

APP gene

amyloid beta precursor protein

Normal Function

The *APP* gene provides instructions for making a protein called amyloid precursor protein. This protein is found in many tissues and organs, including the brain and spinal cord (central nervous system). Little is known about the function of amyloid precursor protein. Researchers speculate that it may bind to other proteins on the surface of cells or help cells attach to one another. Studies suggest that in the brain, it helps direct the movement (migration) of nerve cells (neurons) during early development.

Amyloid precursor protein is cut by enzymes to create smaller fragments (peptides), some of which are released outside the cell. Two of these fragments are called soluble amyloid precursor protein (sAPP) and amyloid beta (β) peptide. Recent evidence suggests that sAPP has growth-promoting properties and may play a role in the formation of neurons in the brain both before and after birth. The sAPP peptide may also control the function of certain other proteins by turning off (inhibiting) their activity. Amyloid β peptide is likely involved in the ability of neurons to change and adapt over time (plasticity). Other functions of sAPP and amyloid β peptide are under investigation.

Health Conditions Related to Genetic Changes

Alzheimer's disease

Many variants (also called mutations) in the *APP* gene can cause early-onset Alzheimer's disease, which begins before age 65. These variants are responsible for less than 10 percent of all early-onset cases of Alzheimer's disease.

The most common *APP* gene variant changes one of the protein building blocks (amino acids) in the amyloid precursor protein. This variant replaces the amino acid valine with the amino acid isoleucine at protein position 717 (written as Val717Ile or V717I). Variants in the *APP* gene can lead to an increased amount of the amyloid β peptide or to the production of a slightly longer and stickier form of the peptide. When these protein fragments are released from the cell, they can accumulate in the brain and form clumps called amyloid plaques. These plaques are characteristic of Alzheimer's disease. A buildup of toxic amyloid β peptide and amyloid plaques may lead to the death of neurons and the progressive signs and symptoms of Alzheimer's disease.

Hereditary cerebral amyloid angiopathy

Variants in the *APP* gene have been found to cause hereditary cerebral amyloid angiopathy, a condition characterized by stroke and a decline in intellectual function (dementia), which begins in mid-adulthood. These variants change single amino acids in the amyloid precursor protein. Each of these variants causes a different type of the condition. The Dutch type, the most common of all the types, is caused by the replacement of the amino acid glutamic acid with the amino acid glutamine at position 22 in the protein sequence (written as Glu22Gln or E22Q). The Italian type and Arctic type are also caused by changes to glutamic acid at position 22. In the Italian type, glutamic acid is replaced with the amino acid lysine (written as Glu22Lys or E22K) and in the Arctic type, glutamic acid is replaced with the amino acid glycine (written as Glu22Gly or E22G). The Flemish type is caused by replacement of the amino acid alanine with glycine at position 21 (written as Ala21Gly or A21G). In the Iowa type, the amino acid aspartic acid is switched with the amino acid asparagine at position 23 (written as Asp23Asn or D23N). The Piedmont type of hereditary cerebral amyloid angiopathy is caused by the replacement of the amino acid leucine at position 34 with the amino acid valine (written as Leu34Val or L34V).

The result of all of these variants is the production of an amyloid β peptide that is more prone to cluster together (aggregate) than the normal peptide. The aggregated protein forms amyloid deposits that accumulate in the blood vessels of the brain. The amyloid deposits replace the muscle fibers and elastic fibers that give blood vessels flexibility, causing the blood vessels to become weak and prone to breakage. In the brain, such a break causes bleeding (hemorrhagic stroke), which can lead to brain damage and dementia or be life-threatening. Amyloid deposits in specific parts of the brain can interfere with normal brain function, leading to dementia, seizures, movement problems, and other neurological features in some people with hereditary cerebral amyloid angiopathy.

Other Names for This Gene

- A4_HUMAN
- AAA
- ABETA
- ABPP
- AD1
- amyloid beta (A4) precursor protein
- amyloid beta-peptide
- amyloid beta-protein precursor
- amyloid precursor protein
- APPI
- cerebral vascular amyloid peptide
- CVAP

- PN-II
- PN2
- protease nexin 2
- protease nexin-II

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of APP ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=351\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=351[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28APP%5BTI%5D%29+OR+%28amyloid+beta+++precursor+protein%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+1080+days%22%5Bdp%5D%29>)

Catalog of Genes and Diseases from OMIM

- AMYLOID BETA A4 PRECURSOR PROTEIN; APP (<https://omim.org/entry/104760>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/351>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=APP\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=APP[gene]))

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Genomic Location

The *APP* gene is found on chromosome 21 (<https://medlineplus.gov/genetics/chromosome/21/>).

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