PTEN gene

phosphatase and tensin homolog

Normal Function

The *PTEN* gene provides instructions for making an enzyme that is found in almost all tissues in the body. The enzyme acts as a tumor suppressor, which means that it helps regulate cell division by keeping cells from growing and dividing too rapidly or in an uncontrolled way. The PTEN enzyme modifies other proteins and fats (lipids) by removing phosphate groups, each of which consists of three oxygen atoms and one phosphorus atom. Enzymes with this function are called phosphatases.

The PTEN enzyme is part of a chemical pathway that signals cells to stop dividing and triggers cells to self-destruct through a process called apoptosis. Evidence suggests that this enzyme also helps control cell movement (migration), the sticking (adhesion) of cells to surrounding tissues, and the formation of new blood vessels (angiogenesis). Additionally, it likely plays a role in maintaining the stability of a cell's genetic information. All of these functions help prevent uncontrolled cell growth that can lead to the formation of tumors.

Health Conditions Related to Genetic Changes

Bannayan-Riley-Ruvalcaba syndrome

More than 30 mutations in the *PTEN* gene have been found to cause Bannayan-Riley-Ruvalcaba syndrome. Common features of this condition include a large head size (macrocephaly), multiple noncancerous tumors and tumor-like growths called hamartomas, and dark freckles on the penis in males. Bannayan-Riley-Ruvalcaba syndrome is one of several related conditions that are often considered together as *PTEN* hamartoma tumor syndrome (described below).

Some of the mutations that cause Bannayan-Riley-Ruvalcaba syndrome change single DNA building blocks (base pairs) in the *PTEN* gene or insert or delete a small number of base pairs. Other mutations result in an abnormally short enzyme or reduce the amount of enzyme that is produced. In about 10 percent of cases, Bannayan-Riley-Ruvalcaba syndrome results from the deletion of a large amount of genetic material that includes part or all of the *PTEN* gene. All of these genetic changes prevent the PTEN enzyme from regulating cell proliferation effectively, which can lead to uncontrolled cell growth and the formation of hamartomas and other types of tumors. It is unclear how *PTEN* gene mutations cause macrocephaly and the other features of Bannayan-Riley-Ruvalcaba syndrome.

Cowden syndrome

Researchers have identified more than 300 mutations in the *PTEN* gene that can cause Cowden syndrome or a similar disorder called Cowden-like syndrome. These conditions are characterized by the growth of multiple hamartomas and an increased risk of developing certain cancers, particularly breast cancer, thyroid cancer, and cancer of the uterine lining (endometrial cancer). Cowden syndrome and Cowden-like syndrome are considered to be part of *PTEN* hamartoma tumor syndrome (described below).

Mutations that cause Cowden syndrome and Cowden-like syndrome include changes in a small number of base pairs and, in some cases, deletions of a larger amount of genetic material from the *PTEN* gene. These mutations lead to the production of a PTEN enzyme that does not function properly or does not work at all. The altered enzyme is unable to restrain cell division or signal abnormal cells to die, which contributes to the development of hamartomas and cancerous tumors.

Breast cancer

Inherited mutations in the *PTEN* gene increase the risk of developing breast cancer. In many cases, this increased risk occurs as part of Cowden syndrome (described above). Inherited mutations in the *PTEN* gene are thought to account for only a small fraction of all breast cancer cases.

Noninherited (somatic) *PTEN* gene mutations occur in some breast cancers in women without a family history of the disease. Somatic mutations are not inherited and do not occur as part of a familial cancer syndrome. They are acquired during a person's lifetime and occur only in certain cells in the breast. These mutations impair the tumor suppressor function of the PTEN enzyme, allowing cells to grow and divide without control or order. This uncontrolled cell growth contributes to the formation of a cancerous tumor. Studies suggest that a loss of functional PTEN enzyme is also related to poor responsiveness to a drug called trastuzumab (Herceptin), which is used to treat breast cancer.

Autism spectrum disorder

Head and neck squamous cell carcinoma

Lung cancer

Prostate cancer

Other disorders

Several related conditions caused by mutations in the *PTEN* gene, including Bannayan-Riley-Ruvalcaba syndrome and Cowden syndrome, are often considered together as *PTEN* hamartoma tumor syndrome. The mutations that cause these

conditions are present in cells throughout the body and are often inherited from a parent. Some of the mutations that cause *PTEN* hamartoma tumor syndrome lead to a defective version of the PTEN enzyme that cannot perform its function as a tumor suppressor. Other mutations prevent the *PTEN* gene from producing any enzyme at all. Without functional PTEN enzyme, cell division is not controlled effectively and damaged cells continue to divide inappropriately, leading to the development of hamartomas and other tumors.

In some published case reports, mutations in the *PTEN* gene have been associated with Proteus syndrome, a rare condition characterized by asymmetric overgrowth of the bones, skin, and other tissues. However, many researchers now believe that individuals with *PTEN* gene mutations and asymmetric overgrowth do not meet the strict guidelines for a diagnosis of Proteus syndrome. Instead, these individuals have a condition that is considered part of *PTEN* hamartoma tumor syndrome. One name that has been proposed for the condition is segmental overgrowth, lipomatosis, arteriovenous malformations, and epidermal nevus (SOLAMEN) syndrome; another is type 2 segmental Cowden syndrome. However, some scientific articles still refer to *PTEN*-related Proteus syndrome.

PTEN gene mutations have been identified in several people who have both macrocephaly and the characteristic features of autism spectrum disorder, which affects communication and social interaction. Many of these mutations change single protein building blocks (amino acids) in the PTEN enzyme or lead to the production of an abnormally short version of the enzyme. It is unknown how changes in the *PTEN* gene are related to the risk of developing autism spectrum disorder. Some of these mutations have also been reported in families with *PTEN* hamartoma tumor syndrome, and it is unclear how these mutations can cause different disorders.

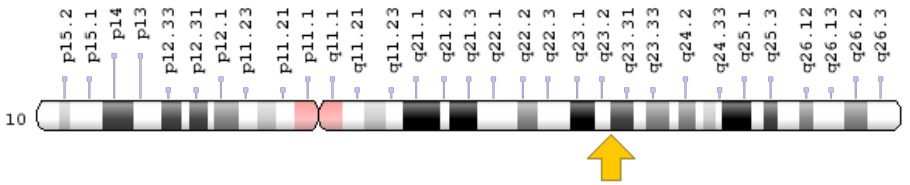
Other cancers

Somatic mutations in the *PTEN* gene are among the most common genetic changes found in human cancers. The cancers associated with somatic mutations are not inherited and do not occur as part of a cancer syndrome. Somatic mutations in the *PTEN* gene have been reported in many types of cancer, and studies suggest that *PTEN* may be the most frequently mutated gene in prostate cancer and endometrial cancer. *PTEN* gene mutations are also commonly found in brain tumors called glioblastomas and astrocytomas, and in an aggressive form of skin cancer called melanoma. Mutations in the *PTEN* gene reduce or eliminate the tumor suppressor function of the PTEN enzyme. The loss of this enzyme's function likely permits certain cells to divide uncontrollably, contributing to the growth of cancerous tumors. In some cases, the presence of *PTEN* gene mutations is associated with more advanced stages of tumor growth.

Chromosomal Location

Cytogenetic Location: 10q23.31, which is the long (q) arm of chromosome 10 at position 23.31

Molecular Location: base pairs 87,863,438 to 87,971,930 on chromosome 10 (Homo sapiens Annotation Release 109, GRCh38.p12) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- MMAC1
- mutated in multiple advanced cancers 1
- phosphatase and tensin homolog (mutated in multiple advanced cancers 1)
- phosphatase and tensin homolog deleted on chromosome 10
- protein-tyrosine phosphatase PTEN
- PTEN-MMAC1 protein
- PTEN1
- PTEN_HUMAN
- TEP1
- TEP1 phosphatase

Additional Information & Resources

Educational Resources

- Molecular Cell Biology (fourth edition, 2000): Deletion of the PTEN Phosphatase Is a Frequent Occurrence in Human Tumors
  https://www.ncbi.nlm.nih.gov/books/NBK21513/#A7132
- National Cancer Institute: Genetics of Breast and Gynecologic Cancers (PDQ)
  https://www.cancer.gov/types/breast/hp/breast-ovarian-genetics-pdq

- Simons VIP Connect: Single Gene - PTEN
  https://www.simonsvipconnect.org/index.php?option=com_content&view=article&id=571&catid=90&Itemid=492&lang=en
- The Cell: A Molecular Approach (second edition, 2000): Suppression of cell survival by PTEN
  https://www.ncbi.nlm.nih.gov/books/NBK9894/figure/A2669/

GeneReviews

- PTEN Hamartoma Tumor Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1488

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28PTEN%5BTI%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+180+days%22%5Bdp%5D

OMIM

- ENDOMETRIAL CANCER
  http://omim.org/entry/608089
- GLIOMA SUSCEPTIBILITY 1
  http://omim.org/entry/137800
- MACROCEPHALY/AUTISM SYNDROME
  http://omim.org/entry/605309
- MELANOMA, CUTANEOUS MALIGNANT, SUSCEPTIBILITY TO, 1
  http://omim.org/entry/155600
- PHOSPHATASE AND TENSIN HOMOLOG
  http://omim.org/entry/601728

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/PTENID158.html
- Cancer Genetics Web
  http://www.cancerindex.org/geneweb/PTEN.htm
- Catalogue of Somatic Mutations in Cancer: PTEN
  https://cancer.sanger.ac.uk/cosmic/gene/analysis?ln=PTEN
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=PTEN%5Bgene%5D
- HGNC Gene Family: C2 tensin-type domain containing
  https://www.genenames.org/cgi-bin/genefamilies/set/837

- HGNC Gene Family: Phosphoinositide phosphatases
  https://www.genenames.org/cgi-bin/genefamilies/set/1079
- HGNC Gene Family: PTEN protein phosphatases
  https://www.genenames.org/cgi-bin/genefamilies/set/902
- HGNC Gene Symbol Report
  https://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=9588
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/5728
- UniProt
  http://www.uniprot.org/uniprot/P60484

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