TSC1 gene

TSC complex subunit 1

Normal Function

The *TSC1* gene provides instructions for producing a protein called hamartin. Within cells, hamartin interacts with a protein called tuberin, which is produced from the *TSC2* gene. These two proteins help control cell growth and division (proliferation) and cell size. Proteins that normally prevent cells from growing and dividing too fast or in an uncontrolled way are known as tumor suppressors. Hamartin and tuberin carry out their tumor suppressor function by interacting with and regulating a wide variety of other proteins.

Health Conditions Related to Genetic Changes

Lymphangioleiomyomatosis

TSC1 gene variants (also known as mutations) can cause a disorder called lymphangioleiomyomatosis (LAM), although variants in the *TSC2* gene appear to be responsible for most cases of this disorder. This destructive lung disease is caused by the abnormal overgrowth of smooth muscle-like tissue in the lungs. It occurs almost exclusively in women, causing coughing, shortness of breath, chest pain, and lung collapse.

LAM can occur alone (isolated or sporadic LAM) or in combination with a condition called tuberous sclerosis complex (described below). Researchers suggest that sporadic LAM can be caused by a random variant in the *TSC1* gene that occurs very early in development. As a result, some of the body's cells have a normal version of the gene, while others have the altered version. This situation is called mosaicism. When a variant occurs in the other copy of the *TSC1* gene in certain cells during a woman's lifetime (a somatic variant), she may develop LAM.

Tuberous sclerosis complex

Hundreds of variants in the *TSC1* gene have been identified in individuals with tuberous sclerosis complex, a condition characterized by developmental problems and the growth of noncancerous (benign) tumors in many parts of the body. Most of these variants involve either small deletions or insertions of DNA in the *TSC1* gene. Some variants create a premature stop signal in the instructions for making hamartin.

People with *TSC1*-related tuberous sclerosis complex are born with one altered copy of the *TSC1* gene in each cell. A *TSC1* gene change prevents the cell from making functional hamartin from that copy of the gene. Enough hamartin is usually produced from the other, normal copy of the *TSC1* gene to regulate cell growth effectively. For some types of tumors to develop, a second variant involving the other copy of the gene must occur in certain cells during a person's lifetime.

When both copies of the *TSC1* gene are altered in a particular cell, that cell cannot produce any functional hamartin. The loss of this protein allows the cell to grow and divide in an uncontrolled way to form a tumor. A shortage of hamartin also interferes with the normal development of certain cells. In people with *TSC1*-related tuberous sclerosis complex, a second *TSC1* gene variant typically occurs in multiple cells over an affected person's lifetime. The loss of hamartin in different types of cells disrupts normal development and leads to the growth of tumors in many different organs and tissues, leading to the signs and symptoms of tuberous sclerosis complex.

Cholangiocarcinoma

MedlinePlus Genetics provides information about Cholangiocarcinoma

Other disorders

Inherited variants in the *TSC1* gene can cause a disorder known as focal cortical dysplasia of Taylor balloon cell type. This disorder involves malformations of the cerebrum, the large, frontal part of the brain that is responsible for thinking and learning. Focal cortical dysplasia causes severe recurrent seizures (epilepsy) in affected individuals.

Other Names for This Gene

- hamartin
- KIAA0243
- TSC1_HUMAN
- tuberous sclerosis 1

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of TSC1 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=7248[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28TSC1%5BTIAB%5D%29+OR+%28hamartin%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AN

D+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- TSC COMPLEX SUBUNIT 1; TSC1 (https://omim.org/entry/605284)
- FOCAL CORTICAL DYSPLASIA, TYPE II; FCORD2 (https://omim.org/entry/607341)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/7248)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=TSC1[gene])

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Genomic Location

The *TSC1* gene is found on chromosome 9 (https://medlineplus.gov/genetics/chromosome/9/).

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