SMN1 gene

survival of motor neuron 1, telomeric

Normal Function

The *SMN1* gene provides instructions for making the survival motor neuron (SMN) protein. The SMN protein is found throughout the body, with highest levels in the spinal cord. This protein is one of a group of proteins called the SMN complex, which is important for the maintenance of specialized nerve cells called motor neurons. These cells are located in the spinal cord and the part of the brain that is connected to the spinal cord (the brainstem). Motor neurons transmit signals from the brain and spinal cord that tell skeletal muscles to tense (contract), which allows the body to move.

In cells, the SMN complex plays an important role in processing molecules called messenger RNA (mRNA), which serve as genetic blueprints for making proteins. Messenger RNA begins as a rough draft (pre-mRNA) and goes through several processing steps to become a final, mature form. The SMN complex helps to assemble the cellular machinery needed to process pre-mRNA. The SMN complex is also important for the development of specialized outgrowths from nerve cells called dendrites and axons. Dendrites and axons are required for the transmission of impulses between neurons and from neurons to muscles.

A small amount of SMN protein is produced from a gene similar to *SMN1* called *SMN2*. Several different versions of the SMN protein are produced from the *SMN2* gene, but only one version is functional; the other versions are smaller and quickly broken down.

Health Conditions Related to Genetic Changes

Amyotrophic lateral sclerosis

MedlinePlus Genetics provides information about Amyotrophic lateral sclerosis

Spinal muscular atrophy

Many mutations in the *SMN1* gene have been found to cause spinal muscular atrophy. This condition is characterized by a loss of motor neurons that leads to weakness and wasting (atrophy) in muscles used for movement (skeletal muscles) that worsens with age. Spinal muscular atrophy has a wide range of severity. There are many types of spinal muscular atrophy that differ in age of onset and level of muscle functioning;

however, there is overlap among the types. About 95 percent of individuals with spinal muscular atrophy have mutations that delete a piece of the *SMN1* gene in both copies of the gene in each cell. As a result, SMN protein production is impaired. In about 5 percent of people with this disorder, one copy of the *SMN1* gene is missing a section, and the other copy has a different kind of mutation that disrupts the production or function of the SMN protein.

Researchers suggest that a shortage of SMN protein leads to the inefficient assembly of the machinery needed to process pre-mRNA. A lack of mature mRNA, and subsequently the proteins needed for normal cell functioning, has damaging effects on motor neuron development and survival. The loss of motor neurons leads to the signs and symptoms of spinal muscular atrophy. However, it is unclear why these cells are particularly sensitive to a reduction in the amount of SMN protein. Some research findings indicate that a shortage of this protein impairs the formation and function of axons and dendrites, leading to the death of motor neurons.

Typically, people have two copies of the *SMN1* gene and one to two copies of the *SMN2* gene in each cell. However, the number of copies of the *SMN2* gene varies, with some people having up to eight copies. Multiple copies of the *SMN2* gene are usually associated with less severe features of the condition that develop later in life. The small amount of SMN protein produced by the *SMN2* genes can help make up for the protein deficiency caused by *SMN1* gene mutations. Other factors, many unknown, also contribute to the variable severity of spinal muscular atrophy.

Other Names for This Gene

- BCD541
- SMA1
- SMA2
- SMA3
- SMA4
- SMN_HUMAN
- SMNT
- T-BCD541
- telomeric SMN

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of SMN1 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=6606[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28SMN1%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+1080+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- SURVIVAL OF MOTOR NEURON 1; SMN1 (https://omim.org/entry/600354)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/6606)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=SMN1[gene])

References

- Blauw HM, Barnes CP, van Vught PW, van Rheenen W, Verheul M, Cuppen E, VeldinkJH, van den Berg LH. SMN1 gene duplications are associated with sporadic ALS.Neurology. 2012 Mar 13;78(11):776-80. doi: 10.1212/WNL.0b013e318249f697. Epub2012 Feb 8. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/22323753) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3304946/)
- Cartegni L, Hastings ML, Calarco JA, de Stanchina E, Krainer AR. Determinantsof exon 7 splicing in the spinal muscular atrophy genes, SMN1 and SMN2. Am J HumGenet. 2006 Jan;78(1):63-77. doi: 10.1086/498853. Epub 2005 Nov 16. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16385450) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1380224/)
- Corcia P, Camu W, Halimi JM, Vourc'h P, Antar C, Vedrine S, Giraudeau B, deToffol B, Andres CR; French ALS Study Group. SMN1 gene, but not SMN2, is a riskfactor for sporadic ALS. Neurology. 2006 Oct 10;67(7):1147-50. doi:10.1212/01.wnl.0000233830.85206.1e. Epub 2006 Aug 23. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16931506)
- Corcia P, Camu W, Praline J, Gordon PH, Vourch P, Andres C. The importance ofthe SMN genes in the genetics of sporadic ALS. Amyotroph Lateral Scler. 2009Oct-Dec;10(5-6):436-40. doi: 10.3109/17482960902759162. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/19922137)
- Farrar MA, Kiernan MC. The Genetics of Spinal Muscular Atrophy: Progress andChallenges. Neurotherapeutics. 2015 Apr;12(2):290-302. doi:10.1007/s13311-014-0314-x. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/25413156) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4404441/)
- Fuller HR, Gillingwater TH, Wishart TM. Commonality amid diversity:Multi-study proteomic identification of conserved disease mechanisms in spinalmuscular atrophy.

Neuromuscul Disord. 2016 Sep;26(9):560-9. doi:10.1016/j.nmd.2016.06.004. Epub 2016 Jun 7. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/27460344)

- Gubitz AK, Feng W, Dreyfuss G. The SMN complex. Exp Cell Res. 2004 May15; 296(1):51-6. doi: 10.1016/j.yexcr.2004.03.022. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/15120993)
- Kolb SJ, Battle DJ, Dreyfuss G. Molecular functions of the SMN complex. JChild Neurol. 2007 Aug;22(8):990-4. doi: 10.1177/0883073807305666. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17761654)
- Kolb SJ, Kissel JT. Spinal Muscular Atrophy. Neurol Clin. 2015Nov;33(4):831-46. doi: 10.1016/j.ncl.2015.07.004. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/26515624) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4628728/)
- Prior TW, Swoboda KJ, Scott HD, Hejmanowski AQ. Homozygous SMN1 deletions inunaffected family members and modification of the phenotype by SMN2. Am J MedGenet A. 2004 Oct 15;130A(3):307-10. doi: 10.1002/ajmg.a.30251. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/15378550) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4349519/)

Genomic Location

The *SMN1* gene is found on chromosome 5 (https://medlineplus.gov/genetics/chromosome/5/).

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