

## ATL1 gene

atlastin GTPase 1

### **Normal Function**

The *ATL1* gene provides instructions for producing a protein called atlastin-1. Atlastin-1 is produced primarily in the brain and spinal cord (central nervous system), particularly in nerve cells (neurons) that extend down the spinal cord (corticospinal tracts). These neurons send electrical signals that lead to voluntary muscle movement. In neurons, this protein is found mainly in the endoplasmic reticulum, which is a structure involved in protein processing and distribution. Atlastin-1 fuses together the network of tubules that make up the structure of the endoplasmic reticulum. Atlastin-1 is also active in compartments called axonal growth cones, which are located at the tip of neurons. The axonal growth cones direct the growth of specialized extensions, called axons, which transmit nerve impulses that signal muscle movement. Within axonal growth cones, atlastin-1 acts during development to help guide the growth of axons.

### **Health Conditions Related to Genetic Changes**

### Spastic paraplegia type 3A

Approximately 60 mutations in the *ATL1* gene have been found to cause spastic paraplegia type 3A. This condition is characterized by muscle stiffness (spasticity) and weakness of the lower limbs (paraplegia), which begin in childhood. Most of the mutations that cause spastic paraplegia type 3A change one protein building block (amino acid) in the atlastin-1 protein. These mutations likely lead to abnormal activity of atlastin-1, which impairs the functioning of neurons, including the distribution of materials within these cells. This lack of functional atlastin-1 protein can also restrict the growth of axons. Within the long neurons of the corticospinal tracts, these problems can lead to cell death. As a result, the neurons are unable to transmit nerve impulses, particularly to other neurons and muscles in the lower extremities. This impaired nerve function leads to the signs and symptoms of spastic paraplegia type 3A.

### Other disorders

Mutations in the *ATL1* gene have been found to cause a condition called hereditary sensory neuropathy type ID. This condition is characterized by nerve abnormalities in the legs and feet (peripheral neuropathy). Many people with this condition experience prickling or tingling sensations (paresthesias), absent reflexes, weakness, and a

reduced ability to feel pain. Affected individuals often get open sores (ulcers) on their feet, and because they cannot feel the pain of these sores, they may not seek immediate treatment. Without treatment, the ulcers can become infected and may require amputation of the surrounding area.

At least four *ATL1* gene mutations have been found to cause hereditary sensory neuropathy type ID. These mutations impair nerve cell function and decrease transmission of nerve impulses, similar to the effects of *ATL1* gene mutations that cause spastic paraplegia type 3A (described above). It is unclear why some *ATL1* gene mutations cause hereditary sensory neuropathy type ID and others cause spastic paraplegia type 3A.

### Other Names for This Gene

- AD-FSP
- ATLA1\_HUMAN
- atlastin
- atlastin1
- FSP1
- GBP3
- guanylate-binding protein 3

### **Additional Information & Resources**

### Tests Listed in the Genetic Testing Registry

Tests of ATL1 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=51062[geneid])

### Scientific Articles on PubMed

PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28SPG3A%5BTIAB%5D%29+OR+%28atlastin%5BTIAB%5D%29+OR+%28ATL1%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D)

### Catalog of Genes and Diseases from OMIM

- ATLASTIN GTPase 1; ATL1 (https://omim.org/entry/606439)
- NEUROPATHY, HEREDITARY SENSORY, TYPE ID; HSN1D (https://omim.org/entry/613708)

### Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/51062)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=ATL1[gene])

### References

- Byrnes LJ, Sondermann H. Structural basis for the nucleotide-dependentdimerization of the large G protein atlastin-1/SPG3A. Proc Natl Acad Sci U S A.2011 Feb 8;108(6):2216-21. doi: 10.1073/pnas.1012792108. Epub 2011 Jan 10. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21220294) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3038741/)
- Ivanova N, Claeys KG, Deconinck T, Litvinenko I, Jordanova A, Auer-Grumbach M, Haberlova J, Lofgren A, Smeyers G, Nelis E, Mercelis R, Plecko B, Priller J, Zamecnik J, Ceulemans B, Erichsen AK, Bjorck E, Nicholson G, Sereda MW, Seeman P,Kremensky I, Mitev V, De Jonghe P. Hereditary spastic paraplegia 3A associatedwith axonal neuropathy. Arch Neurol. 2007 May;64(5):706-13. doi:10. 1001/archneur.64.5.706. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/1750 2470)
- Leonardis L, Auer-Grumbach M, Papic L, Zidar J. The N355K atlastin 1 mutationis associated with hereditary sensory neuropathy and pyramidal tract features. Eur J Neurol. 2012 Jul;19(7):992-8. doi: 10.1111/j.1468-1331.2012.03665.x. Epub2012 Feb 16. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/22340599)
- McCorquodale DS 3rd, Ozomaro U, Huang J, Montenegro G, Kushman A, Citrigno L,Price J, Speziani F, Pericak-Vance MA, Zuchner S. Mutation screening of spastin, atlastin, and REEP1 in hereditary spastic paraplegia. Clin Genet. 2011Jun;79(6):523-30. doi: 10.1111/j.1399-0004.2010.01501.x. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20718791) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2990804/)
- Moss TJ, Daga A, McNew JA. Fusing a lasting relationship between ER tubules. Trends Cell Biol. 2011 Jul;21(7):416-23. doi: 10.1016/j.tcb.2011.03.009. Epub2011 May 6. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21550242) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3128651/)
- Zhu PP, Soderblom C, Tao-Cheng JH, Stadler J, Blackstone C. SPG3A proteinatlastin-1 is enriched in growth cones and promotes axon elongation duringneuronal development. Hum Mol Genet. 2006 Apr 15;15(8):1343-53. doi:10. 1093/hmg/ddl054. Epub 2006 Mar 14. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16537571)

### **Genomic Location**

The *ATL1* gene is found on chromosome 14 (https://medlineplus.gov/genetics/chromosome/14/).

# Last updated March 1, 2015