

# SLC26A2 Gene

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solute carrier family 26 member 2

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## 1. Normal Function

The *SLC26A2* gene provides instructions for making a protein that transports charged molecules (ions), particularly sulfate ions, across cell membranes. This protein appears to be active in many of the body's tissues, including developing cartilage. Cartilage is a tough, flexible tissue that makes up much of the skeleton during early development. Most cartilage is later converted to bone, except for the cartilage that continues to cover and protect the ends of bones and is present in the nose and external ears.

Cartilage cells use sulfate ions transported by the *SLC26A2* protein to build molecules called proteoglycans. These molecules, which each consist of several sugars attached to a protein, help give cartilage its rubbery, gel-like structure. Because sulfate ions are required to make proteoglycans, the transport activity of the *SLC26A2* protein is essential for normal cartilage formation.

## 2. Health Conditions Related to Genetic Changes

### 2.1. Achondrogenesis

At least eight mutations in the *SLC26A2* gene have been found to cause a form of achondrogenesis known as type 1B or the Parenti-Fraccaro type. This rare disorder of bone development is characterized by extremely short limbs, short fingers and toes, a narrow chest, and a prominent, rounded abdomen. Serious health problems result from these abnormalities, and infants with achondrogenesis usually die before or soon after birth.

Two *SLC26A2* gene mutations appear to be relatively common causes of achondrogenesis type 1B. One of these mutations deletes a single protein building block (amino acid) at position 341 in the *SLC26A2* protein. This genetic change is written as Val341del. The other mutation deletes three DNA building blocks (base pairs) at a specific place in the *SLC26A2* gene. This genetic change is written as c.1020\_1022delTGT.

The *SLC26A2* gene mutations that cause achondrogenesis type 1B prevent the production of any functional protein from the *SLC26A2* gene. Without this protein, cartilage cells are unable to take up the necessary sulfate ions, and cells cannot produce normal proteoglycans. A lack of these important molecules severely disrupts the structure of cartilage, making it look coarse and spongelike under a microscope. Because much of the skeleton develops from cartilage before birth and in early childhood, *SLC26A2* gene mutations prevent bones from developing and growing normally, causing the severe skeletal abnormalities seen in achondrogenesis type 1B.

### 2.2. Atelosteogenesis type 2

At least eight *SLC26A2* gene mutations have been identified in people with atelosteogenesis type 2, another severe disorder of cartilage and bone development. Affected individuals typically have a mutation in one copy of the gene that disrupts the normal structure of the *SLC26A2* protein, and a mutation in the other copy of the gene that prevents the production of any functional protein.

One common mutation that causes atelosteogenesis type 2 replaces the amino acid arginine with the amino acid tryptophan at position 279 in the protein (written as Arg279Trp or R279W). In the Finnish population, the most common mutation (usually written as IVS1+2T>C) interferes with the normal processing of the *SLC26A2* protein.

*SLC26A2* gene mutations alter the structure and function of the *SLC26A2* transporter protein, which disrupts the ability of cartilage cells to take up the necessary sulfate ions. The cell is then unable to produce normal proteoglycans, which affects the structure of cartilage and the normal formation and growth of bones.

### 2.3. Diastrophic dysplasia

More than 20 *SLC26A2* gene mutations have been identified in people with diastrophic dysplasia. This disorder of cartilage and bone development has features similar to those of atelosteogenesis type 2 (described above), although diastrophic dysplasia tends to be less severe. Like people with atelosteogenesis type 2, people with diastrophic dysplasia usually have a mutation in one copy of the gene that disrupts the normal structure of the *SLC26A2* protein and a mutation in the other copy of the gene that prevents the production of any functional protein. Mutations common in atelosteogenesis type 2 (including the R279W and IVS1+2T>C mutations) can also occur in diastrophic dysplasia.

The *SLC26A2* gene mutations that cause diastrophic dysplasia disrupt the ability of cartilage cells to take up the necessary sulfate ions. Without enough sulfate, the cell is unable to produce normal proteoglycans. A lack of these essential molecules affects the structure of cartilage and the normal formation and growth of bones.

### 2.4. Multiple epiphyseal dysplasia

At least four mutations in the *SLC26A2* gene have been found in people with multiple epiphyseal dysplasia, a disorder of cartilage and bone development that primarily affects the ends of the long bones in the arms and legs (epiphyses). *SLC26A2* gene mutations cause the recessive form of the disorder, which is also characterized by malformations of the hands, feet, and knees; abnormal curvature of the spine (scoliosis); and other birth defects.

Mutations that cause recessive multiple epiphyseal dysplasia typically replace one amino acid with another amino acid in the *SLC26A2* protein. The most common mutation replaces the amino acid arginine with the amino acid tryptophan at position 279 in the protein (written as Arg279Trp or R279W). (This mutation can also occur in atelosteogenesis type 2 and diastrophic dysplasia, described above). Another mutation that commonly causes recessive multiple epiphyseal dysplasia replaces the amino acid cysteine with the amino acid serine at position 653 in the *SLC26A2* protein (written as Cys653Ser or C653S).

The *SLC26A2* gene mutations that result in recessive multiple epiphyseal dysplasia tend to have less serious effects than mutations that cause life-threatening skeletal disorders such as achondrogenesis type 1B (described above). As a result of these milder mutations, the *SLC26A2* protein likely retains some of its function as a transporter of sulfate ions. Cartilage and bone formation are impaired to a lesser degree, which may help explain the less severe signs and symptoms of recessive multiple epiphyseal dysplasia.

## 3. Other Names for This Gene

- diastrophic dysplasia sulfate transporter
- DTD
- DTDST
- EDM4
- S26A2\_HUMAN
- solute carrier family 26 (anion exchanger), member 2
- solute carrier family 26 (sulfate transporter), member 2
- sulfate anion transporter 1
- sulfate transporter

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