

THAP1 Gene

Subjects: **Genetics & Heredity**

Contributor: Rui Liu

THAP domain containing 1: The THAP1 gene provides instructions for making a protein that is a transcription factor, which means that it attaches (binds) to specific regions of DNA and regulates the activity of other genes.

genes

1. Normal Function

The *THAP1* gene provides instructions for making a protein that is a transcription factor, which means that it attaches (binds) to specific regions of DNA and regulates the activity of other genes. Through this function, it is thought to help control several processes in the body, including the growth and division (proliferation) of endothelial cells, which line the inside surface of blood vessels and other circulatory system structures called lymphatic vessels. The THAP1 protein also plays a role in the self-destruction of cells that are no longer needed (apoptosis).

2. Health Conditions Related to Genetic Changes

2.1. Dystonia 6

More than 70 *THAP1* gene mutations have been identified in people with dystonia 6. Dystonia 6 is one of many forms of dystonia, which is a group of conditions characterized by involuntary movements, twisting (torsion) and tensing of various muscles, and unusual positioning of affected body parts.

Most of the *THAP1* gene mutations that cause dystonia 6 change single protein building blocks (amino acids) in the THAP1 protein or result in a premature stop signal that leads to an abnormally short protein. Studies indicate that many of the mutations affect the stability of the THAP1 protein, reducing the amount of functional THAP1 protein available for DNA binding. Others may impair the protein's ability to bind with the correct regions of DNA. Problems with DNA binding likely disrupt the proper regulation of gene activity, leading to the signs and symptoms of dystonia 6.

A particular *THAP1* gene mutation is specific to a Mennonite population in the Midwestern United States in which dystonia 6 was first described. This mutation changes the DNA sequence in a region of the gene known as exon 2. Some researchers use the term DYT6 dystonia to refer to dystonia caused by this particular mutation, and the broader term THAP1 dystonia to refer to dystonia caused by any *THAP1* gene mutation. In general, mutations

affecting the region of the THAP1 protein that binds to DNA, including the mutation found in the Mennonite population, tend to result in more severe signs and symptoms than mutations affecting other regions of the protein.

3. Other Names for This Gene

- 4833431A01Rik
- DYT6
- FLJ10477
- nuclear proapoptotic factor
- THAP domain containing, apoptosis associated protein 1
- THAP domain protein 1
- THAP domain-containing protein 1
- THAP1_HUMAN

References

1. Blanchard A, Ea V, Roubertie A, Martin M, Coquart C, Claustres M, Bérout C, Collod-Bérout G. DYT6 dystonia: review of the literature and creation of the UMD Locus-Specific Database (LSDB) for mutations in the THAP1 gene. *Hum Mutat.* 2011Nov;32(11):1213-24. doi: 10.1002/humu.21564.
2. Bressman SB, Raymond D, Fuchs T, Heiman GA, Ozelius LJ, Saunders-Pullman R. Mutations in THAP1 (DYT6) in early-onset dystonia: a genetic screening study. *Lancet Neurol.* 2009 May;8(5):441-6. doi: 10.1016/S1474-4422(09)70081-X.
3. Campagne S, Muller I, Milon A, Gervais V. Towards the classification of DYT6 dystonia mutants in the DNA-binding domain of THAP1. *Nucleic Acids Res.* 2012Oct;40(19):9927-40. doi: 10.1093/nar/gks703.
4. Cheng FB, Ozelius LJ, Wan XH, Feng JC, Ma LY, Yang YM, Wang L. THAP1/DYT6 sequence variants in non-DYT1 early-onset primary dystonia in China and their effects on RNA expression. *J Neurol.* 2012 Feb;259(2):342-7. doi:10.1007/s00415-011-6196-5.
5. Djarmati A, Schneider SA, Lohmann K, Winkler S, Pawlack H, Hagenah J, Brüggemann N, Zittel S, Fuchs T, Raković A, Schmidt A, Jabusch HC, Wilcox R, Kostić VS, Siebner H, Altenmüller E, Münchau A, Ozelius LJ, Klein C. Mutations in THAP1 (DYT6) and generalised dystonia with prominent spasmodic dysphonia: a genetic screening study. *Lancet Neurol.* 2009 May;8(5):447-52. doi:10.1016/S1474-4422(09)70083-3.
6. Houlden H, Schneider SA, Paudel R, Melchers A, Schwingenschuh P, Edwards M, Hardy J, Bhatia KP. THAP1 mutations (DYT6) are an additional cause of early-onset dystonia. *Neurology.* 2010 Mar 9;74(10):846-50. doi: 10.1212/WNL.0b013e3181d5276d.

7. LeDoux MS, Xiao J, Rudzińska M, Bastian RW, Wszolek ZK, Van Gerpen JA, Puschmann A, Momčilović D, Vemula SR, Zhao Y. Genotype-phenotype correlations in THAP1 dystonia: molecular foundations and description of new cases. *Parkinsonism Relat Disord*. 2012 Jun;18(5):414-25. doi: 10.1016/j.parkreldis.2012.02.001.
 8. Xiomerisiou G, Houlden H, Scarneas N, Stamelou M, Kara E, Hardy J, Lees AJ, Korlipara P, Limousin P, Paudel R, Hadjigeorgiou GM, Bhatia KP. THAP1 mutations and dystonia phenotypes: genotype phenotype correlations. *Mov Disord*. 2012 Sep;27(10):1290-4. doi: 10.1002/mds.25146.
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