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%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])

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Genomic Location

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

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