
Published: April 15, 2020

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