APC gene

APC regulator of WNT signaling pathway

Normal Function

The *APC* gene provides instructions for making the APC protein, which plays a critical role in several cellular processes. The APC protein acts as a tumor suppressor, which means that it keeps cells from growing and dividing too fast or in an uncontrolled way. It helps control how often a cell divides, how it attaches to other cells within a tissue, and whether a cell moves within or away from a tissue. This protein also helps ensure that the number of chromosomes in a cell is correct following cell division. The APC protein accomplishes these tasks mainly through association with other proteins, especially those that are involved in cell attachment and signaling.

One protein with which APC associates is beta-catenin. Beta-catenin helps control the activity (expression) of particular genes and promotes the growth and division (proliferation) of cells and the process by which cells mature to carry out specific functions (differentiation). Beta-catenin also helps cells attach to one another and is important for tissue formation. Association of APC with beta-catenin signals for beta-catenin to be broken down when it is no longer needed.

Health Conditions Related to Genetic Changes

Desmoid tumor

Several mutations in the *APC* gene have been found in people with a type of aggressive but noncancerous (benign) growth called a desmoid tumor. These rare tumors arise from connective tissue, which provides strength and flexibility to structures such as bones, ligaments, and muscles. *APC* gene mutations typically cause formation of desmoid tumors in the abdomen, but these tumors can also occur in other parts of the body. Although *APC*-related desmoid tumors are commonly associated with a form of colon cancer called familial adenomatous polyposis (described below), *APC* gene mutations can cause tumors in individuals without this inherited disease. *APC* gene mutations are found in about 10 to 15 percent of non-inherited (sporadic) desmoid tumors; these mutations are somatic, which means they are acquired during a person's lifetime and are present only in tumor cells.

Most *APC* gene mutations that cause sporadic desmoid tumors lead to an abnormally short APC protein. The shortened protein is unable to interact with the beta-catenin

protein, which prevents the breakdown of beta-catenin when it is no longer needed. Excess beta-catenin promotes uncontrolled growth and division of cells, allowing the formation of desmoid tumors.

Familial adenomatous polyposis

More than 700 mutations in the *APC* gene have been identified in families with the classic and attenuated types of familial adenomatous polyposis (FAP). Most of these mutations lead to the production of an abnormally short, nonfunctional version of the APC protein. This short protein cannot suppress the cellular overgrowth that leads to the formation of abnormal growths (polyps) in the colon, which can become cancerous. The most common mutation in FAP is a deletion of five building blocks of DNA (nucleotides) in the *APC* gene. This mutation changes the sequence of the building blocks of proteins (amino acids) in the resulting APC protein.

Although most people with FAP will develop colorectal cancer, the number of polyps and the time frame in which they become cancerous depend on the location of the mutation in the *APC* gene. The location of the mutation also determines whether an individual with FAP is predisposed to developing desmoid tumors (described above).

Primary macronodular adrenal hyperplasia

MedlinePlus Genetics provides information about Primary macronodular adrenal hyperplasia

Other cancers

Mutations in the *APC* gene are also responsible for a disorder called Turcot syndrome, which is closely related to familial adenomatous polyposis. Turcot syndrome is an association of colorectal cancer with a type of cancerous brain tumor called a medulloblastoma. Approximately two-thirds of people with Turcot syndrome have mutations in the *APC* gene.

A certain mutation in the *APC* gene (unrelated to Turcot syndrome) is found in approximately 6 percent of people with Ashkenazi (eastern and central European) Jewish heritage. This mutation replaces the amino acid isoleucine with the amino acid lysine at position 1307 in the APC protein (written as Ile1307Lys or I1307K). This change was initially thought to be harmless, but has been shown to be associated with a 10 percent to 20 percent increased risk of colon cancer.

Somatic mutations in the *APC* gene may be involved in the development of a small percentage of stomach (gastric) cancers.

Other Names for This Gene

- adenomatous polyposis coli
- APC_HUMAN
- DP2

- DP2.5
- DP3
- FAP
- FPC
- GS
- PPP1R46
- WNT signaling pathway regulator

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of APC (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=324[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28APC%5BTI%5D%29+OR+%28adenomatosis+polyposis+coli%5BTI%5D%29%29+AND+%28apc+gene%5BMAJR%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+360+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- DIFFUSE GASTRIC AND LOBULAR BREAST CANCER SYNDROME; DGLBC (https://omim.org/entry/137215)
- MISMATCH REPAIR CANCER SYNDROME 1; MMRCS1 (https://omim.org/entry/276300)
- APC REGULATOR OF WNT SIGNALING PATHWAY; APC (https://omim.org/entry/611731)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/324)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=APC[gene])

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Genomic Location

The *APC* gene is found on chromosome 5 (https://medlineplus.gov/genetics/chromosome/5/).

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