



TTR gene

transthyretin

Normal Function

The *TTR* gene provides instructions for producing a protein called transthyretin. This protein transports vitamin A (retinol) and a hormone called thyroxine throughout the body. To transport thyroxine, four transthyretin proteins must be attached (bound) to each other to form a four-protein unit (tetramer). To transport retinol, transthyretin must form a tetramer and also bind to retinol binding protein. Transthyretin is produced primarily in the liver. A small amount of this protein is produced in an area of the brain called the choroid plexus and in the light-sensitive tissue that lines the back of the eye (the retina).

Health Conditions Related to Genetic Changes

Transthyretin amyloidosis

More than 100 mutations in the *TTR* gene have been found to cause transthyretin amyloidosis. Nearly all of these mutations change one protein building block (amino acid) in the transthyretin protein. The most common mutation found in people with transthyretin amyloidosis replaces the amino acid valine with the amino acid methionine at position 30 in the transthyretin protein (written as Val30Met or V30M). This mutation is seen most commonly in the Portuguese and Swedish populations, although it is found in affected people worldwide. Another common mutation replaces the amino acid valine with the amino acid isoleucine at position 122 in the transthyretin protein (written as Val122Ile or V122I). It is estimated that 3 percent to 3.9 percent of African Americans and 5 percent of some West African populations have this mutation.

Most of the *TTR* gene mutations that cause transthyretin amyloidosis are thought to alter the structure of transthyretin, impairing its ability to bind to other transthyretin proteins and altering its normal function.

Carpal tunnel syndrome

Other disorders

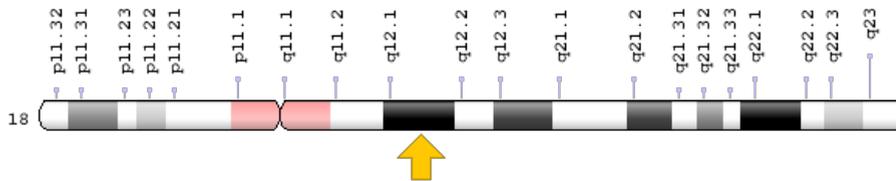
In older adults, deposits of transthyretin protein cause a condition called senile systemic amyloidosis. People with this condition do not have a mutation in the *TTR* gene; for reasons that are unclear, the transthyretin protein abnormally begins to form protein deposits. The most common place for amyloidosis in people with this condition is the heart, causing slowly progressive heart failure. Other sites of

amyloidosis may include the lungs, blood vessels, and kidneys. It is estimated that 10 percent to 25 percent of people older than 80 have senile systemic amyloidosis.

Chromosomal Location

Cytogenetic Location: 18q12.1, which is the long (q) arm of chromosome 18 at position 12.1

Molecular Location: base pairs 31,591,767 to 31,599,024 on chromosome 18 (Homo sapiens Updated Annotation Release 109.20190607, GRCh38.p13) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- ATTR
- PALB
- prealbumin, amyloidosis type I
- TBPA
- TTHY_HUMAN

Additional Information & Resources

Educational Resources

- Neuromuscular Disease Center, Washington University
<https://neuromuscular.wustl.edu/nother/amyloid.htm#transthyretin>

Clinical Information from GeneReviews

- Hereditary Transthyretin Amyloidosis
<https://www.ncbi.nlm.nih.gov/books/NBK1194>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28TTR%5BTI%5D%29+OR+%28transthyretin%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+720+days%22%5Bdp%5D>

Catalog of Genes and Diseases from OMIM

- TRANSTHYRETIN
<http://omim.org/entry/176300>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
http://atlasgeneticsoncology.org/Genes/GC_TTR.html
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=TTR%5Bgene%5D>
- HGNC Gene Symbol Report
https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:12405
- Monarch Initiative
<https://monarchinitiative.org/gene/NCBIGene:7276>
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/7276>
- UniProt
<https://www.uniprot.org/uniprot/P02766>

Sources for This Summary

- Benson MD, Kincaid JC. The molecular biology and clinical features of amyloid neuropathy. *Muscle Nerve*. 2007 Oct;36(4):411-23. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/17554795>
- Buxbaum J, Koziol J, Connors LH. Serum transthyretin levels in senile systemic amyloidosis: effects of age, gender and ethnicity. *Amyloid*. 2008 Dec;15(4):255-61. doi: 10.1080/13506120802525285.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/19065297>
- Hou X, Aguilar MI, Small DH. Transthyretin and familial amyloidotic polyneuropathy. Recent progress in understanding the molecular mechanism of neurodegeneration. *FEBS J*. 2007 Apr; 274(7):1637-50. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/17381508>
- Saraiva MJ. Hereditary transthyretin amyloidosis: molecular basis and therapeutical strategies. *Expert Rev Mol Med*. 2002 May 14;4(12):1-11. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/14987380>
- OMIM: TRANSTHYRETIN
<http://omim.org/entry/176300>
- Wiseman RL, Powers ET, Kelly JW. Partitioning conformational intermediates between competing refolding and aggregation pathways: insights into transthyretin amyloid disease. *Biochemistry*. 2005 Dec 20;44(50):16612-23.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16342952>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2532856/>

Reprinted from Genetics Home Reference:
<https://ghr.nlm.nih.gov/gene/TTR>

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