SPAST gene

spastin

Normal Function

The *SPAST* gene provides instructions for producing a protein called spastin, which is a member of the AAA protein family. This protein family plays a role in many cellular activities, including regulation of cell components and proteins. Spastin is found throughout the body, particularly in certain nerve cells (neurons). The spastin protein plays a role in the function of microtubules, which are rigid, hollow fibers that make up the cell's structural framework (the cytoskeleton). Microtubules are also involved in transporting cell compartments (organelles) and facilitating cell division. Spastin likely helps regulate microtubule length and disassemble microtubule structures when they are no longer needed.

Health Conditions Related to Genetic Changes

Spastic paraplegia type 4

Several hundred mutations in the *SPAST* gene have been found to cause spastic paraplegia type 4. This condition is characterized by muscle weakness, progressive muscle stiffness (spasticity) in the legs, and difficulty walking. Most of these mutations alter the structure or disrupt the production of spastin, impairing its ability to regulate microtubules. The inability of the microtubules to transport organelles, especially in nerve cells, is thought to contribute to the major signs and symptoms of spastic paraplegia type 4.

Mutation in the *SPAST* gene account for approximately 40 percent of autosomal dominant hereditary spastic paraplegias.

Other Names for This Gene

- ADPSP
- FSP2
- KIAA1083
- SPAST_HUMAN
- spastic paraplegia 4 (autosomal dominant; spastin)
- SPG4

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of SPAST (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=6683[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28SPAST%5BTIAB%5D%29+OR+%28spastin%5BTIAB%5D%29+OR+%28SPG4%5BTIAB%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)

Catalog of Genes and Diseases from OMIM

- SPASTIN; SPAST (https://omim.org/entry/604277)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/6683)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=SPAST[gene])

References

- Blackstone C. Hereditary spastic paraplegia. Handb Clin Neurol.2018;148:633-652. doi: 10.1016/B978-0-444-64076-5.00041-7. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/29478605)
- Claudiani P, Riano E, Errico A, Andolfi G, Rugarli EI. Spastin subcellularlocalization is regulated through usage of different translation start sites andactive export from the nucleus. Exp Cell Res. 2005 Oct 1;309(2):358-69. doi:10.1016/j.yexcr.2005.06.009. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16026783)
- Kuo YW, Trottier O, Mahamdeh M, Howard J. Spastin is a dual-function enzymethat severs microtubules and promotes their regrowth to increase the number andmass of microtubules. Proc Natl Acad Sci U S A. 2019 Mar 19;116(12):5533-5541.doi: 10.1073/pnas.1818824116. Epub 2019 Mar 5. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/30837315) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6431158/)
- McNally FJ, Roll-Mecak A. Microtubule-severing enzymes: From cellularfunctions to molecular mechanism. J Cell Biol. 2018 Dec 3;217(12):4057-4069. doi:10.1083/jcb.201612104. Epub 2018 Oct 29. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/30373906) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6279391/)

- Roll-Mecak A, Vale RD. Structural basis of microtubule severing by thehereditary spastic paraplegia protein spastin. Nature. 2008 Jan17;451(7176):363-7. doi: 10.1038/nature06482. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18202664) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2882799/)
- Sandate CR, Szyk A, Zehr EA, Lander GC, Roll-Mecak A. An allosteric network inspastin couples multiple activities required for microtubule severing. Nat StructMol Biol. 2019 Aug;26(8):671-678. doi: 10.1038/s41594-019-0257-3. Epub 2019 Jul8. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/31285604) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6761829/)

Genomic Location

The *SPAST* gene is found on chromosome 2 (https://medlineplus.gov/genetics/chromosome/2/).

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