



SMARCB1 gene

SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily b, member 1

Normal Function

The *SMARCB1* gene provides instructions for making a protein that forms one piece (subunit) of several different protein groupings called SWI/SNF protein complexes. SWI/SNF complexes regulate gene activity (expression) by a process known as chromatin remodeling. Chromatin is the network of DNA and protein that packages DNA into chromosomes. The structure of chromatin can be changed (remodeled) to alter how tightly DNA is packaged. Chromatin remodeling is one way gene expression is regulated during development; when DNA is tightly packed, gene expression is lower than when DNA is loosely packed.

Through their ability to regulate gene activity, SWI/SNF complexes are involved in many processes, including repairing damaged DNA; copying (replicating) DNA; and controlling the growth, division, and maturation (differentiation) of cells. Through these processes, the SMARCB1 protein and other SWI/SNF subunits are thought to act as tumor suppressors, which keep cells from growing and dividing too rapidly or in an uncontrolled way.

The role of the SMARCB1 protein within the SWI/SNF complex is not fully understood.

Health Conditions Related to Genetic Changes

Coffin-Siris syndrome

At least five mutations in the *SMARCB1* gene have been found to cause Coffin-Siris syndrome. This condition is characterized by delayed development, abnormalities of the fifth (pinky) fingers or toes, and characteristic facial features that are described as coarse. The *SMARCB1* gene mutations involved in Coffin-Siris syndrome are germline mutations, which means that they are present in cells throughout the body. The mutations change or remove single protein building blocks (amino acids) in the SMARCB1 protein. Although it is unclear how these changes affect SWI/SNF complexes, researchers suggest that *SMARCB1* gene mutations result in abnormal chromatin remodeling. Disturbance of this process alters the activity of many genes and disrupts several cell activities, which could explain the diverse signs and symptoms of Coffin-Siris syndrome. People with Coffin-Siris syndrome do not appear to have an increased risk of cancer (see below).

Rhabdoid tumor predisposition syndrome

More than 50 germline mutations in the *SMARCB1* gene have been identified in people with rhabdoid tumor predisposition syndrome (RTPS). RTPS is characterized by a high risk of developing cancerous (malignant) growths called rhabdoid tumors. These tumors most often occur in the brain and spinal cord (central nervous system) or in the kidney, but they can occur in other organs and tissues of the body. Some affected children also develop noncancerous (benign) tumors called schwannomas, which grow on nerves. Women with RTPS are at increased risk of developing a rare type of ovarian cancer called small cell cancer of the ovary, hypercalcemic type (SCCOHT).

In addition to the germline mutation affecting one copy of the *SMARCB1* gene in each cell, an additional genetic change that deletes the normal copy of the gene is needed for a tumor to develop. This additional change is present only in the cancerous cells. Such changes are known as somatic mutations. In combination, the germline and somatic mutations lead to the absence or dysfunction of SMARCB1 protein. This deficiency likely impairs the tumor suppressor functions of the proteins, but the specific mechanism that leads to rhabdoid tumors is unknown.

Schwannomatosis

More than two dozen mutations in the *SMARCB1* gene have been found in people with schwannomatosis, a disorder characterized by multiple noncancerous (benign) tumors called schwannomas that grow on nerves. This type of tumor arises from Schwann cells, which are specialized cells that normally form an insulating layer around the nerve.

SMARCB1 gene mutations associated with schwannomatosis lead to production of an altered SMARCB1 protein whose function is reduced but not eliminated. The altered protein is less able to control how cells grow and divide, which can allow tumors to develop. However, it is unknown why these mutations are predominantly associated with schwannomas, instead of other tumor types, in people with schwannomatosis.

It appears that germline mutations in *SMARCB1* alone are not enough to trigger the development of schwannomas. Additional somatic mutations that are acquired during a person's lifetime and are present only in certain cells may also be required for schwannomas to form.

Some people who have a mutation in the *SMARCB1* gene never develop tumors, which is a situation known as reduced penetrance.

Other cancers

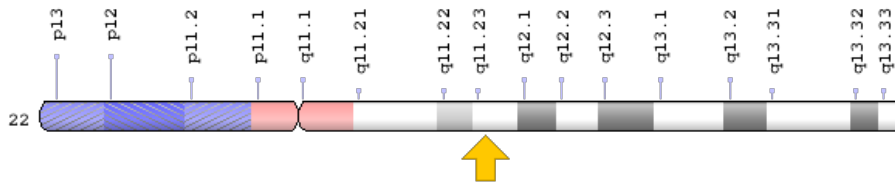
Somatic mutations in both copies of the *SMARCB1* gene, which result in the absence of SMARCB1 protein, cause noninherited (sporadic) rhabdoid tumors in children. As in RTPS (described above), the absence of SMARCB1 protein likely impairs the

tumor suppressor functions of the proteins, but the specific mechanism that leads to rhabdoid tumors is unknown.

Chromosomal Location

Cytogenetic Location: 22q11.23, which is the long (q) arm of chromosome 22 at position 11.23

Molecular Location: base pairs 23,786,931 to 23,834,518 on chromosome 22 (Homo sapiens Annotation Release 109, GRCh38.p12) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- BAF47
- BRG1-associated factor 47
- hSNF5
- hSNFS
- INI1
- integrase interactor 1 protein
- MRD15
- PPP1R144
- RDT
- RTPS1
- Sfh1p
- SNF5
- SNF5 homolog
- SNF5_HUMAN
- SNF5L1
- Snr1

- sucrose nonfermenting, yeast, homolog-like 1
- SWI/SNF-related matrix-associated actin-dependent regulator of chromatin subfamily B member 1

Additional Information & Resources

Educational Resources

- Molecular Biology of the Cell (fourth edition, 2002): ATP-Driven Chromatin Remodeling Machines Change Nucleosome Structure
<https://www.ncbi.nlm.nih.gov/books/NBK26834/#A644>
- Molecular Biology of the Cell (fourth edition, 2002): Chromosomal DNA and Its Packaging in the Chromatin Fiber
<https://www.ncbi.nlm.nih.gov/books/NBK26834/>

Clinical Information from GeneReviews

- Coffin-Siris Syndrome
<https://www.ncbi.nlm.nih.gov/books/NBK131811>
- Rhabdoid Tumor Predisposition Syndrome
<https://www.ncbi.nlm.nih.gov/books/NBK469816>
- Schwannomatosis
<https://www.ncbi.nlm.nih.gov/books/NBK487394>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28SMARCB1%5BTIAB%5D%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

- SWI/SNF-RELATED, MATRIX-ASSOCIATED, ACTIN-DEPENDENT REGULATOR OF CHROMATIN, SUBFAMILY B, MEMBER 1
<http://omim.org/entry/601607>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
<http://atlasgeneticsoncology.org/Genes/SMARCB1ID169.html>
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=SMARCB1%5Bgene%5D>
- HGNC Gene Symbol Report
https://www.genenames.org/data/gene-symbol-report#!/hgnc_id/HGNC:11103

- Monarch Initiative
<https://monarchinitiative.org/gene/NCBIGene:6598>
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/6598>
- UniProt
<https://www.uniprot.org/uniprot/Q12824>

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