Genetics
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Your Guide to Understanding Genetic Conditions

TP53 gene
tumor protein p53

Normal Function

The TP53 gene provides instructions for making a protein called tumor protein p53 (or p53). This protein acts as a tumor suppressor, which means that it regulates cell division by keeping cells from growing and dividing (proliferating) too fast or in an uncontrolled way.

The p53 protein is located in the nucleus of cells throughout the body, where it attaches (binds) directly to DNA. When the DNA in a cell becomes damaged by agents such as toxic chemicals, radiation, or ultraviolet (UV) rays from sunlight, this protein plays a critical role in determining whether the DNA will be repaired or the damaged cell will self-destruct (undergo apoptosis). If the DNA can be repaired, p53 activates other genes to fix the damage. If the DNA cannot be repaired, this protein prevents the cell from dividing and signals it to undergo apoptosis. By stopping cells with mutated or damaged DNA from dividing, p53 helps prevent the development of tumors.

Because p53 is essential for regulating cell division and preventing tumor formation, it has been nicknamed the "guardian of the genome."

Health Conditions Related to Genetic Changes

Breast cancer

Inherited changes in the TP53 gene greatly increase the risk of developing breast cancer, as well as several other forms of cancer, as part of a rare cancer syndrome called Li-Fraumeni syndrome (described below). These mutations are thought to account for only a small fraction of all breast cancer cases.

Noninherited (somatic) mutations in the TP53 gene are much more common than inherited mutations, occurring in 20 to 40 percent of all breast cancers. These somatic mutations are acquired during a person's lifetime and are present only in cells that become cancerous. The cancers associated with somatic mutations do not occur as part of a cancer syndrome. Most of these mutations change single protein building blocks (amino acids) in the p53 protein, which reduces or eliminates the protein's tumor suppressor function. This altered p53 protein cannot regulate cell proliferation effectively. Specifically, it is unable to trigger apoptosis in cells with mutated or damaged DNA. As a result, DNA damage can accumulate in cells. Such cells may continue to divide in an uncontrolled way, leading to tumor growth.

Compared with breast cancers without TP53 gene mutations, tumors with these genetic changes tend to have a poorer prognosis. They are more likely to be
aggressive, to be resistant to treatment with certain anti-cancer drugs and radiation, and to come back (recur) after treatment.

**Bladder cancer**

Somatic TP53 gene mutations have been found in some cases of bladder cancer. Most of these mutations change single amino acids in p53. This altered p53 protein cannot regulate cell proliferation and it is unable to trigger apoptosis in cells with mutated or damaged DNA. As a result, DNA damage can accumulate in cells. Such cells may continue to divide in an uncontrolled way, leading to tumor growth. Mutations in the TP53 gene may help predict whether bladder cancer will progress and spread to nearby tissues, and whether the disease will recur after treatment.

**Cholangiocarcinoma**

**Head and neck squamous cell carcinoma**

Somatic mutations in the TP53 gene have been found in nearly half of all head and neck squamous cell carcinomas (HNSCC). This type of cancerous tumor occurs in the moist lining of the mouth, nose, and throat. Most of the TP53 gene mutations involved in HNSCC change single amino acids in p53; these changes impair the protein's function. Without functioning p53, cell proliferation is not regulated. As a result, cells accumulate DNA damage and continue to divide in an uncontrolled way, leading to tumor growth.

**Li-Fraumeni syndrome**

Although somatic mutations in the TP53 gene are found in many types of cancer, Li-Fraumeni syndrome appears to be the only cancer syndrome associated with inherited mutations in this gene. This condition greatly increases the risk of developing several types of cancer, including breast cancer; bone cancer; and cancers of soft tissues (such as muscle) called soft tissue sarcomas, particularly in children and young adults. At least 140 different mutations in the TP53 gene have been identified in individuals with Li-Fraumeni syndrome.

Many of the mutations associated with Li-Fraumeni syndrome change single amino acids in the part of the p53 protein that binds to DNA. Other mutations delete small amounts of DNA from the gene. These mutations result in an altered p53 protein that cannot regulate cell proliferation effectively and is unable to trigger apoptosis in cells with mutated or damaged DNA. As a result, DNA damage can accumulate in cells. Such cells may continue to divide in an uncontrolled way, leading to the growth of tumors.

**Lung cancer**

Somatic mutations in the TP53 gene have been found in nearly half of all lung cancer. Lung cancer is a disease in which certain cells in the lungs become abnormal
and multiply uncontrollably to form a tumor. Signs and symptoms may not occur in early stages of the disease.

Lung cancer is generally divided into two types, small cell lung cancer and non-small cell lung cancer, based on the size of the affected cells when viewed under a microscope. Small cell lung cancers nearly always have TP53 gene mutations; however, these mutations may also occur in non-small cell lung cancer. TP53 gene mutations change single amino acids in p53, which impair the protein's function. Without functioning p53, cell proliferation is not regulated effectively and DNA damage can accumulate in cells. Such cells may continue to divide in an uncontrolled way, leading to tumor growth. Additional genetic, environmental, and lifestyle factors contribute to a person's cancer risk; in lung cancer, the greatest risk factor is being a long-term tobacco smoker.

**Melanoma**

**Ovarian cancer**

Somatic TP53 gene mutations are common in ovarian cancer, occurring in almost half of ovarian tumors. These mutations result in a p53 protein that is less able to control cell proliferation. Specifically, it is unable to trigger apoptosis in cells with mutated or damaged DNA. As a result, DNA damage can accumulate in cells. Such cells may continue to divide in an uncontrolled way, leading to tumor growth.

**Wilms tumor**

**Other cancers**

Somatic mutations in the TP53 gene are the most common genetic changes found in human cancer, occurring in about half of all cancers. In addition to the cancers described above, somatic TP53 gene mutations have been identified in several types of brain tumor, colorectal cancer, liver cancer, a type of bone cancer called osteosarcoma, a cancer of muscle tissue called rhabdomyosarcoma, and a cancer called adrenocortical carcinoma that affects the outer layer of the adrenal glands (small hormone-producing glands on top of each kidney).

Most TP53 mutations change single amino acids in the p53 protein, which leads to the production of an altered version of the protein that cannot control cell proliferation and is unable to trigger apoptosis in cells with mutated or damaged DNA. As a result, DNA damage can accumulate in cells. Such cells may continue to divide in an uncontrolled way, leading to tumor growth.
Chromosomal Location

Cytogenetic Location: 17p13.1, which is the short (p) arm of chromosome 17 at position 13.1

Molecular Location: base pairs 7,668,402 to 7,687,550 on chromosome 17 (Homo sapiens Annotation Release 109, GRCh38.p12) (NCBI)

Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- antigen NY-CO-13
- cellular tumor antigen p53
- P53
- P53 tumor suppressor
- P53_HUMAN
- phosphoprotein p53
- transformation-related protein 53
- TRP53
- tumor protein p53 (Li-Fraumeni syndrome)
- tumor suppressor p53

Additional Information & Resources

Educational Resources

  https://www.ncbi.nlm.nih.gov/books/NBK26856/#A3240
  https://www.ncbi.nlm.nih.gov/books/NBK21551/#A7158
• National Cancer Institute: Genetics of Breast and Gynecologic Cancers (PDQ)  

• The TP53 Website: p53 Mutations in Lung Cancer 
http://p53.free.fr/Database/p53_cancer/p53_Lung.html

Clinical Information from GeneReviews
• Li-Fraumeni Syndrome  
https://www.ncbi.nlm.nih.gov/books/NBK1311

Scientific Articles on PubMed
• PubMed  
https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28TP53%5BTI%5D%29+OR+%28p53%5BTI%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+180+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM
• TUMOR PROTEIN p53  
http://omim.org/entry/191170

Research Resources
• Atlas of Genetics and Cytogenetics in Oncology and Haematology  
http://atlasgeneticsoncology.org/Genes/P53ID88.html

• Cancer Genetics Web: TP53  
http://www.cancerindex.org/geneweb/TP53.htm

• ClinVar  

• HGNC Gene Symbol Report  

• Monarch Initiative  
https://monarchinitiative.org/gene/NCBIGene:7157

• NCBI Gene  

• UniProt  
https://www.uniprot.org/uniprot/P04637
Sources for This Summary


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