TSC2 gene

TSC complex subunit 2

Normal Function

The *TSC2* gene provides instructions for producing a protein called tuberin. Within cells, tuberin interacts with a protein called hamartin, which is produced from the *TSC1* 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

TSC2 gene variants (also known as mutations) cause most cases of a disorder called lymphangioleiomyomatosis (LAM). This destructive lung disease is characterized 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 is caused by a random variant in the *TSC2* 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 *TSC2* gene in certain cells during a woman's lifetime (a somatic variant), she may develop LAM.

Tuberous sclerosis complex

More than a thousand variants in the *TSC2* gene have been identified in individuals with tuberous sclerosis complex, a condition characterized by developmental problems and the growth of noncancerous tumors in many parts of the body. Most of these variants insert or delete a small number of DNA building blocks (base pairs) in the *TSC2* gene. Other variants change a single base pair in the *TSC2* gene or create a premature stop signal in the instructions for making tuberin.

People with *TSC2*-related tuberous sclerosis complex are born with one altered copy of the *TSC2* gene in each cell. A *TSC2* gene variant prevents the cell from making functional tuberin from that copy of the gene. Enough tuberin is usually produced from the other, normal copy of the *TSC2* 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 *TSC2* gene are altered in a particular cell, that cell cannot produce any functional tuberin. The loss of this protein allows the cell to grow and divide in an uncontrolled way to form a tumor. A shortage of tuberin also interferes with the normal development of certain cells. In people with *TSC2*-related tuberous sclerosis complex, a second *TSC2* gene variant typically occurs in multiple cells over an affected person's lifetime. The loss of tuberin 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.

Other Names for This Gene

- PPP1R160
- TSC2_HUMAN
- tuberin
- tuberous sclerosis 2

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of TSC2 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=7249[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28TSC2%5BTIAB%5D%29+OR+%28tuberous+sclerosis+2%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+720+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- TSC COMPLEX SUBUNIT 2; TSC2 (https://omim.org/entry/191092)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/7249)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=TSC2[gene])

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Genomic Location

The *TSC2* gene is found on chromosome 16 (https://medlineplus.gov/genetics/chromosome/16/).

Last updated January 4, 2022