COL11A2 Gene

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Contributor: Vicky Zhou

collagen type XI alpha 2 chain

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1. Normal Function

The *COL11A2* gene provides instructions for making a component of type XI collagen called the pro-alpha2(XI) chain. Collagens are molecules that provide structure and strength to the connective tissues that support the body's muscles, joints, organs, and skin. Type XI collagen is normally found in cartilage, a tough but 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. Type XI collagen made with the pro-alpha2(XI) chain is also part of the inner ear and the nucleus pulposus, which is the center portion of the discs between the bones of the spine (vertebrae).

Collagens begin as rope-like procollagen molecules that are each made up of three chains. The pro-alpha2(XI) chain combines with two other collagen chains, pro-alpha1(XI) and pro-alpha1(II), to form a triple-stranded procollagen molecule. Then the ropelike procollagen is processed by enzymes to create mature collagen. Mature collagen molecules arrange themselves into long, thin fibrils that form stable interactions (cross-links) with one another in the spaces between cells (the extracellular matrix). The cross-links result in the formation of very strong type XI collagen fibers.

Type XI collagen also helps maintain the spacing and width (diameter) of another type of collagen molecule, type II collagen. Type II collagen is an important component of mature cartilage. The arrangement and size of type II collagen fibrils is essential for the normal structure of these tissues.

2. Health Conditions Related to Genetic Changes

2.1. Fibrochondrogenesis

At least two mutations in the *COL11A2* gene have been identified in people with fibrochondrogenesis type 2, a disorder of bone growth characterized by severe skeletal abnormalities and hearing loss. Infants with fibrochondrogenesis type 2 have a very narrow chest that prevents the lungs from developing normally. Most infants with this condition are stillborn or die shortly after birth from respiratory failure, although some have lived into childhood.

The *COL11A2* gene mutations that cause fibrochondrogenesis type 2 lead to the production of an abnormal version of the pro-alpha2(XI) chain. When this abnormal chain is incorporated into collagen molecules, it creates defective type XI collagen. The abnormal collagen weakens connective tissues, impairing the formation of bones throughout the skeleton and causing changes in the inner ear that lead to hearing problems.

2.2. Nonsyndromic Hearing Loss

Mutations in the *COL11A2* gene have been identified in people with nonsyndromic hearing loss, which is loss of hearing that is not associated with other signs and symptoms. Mutations in this gene can cause two forms of nonsyndromic hearing loss: DFNA13 and DFNB53.

DFNA13 is inherited in an autosomal dominant pattern, which means only one mutated copy of the *COL11A2* gene in each cell is sufficient to cause the condition. This type of hearing loss begins in childhood or adolescence. It is classified as postlingual because it starts after a child learns to speak.

At least two *COL11A2* gene mutations have been identified in people with DFNA13. Both of these mutations change a single protein building block (amino acid) in the pro-alpha2(XI) chain of type XI collagen. These mutations are thought to change the structure of type XI collagen, which plays an important role in the structure and function of the inner ear.

DFNB53 is inherited in an autosomal recessive pattern, which means both copies of the *COL11A2* gene are mutated in each cell. It is characterized by profound hearing loss that is present before a child learns to speak (prelingual).

At least three mutations in the *COL11A2* gene have been found to cause DFNB53. Each of these mutations changes a single amino acid in the pro-alpha2(XI) chain of type XI collagen. Studies suggest that the altered protein causes hearing loss by changing the structure of type XI collagen and impairing its ability to interact with other proteins.

2.3. Otospondylomegaepiphyseal Dysplasia

At least 14 mutations in the *COL11A2* gene have been found to cause otospondylomegaepiphyseal dysplasia (OSMED), a disorder characterized by skeletal abnormalities, distinctive facial features, and severe hearing loss. These signs and symptoms are similar to those of Weissenbacher-Zweymüller syndrome (described below) and to a form of Stickler syndrome classified as type III. In some cases, it can be difficult to tell these conditions apart. Some researchers believe they represent a single disorder with a range of signs and symptoms.

Most of the reported *COL11A2* gene mutations that cause OSMED lead to the production of an abnormally short version of the pro-alpha2(XI) chain that is probably not incorporated into type XI collagen molecules. The defective collagen impairs the normal development of several tissues, including bones and the inner ear.

2.4. Stickler Syndrome

Stickler syndrome

2.5. Weissenbacher-Zweymüller Syndrome

At least one mutation in the *COL11A2* gene has been associated with Weissenbacher-Zweymüller syndrome, a disorder of bone growth characterized by skeletal abnormalities, hearing loss, and distinctive facial features. These signs and symptoms are similar to those of OSMED (described above) and to a form of Stickler syndrome classified as type III.

Like the other mutations that cause OSMED, this mutation leads to defective type XI collagen. The abnormal collagen impairs the normal development of several tissues, including bones and the inner ear.

3. Other Names for This Gene

- collagen type XI alpha 2
- collagen, type XI, alpha 2
- HKE5
- PARP
- STL3

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