CTNNB1 gene

catenin beta 1

Normal Function

The *CTNNB1* gene provides instructions for making a protein called beta-catenin. This protein is present in many types of cells and tissues, where it is primarily found at junctions that connect neighboring cells (adherens junctions). Beta-catenin plays an important role in sticking cells together (cell adhesion) and in communication between cells.

The beta-catenin protein is also involved in cell signaling as an essential part of the Wnt signaling pathway. Certain proteins in this pathway attach (bind) to beta-catenin, which triggers a multistep process that allows the protein to move into the cell nucleus. Once in the nucleus, beta-catenin interacts with other proteins to control the activity (expression) of particular genes. The Wnt signaling pathway promotes the growth and division (proliferation) of cells and helps determine the specialized functions a cell will have (differentiation). Wnt signaling is known to be involved in many aspects of development before birth. In adult tissues, this pathway plays a role in the maintenance and renewal of stem cells, which are cells that help repair tissue damage and can give rise to other types of cells.

Among its many activities, beta-catenin appears to play an important role in the normal function of hair follicles, which are specialized structures in the skin where hair growth occurs. This protein is active in cells that make up a part of the hair follicle known as the matrix. These cells divide and mature to form the different components of the hair follicle and the hair shaft. As matrix cells divide, the hair shaft is pushed upward and extends beyond the skin.

Health Conditions Related to Genetic Changes

Desmoid tumor

Mutations in the *CTNNB1* gene can cause a type of aggressive but noncancerous (benign) growth called a desmoid tumor. *CTNNB1* gene mutations are found in about 85 percent of all noninherited (sporadic) desmoid tumors. These rare tumors arise from connective tissue, which provides strength and flexibility to structures such as bones, ligaments, and muscles. The tumors are often found in the abdomen, shoulders, upper arms, or upper legs. The *CTNNB1* gene mutations that cause desmoid tumors are somatic, which means they are acquired during a person's lifetime and are present only in tumor cells. Somatic mutations are not inherited.

The *CTNNB1* gene mutations that cause desmoid tumors usually occur in a region of the gene called exon 3. They change single protein building blocks (amino acids) in

the beta-catenin protein. These mutations lead to an abnormally stable beta-catenin protein that is not broken down when it is no longer needed. As a result, the protein accumulates within cells. Excess beta-catenin promotes the uncontrolled proliferation of cells, allowing the formation of desmoid tumors.

Pilomatricoma

Somatic mutations in the *CTNNB1* gene are found in almost all pilomatricomas, a type of benign skin tumor associated with hair follicles.

The *CTNNB1* gene mutations found in pilomatricomas are described as gain-of-function mutations. They cause the beta-catenin protein to be turned on all the time (constitutively active), which leads to the abnormal activation of certain genes. These genes increase the proliferation and differentiation of cells associated with the hair follicle matrix. The cells divide too quickly and in an uncontrolled way, leading to the formation of a pilomatricoma.

Almost all pilomatricomas are benign, but a very small percentage are cancerous (malignant). The malignant version of this tumor is known as a pilomatrix carcinoma. Like pilomatricomas, pilomatrix carcinomas have somatic mutations in the *CTNNB1* gene. It is unclear why some of these tumors are cancerous but most others are not.

Wilms tumor

Mutations in the *CTNNB1* gene have been found in Wilms tumor, a rare form of kidney cancer that occurs almost exclusively in children. These mutations are somatic and occur only in kidney cells that give rise to the tumor. *CTNNB1* gene mutations in Wilms tumor result in an overly active protein. This active beta-catenin protein promotes Wnt signaling longer than normal, which leads to the unchecked proliferation of kidney cells and tumor development.

Aldosterone-producing adenoma

Ovarian cancer

Other cancers

Somatic mutations in the *CTNNB1* gene have been identified in several other types of cancer. These include colorectal, liver, thyroid, ovarian, endometrial, and skin cancers, as well as a type of brain tumor called a medulloblastoma, among others. Studies suggest that gain-of-function mutations in the *CTNNB1* gene prevent the breakdown of beta-catenin when it is no longer needed, which allows the protein to accumulate within cells. The excess beta-catenin moves into the cell nucleus and promotes the unchecked proliferation of cells, allowing cancerous tumors to develop.

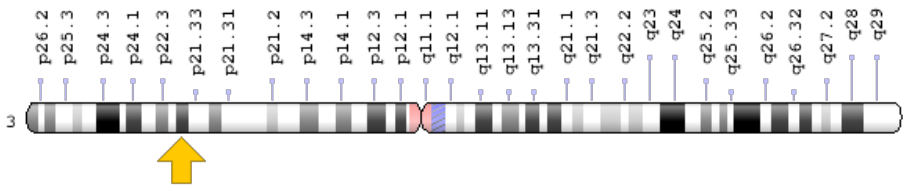
Because mutations in the *CTNNB1* gene can cause normal cells to become cancerous, *CTNNB1* belongs to a class of genes known as oncogenes. Sometimes, mutations in other oncogenes occur together with *CTNNB1* gene mutations to cause

cancer. It is not well understood why mutations in the *CTNNB1* gene are associated with several different types of cancerous and noncancerous tumors.

Chromosomal Location

Cytogenetic Location: 3p22.1, which is the short (p) arm of chromosome 3 at position 22.1

Molecular Location: base pairs 41,199,422 to 41,240,445 on chromosome 3 (Homo sapiens Updated Annotation Release 109.20190905, GRCh38.p13) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- armadillo
- beta-catenin
- catenin (cadherin-associated protein), beta 1
- catenin (cadherin-associated protein), beta 1, 88kDa
- catenin beta-1
- CTNB1_HUMAN
- CTNNB

Additional Information & Resources

Educational Resources

- Developmental Biology (sixth edition, 2000): The Wnt Pathway
  https://www.ncbi.nlm.nih.gov/books/NBK10043/#A1061
- Simons Searchlight
  https://www.simonssearchlight.org/research/what-we-study/ctnnb1/
- Wnt/β-Catenin Signaling in Vertebrate Posterior Neural Development (2010): The Wnt/β-Catenin Signaling Pathway
  https://www.ncbi.nlm.nih.gov/books/NBK53464/figure/fig1.4/

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28CTNNB1%5BTI%5D%29+OR+%28beta+catenin%5BTI%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+180+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- CATENIN, BETA-1
  http://omim.org/entry/116806
- COLORECTAL CANCER
  http://omim.org/entry/114500
- HEPATOCELLULAR CARCINOMA
  http://omim.org/entry/114550
- MEDULLOBLASTOMA
  http://omim.org/entry/155255
- OVARIAN CANCER
  http://omim.org/entry/167000

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/CTNNB1ID71.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=CTNNB1%5Bgene%5D
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:2514
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:1499
- NCBI Gene
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- UniProt
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