SF3B4 Gene

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splicing factor 3b subunit 4

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1. Normal Function

The *SF3B4* gene provides instructions for making the SAP49 protein, which is part of a complex called a spliceosome. Spliceosomes help process messenger RNA (mRNA), which is a chemical cousin of DNA that serves as a genetic blueprint for making proteins. The spliceosomes recognize and then remove regions from mRNA molecules that are not used in the blueprint (which are called introns).

The SAP49 protein may also be involved in a chemical signaling pathway known as the bone morphogenic protein (BMP) pathway. This signaling pathway regulates various cellular processes and is involved in the growth of cells. The SAP49 protein is particularly important for the maturation of cells that build bones and cartilage (osteoblasts and chondrocytes).

2. Health Conditions Related to Genetic Changes

2.1. Nager syndrome

More than 30 mutations in the *SF3B4* gene have been found to cause Nager syndrome, which is primarily characterized by abnormalities of the face, hands, and arms, such as underdeveloped cheek bones (malar hypoplasia), a small lower jaw (micrognathia), and malformed or absent thumbs. The condition can also affect development of other parts of the body. More than half of people with this condition have a mutation in the *SF3B4* gene. These mutations prevent the production of SAP49 protein or lead to production of a nonfunctional protein. It is unclear how a shortage of functional SAP49 protein leads to the development problems in Nager syndrome. Researchers suspect that problems with spliceosome formation may impair mRNA processing and alter the activity of genes involved in development of several parts of the body. A loss of SAP49 may also impair BMP pathway signaling, leading to abnormal development of bones in the face, hands, and arms.

2.2. Other disorders

At least four *SF3B4* gene mutations have been found to cause acrofacial dysostosis of Rodriguez, a severe disorder that causes underdevelopment of bones in the face, arms, and legs as well as lung abnormalities. Affected individuals have abnormally short arm bones, such that the hands are located very close to the body (phocomelia). In addition, the fingers, toes, and a bone in the lower leg called the fibula are usually missing. Affected individuals also have an opening in the roof of the mouth (cleft palate), small external ears (microtia), and micrognathia. In this condition, micrognathia is severe and leads to life-threatening breathing problems; most affected babies do not survive past birth.

The effects of the *SF3B4* gene mutations that cause acrofacial dysostosis of Rodriguez are not understood. Similar to Nager syndrome (described above), researchers suspect that abnormal spliceosome function and disruption of the BMP signaling pathway impair normal bone development and limb formation in babies with this condition.

3. Other Names for This Gene

- AFD1
- Hsh49
- pre-mRNA-splicing factor SF3b 49 kDa subunit
- SAP 49
- SAP49

- SF3b49
- SF3b50
- spliceosomal protein
- spliceosome-associated protein (U2 snRNP)
- spliceosome-associated protein 49
- splicing factor 3B subunit 4
- splicing factor 3b, subunit 4, 49kD
- splicing factor 3b, subunit 4, 49kDa

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