MAPT gene
microtubule associated protein tau

Normal Function

The *MAPT* gene provides instructions for making a protein called tau. This protein is found throughout the nervous system, including in nerve cells (neurons) in the brain. It is involved in assembling and stabilizing microtubules, which are rigid, hollow fibers that make up the cell's structural framework (the cytoskeleton). Microtubules help cells maintain their shape, assist in the process of cell division, and are essential for the transport of materials within cells.

Six different versions (isoforms) of the tau protein are produced in the adult brain. The isoforms vary in length from 352 to 441 protein building blocks (amino acids). A region of the protein called the microtubule-binding domain, which is the part of the protein that attaches (binds) to microtubules, also varies among the isoforms. In three of the isoforms, the microtubule-binding domain contains three repeated segments. In the other three isoforms, this domain contains four repeated segments. Typically, the brain has approximately the same amount of three-repeat isoforms and four-repeat isoforms. This balance appears to be essential for the normal function of neurons.

Health Conditions Related to Genetic Changes

Frontotemporal dementia with parkinsonism-17

More than 40 mutations in the *MAPT* gene have been found to cause frontotemporal dementia with parkinsonism-17 (FTDP-17). Some of these mutations change single amino acids in the tau protein, most often in the microtubule-binding region. These mutations reduce tau's ability to bind to microtubules, which disrupts many important cell functions.

Other *MAPT* gene mutations change the way the gene's instructions are used to build the tau protein. Most of these mutations increase the production of tau with four repeated segments compared to the production of tau with three repeated segments. The resulting imbalance of tau isoforms in the brain interferes with the normal functions of brain cells.

In ways that are not fully understood, the *MAPT* gene mutations responsible for FTDP-17 lead to an accumulation of abnormal tau in neurons and other brain cells. These clumps of defective tau build up over time, although it is unclear what effect they have on cell function and survival. FTDP-17 is characterized by the gradual death of cells in areas of the brain called the frontal and temporal lobes. The frontal lobes are involved in reasoning, planning, judgment, and problem-solving, while the temporal lobes help process hearing, speech, memory, and emotion. The loss of cells
in these brain regions leads to the major features of FTDP-17, including changes in 
personality and behavior, speech and language abnormalities, and problems with 
movement.

Progressive supranuclear palsy

Several mutations in the MAPT gene have been found to cause progressive 
supranuclear palsy. However, mutations in this gene appear to be a rare cause of this 
disorder.

At least one normal variation (polymorphism) in the MAPT gene has been 
associated with an increased risk of developing progressive supranuclear palsy. This 
polymorphism, known as the H1 haplotype, is found much more frequently in people 
with progressive supranuclear palsy than in the general population. It is unclear 
exactly how this genetic variation increases the risk of developing this disease.

The features of progressive supranuclear palsy appear to be related to abnormalities 
in the tau protein. In people with MAPT gene mutations, genetic changes disrupt 
the protein's normal structure and function. However, abnormal tau is also found 
in people without MAPT gene mutations. The defective tau protein assembles into 
abnormal clumps within neurons and other brain cells, although it is unclear what 
effect these clumps have on cell function and survival. Progressive supranuclear 
palsy is characterized by the gradual death of brain cells, particularly in structures 
deep within the brain that are essential for coordinating movement. This loss of 
brain cells underlies the major features of progressive supranuclear palsy, including 
problems with movement, vision, speech, and thinking (cognition).

Idiopathic pulmonary fibrosis

Other disorders

Mutations in the MAPT gene have also been found to cause other brain disorders 
similar to FTDP-17 and progressive supranuclear palsy. These disorders include 
corticobasal degeneration, tauopathy with respiratory failure, and a form of dementia 
with seizures (epilepsy). Although these conditions have somewhat different patterns 
of signs and symptoms, they all involve changes in personality, behavior, or cognition 
and problems with movement. The MAPT gene mutations responsible for these 
disorders lead to a buildup of abnormal tau in brain cells. Although the effect of 
tau accumulation on cell function and survival is unknown, these disorders are 
characterized by the death of brain cells in regions of the brain essential for cognition, 
emotion, and coordinating movement.

Because all of these diseases are characterized by an abnormal buildup of tau in 
the brain, they are known as tauopathies. Some researchers suggest that, instead of 
being described as separate disorders, the group of tauopathies caused by mutations 
in the MAPT gene should be considered as part of a spectrum with varying signs and 
symptoms.
Chromosomal Location

Cytogenetic Location: 17q21.31, which is the long (q) arm of chromosome 17 at position 21.31

Molecular Location: base pairs 45,894,382 to 46,028,334 on chromosome 17 (Homo sapiens Updated Annotation Release 109.20200522, GRCh38.p13) (NCBI)

Credit: Genome Decoration Page/NCBI

Other Names for This Gene

• DDPAC
• FLJ31424
• FTDP-17
• G protein beta1/gamma2 subunit-interacting factor 1
• MAPTL
• MGC138549
• microtubule-associated protein tau
• MSTD
• MTBT1
• MTBT2
• neurofibrillary tangle protein
• paired helical filament-tau
• PHF-tau
• PPND
• PPP1R103
• TAU
• TAU_HUMAN
Additional Information & Resources

Educational Resources

• Basic Neurochemistry (sixth edition, 1999): Microtubules Act as Both Dynamic Structural Elements and Tracks for Organelle Traffic

  https://www.ncbi.nlm.nih.gov/books/NBK9932/

Scientific Articles on PubMed

• PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28MAPT%5BTI%5D%29+OR+%28microtubule-associated+protein+tau%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+1800+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

• FRONTOTEMPORAL DEMENTIA
  http://omim.org/entry/600274

• MICROTUBULE-ASSOCIATED PROTEIN TAU
  http://omim.org/entry/157140

Research Resources

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

• ClinVar

• HGNC Gene Symbol Report

• Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:4137

• NCBI Gene

• UniProt
  https://www.uniprot.org/uniprot/P10636
Sources for This Summary


Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10983715

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