TTR Gene

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Transthyretin

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1. 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).

2. Health Conditions Related to Genetic Changes

2.1. 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.

2.2. Carpal tunnel syndrome

2.3. 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.

3. Other Names for This Gene

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

References

1. 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
2. Buxbaum J, Koziol J, Connors LH. Serum transthyretin levels in senile systemicamyloidosis: effects of age, gender and ethnicity. Amyloid. 2008Dec;15(4):255-61. doi: 10.1080/13506120802525285. Citation on PubMed
3. Hou X, Aguilar MI, Small DH. Transthyretin and familial amyloidoticpolyneuropathy. Recent progress in understanding t he molecular mechanism ofneurodegeneration. FEBS J. 2007 Apr;274(7):1637-50. Review. Citation on PubMed
4. Saraiva MJ. Hereditary transthyretin amyloidosis: molecular basis andtherapeutical strategies. Expert Rev Mol Med. 20 02 May 14;4(12):1-11. doi:10.1017/S1462399402004647. Review. Citation on PubMed
5. Wiseman RL, Powers ET, Kelly JW. Partitioning conformational intermediatesbetween competing refolding and aggreg ation pathways: insights into transthyretinamyloid disease. Biochemistry. 2005 Dec 20;44(50):16612-23. Citation on Pu bMed or Free article on PubMed Central

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