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.

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

Tests Listed in the Genetic Testing Registry

- Tests of SAMD9L (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=219285[geneid])

Scientific Articles on PubMed

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

Catalog of Genes and Diseases from OMIM

- STERILE ALPHA MOTIF DOMAIN-CONTAINING PROTEIN 9-LIKE; SAMD9L (https://omim.org/entry/611170)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/219285)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=SAMD9L[gene])

References

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Genomic Location

The *SAMD9L* gene is found on chromosome 7 (https://medlineplus.gov/genetics/chromosome/7/).

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