

# SMN2 Gene

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## 1. Normal Function

The *SMN2* 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.

Several different versions of the SMN protein are produced from the *SMN2* gene, but only one version (called isoform d) is full size and functional. The other versions are smaller and quickly broken down. The full-size protein made from the *SMN2* gene is identical to the protein made from a similar gene called *SMN1*; however, only 10 to 15 percent of all functional SMN protein is produced from the *SMN2* gene (the rest is produced from the *SMN1* gene). 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. The more *SMN2* gene copies a person has, the more SMN protein they produce.

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.

## 2. Health Conditions Related to Genetic Changes

### 2.1. Spinal muscular atrophy

Extra copies of the *SMN2* gene do not cause spinal muscular atrophy, but they modify the severity of the disorder. 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. All individuals with spinal muscular atrophy have mutations in both copies of the *SMN1* gene. As a result, little or no SMN protein is produced from this gene. The *SMN2* gene can help replace some of the missing SMN protein. In people with spinal muscular atrophy, having multiple copies of the *SMN2* gene is usually associated with less severe features of the condition that develop later in life. Affected individuals with one or two functional copies of the *SMN2* gene generally have severe muscle weakness that begins at birth or in infancy. Affected individuals with four or more copies of the *SMN2* gene typically have mild muscle weakness that may not become noticeable until adulthood. Other factors, many unknown, also contribute to the variable severity of spinal muscular atrophy.

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 SMN protein impairs the formation and function of axons and

dendrites, leading to the death of motor neurons. While the mechanism is not clear, it is apparent that increased *SMN2* gene copy number leads to an increase in SMN protein production, which improves the function and survival of motor neurons and results in less severe disease.

### 3. Other Names for This Gene

- BCD541
- C-BCD541
- centromeric SMN
- SMN\_HUMAN
- SMNC

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