

HTT gene

huntingtin

Normal Function

The *HTT* gene provides instructions for making a protein called huntingtin. Although the exact function of this protein is unknown, it appears to play an important role in nerve cells (neurons) in the brain and is essential for normal development before birth. Huntingtin is found in many of the body's tissues, with the highest levels of activity in the brain. Within cells, this protein may be involved in chemical signaling, transporting materials, attaching (binding) to proteins and other structures, and protecting the cell from self-destruction (apoptosis). Some studies suggest it plays a role in repairing damaged DNA.

One region of the *HTT* gene contains a particular DNA segment known as a CAG trinucleotide repeat. This segment is made up of a series of three DNA building blocks (cytosine, adenine, and guanine) that appear multiple times in a row. Normally, the CAG segment is repeated 10 to 35 times within the gene.

Health Conditions Related to Genetic Changes

Huntington's disease

The inherited variant (also called mutation) that causes Huntington's disease is known as a CAG trinucleotide repeat expansion. This variant increases the size of the CAG segment in the *HTT* gene. People with Huntington's disease have 36 to more than 120 CAG repeats. People with 36 to 39 CAG repeats may or may not develop the signs and symptoms of Huntington's disease, while people with 40 or more repeats almost always develop the disorder.

The expanded CAG segment leads to the production of an abnormally long version of the huntingtin protein. The elongated protein is cut into smaller, toxic fragments that bind together and accumulate in neurons, disrupting the normal functions of these cells. It has also been suggested that loss of the huntingtin protein's DNA repair function may result in the accumulation of DNA damage in neurons, particularly as damaging molecules increase during aging. Regions of the brain that help coordinate movement and control thinking and emotions (the striatum and cerebral cortex) are particularly affected. The dysfunction and eventual death of neurons in these areas of the brain underlie the signs and symptoms of Huntington's disease.

As the altered *HTT* gene is passed from one generation to the next, the size of the CAG trinucleotide repeat often increases in size. A larger number of repeats is usually associated with an earlier onset of signs and symptoms. This phenomenon is called anticipation. People with the adult-onset form of Huntington's disease (which appears in mid-adulthood) typically have 40 to 50 CAG repeats in the *HTT* gene, while people with the less common, juvenile form of the disorder (which appears in childhood or adolescence) tend to have more than 60 CAG repeats.

Individuals who have 27 to 35 CAG repeats in the *HTT* gene do not develop Huntington's disease, but they are at risk of having children who will develop the disorder. As the gene is passed from parent to child, the size of the CAG trinucleotide repeat may lengthen into the range associated with Huntington's disease (36 repeats or more).

Other Names for This Gene

- HD
- HD_HUMAN
- huntingtin (Huntington disease)
- Huntington's disease protein
- IT15

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of HTT ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=3064\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=3064[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28HD%5BTI%5D%29+OR+%28huntingtin%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

- HUNTINGTIN; HTT (<https://omim.org/entry/613004>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/3064>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=HTT\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=HTT[gene]))

References

- Bates G. Huntingtin aggregation and toxicity in Huntington's disease. *Lancet*. 2003 May 10;361(9369):1642-4. doi: 10.1016/S0140-6736(03)13304-1. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12747895>)
- Borrell-Pages M, Zala D, Humbert S, Saudou F. Huntington's disease: from huntingtin function and dysfunction to therapeutic strategies. *Cell Mol Life Sci*. 2006 Nov;63(22):2642-60. doi: 10.1007/s00018-006-6242-0. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/17041811>)
- Cattaneo E. Dysfunction of wild-type huntingtin in Huntington disease. *News Physiol Sci*. 2003 Feb;18:34-7. doi: 10.1152/nips.01410.2002. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12531930>)
- Gardian G, Vecsei L. Huntington's disease: pathomechanism and therapeutic perspectives. *J Neural Transm (Vienna)*. 2004 Oct;111(10-11):1485-94. doi:10.1007/s00702-004-0201-4. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15480847>)
- Imarisio S, Carmichael J, Korolchuk V, Chen CW, Saiki S, Rose C, Krishna G, Davies JE, Ttofi E, Underwood BR, Rubinsztein DC. Huntington's disease: from pathology and genetics to potential therapies. *Biochem J*. 2008 Jun 1;412(2):191-209. doi: 10.1042/BJ20071619. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/18466116>)
- Jones L, Hughes A. Pathogenic mechanisms in Huntington's disease. *Int Rev Neurobiol*. 2011;98:373-418. doi: 10.1016/B978-0-12-381328-2.00015-8. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/21907095>)
- Landles C, Bates GP. Huntingtin and the molecular pathogenesis of Huntington's disease. Fourth in molecular medicine review series. *EMBO Rep*. 2004 Oct;5(10):958-63. doi: 10.1038/sj.embor.7400250. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15459747>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1299150/>)
- Li SH, Li XJ. Huntingtin and its role in neuronal degeneration. *Neuroscientist*. 2004 Oct;10(5):467-75. doi: 10.1177/1073858404266777. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15359012>)
- MacDonald ME. Huntingtin: alive and well and working in middle management. *SciSTKE*. 2003 Nov 4;2003(207):pe48. doi: 10.1126/stke.2003.207.pe48. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/14600292>)
- Maiuri T, Mocle AJ, Hung CL, Xia J, van Roon-Mom WM, Truant R. Huntingtin is a scaffolding protein in the ATM oxidative DNA damage response complex. *Hum Mol Genet*. 2017 Jan 15;26(2):395-406. doi: 10.1093/hmg/ddw395. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/28017939>)
- Rangone H, Humbert S, Saudou F. Huntington's disease: how does huntingtin, an anti-apoptotic protein, become toxic? *Pathol Biol (Paris)*. 2004 Jul;52(6):338-42. doi: 10.1016/j.patbio.2003.06.004. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15261377>)
- Slow EJ, Graham RK, Hayden MR. To be or not to be toxic: aggregations

inHuntington and Alzheimer disease. Trends Genet. 2006 Aug;22(8):408-11. doi:10.1016/j.tig.2006.05.008. Epub 2006 Jun 27. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16806565>)

- van Dellen A, Grote HE, Hannan AJ. Gene-environment interactions, neuronal dysfunction and pathological plasticity in Huntington's disease. Clin Exp Pharmacol Physiol. 2005 Dec;32(12):1007-19. doi:10.1111/j.1440-1681.2005.04313.x. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16445565>)
- Young AB. Huntingtin in health and disease. J Clin Invest. 2003 Feb;111(3):299-302. doi: 10.1172/JCI17742. No abstract available. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12569151>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC151871/>)

Genomic Location

The *HTT* gene is found on chromosome 4 (<https://medlineplus.gov/genetics/chromosome/4/>).

Last updated July 1, 2020