COL1A2 Gene

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collagen type I alpha 2 chain

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1. Normal Function

The *COL1A2* gene provides instructions for making part of a large molecule called type I collagen. Collagens are a family of proteins that strengthen and support many tissues in the body, including cartilage, bone, tendon, skin, and the white part of the eye (the sclera). Type I collagen is the most abundant form of collagen in the human body.

A component of type I collagen called the pro-α2(I) chain is produced from the *COL1A2* gene. Collagens begin as rope-like procollagen molecules that are each made up of three chains. Type I collagen is composed of two pro-α1(I) chains (which are produced from the *COL1A1* gene) and one pro-α2(I) chain.

The triple-stranded procollagen molecules are processed by enzymes in a series of steps inside and outside the cell to create mature collagen. The collagen molecules then arrange themselves into long, thin fibrils that form stable interactions (cross-links) with one another in the spaces between cells. The cross-links result in the formation of very strong type I collagen fibers.

2. Health Conditions Related to Genetic Changes

2.1. Ehlers-Danlos Syndrome

Several mutations in the *COL1A2* gene can cause a form of Ehlers-Danlos syndrome known as the arthrochalasia type. Ehlers-Danlos syndrome is a group of disorders that affect the connective tissues that support the skin, bones, blood vessels, and many other organs and tissues. The arthrochalasia type is characterized by an unusually large range of joint movement (hypermobility) and dislocations of both hips at birth. The genetic changes, which affect one copy of the *COL1A2* gene in each cell, lead to the production of a pro-α2(I) chain that is missing a critical segment. The absence of this segment interferes with the assembly and processing of pro-α2(I) chains into mature type I collagen molecules. These changes mainly affect tissues that are rich in type I collagen, such as the skin, bones, and tendons.

Rarely, mutations in both copies of the *COL1A2* gene in each cell have been reported in people with a form of Ehlers-Danlos syndrome described as the cardiac-valvular type. This rare condition is characterized by abnormalities of the valves in the heart, highly stretchy (elastic) skin, and joint hypermobility. The mutations that cause this form of the disorder prevent cells from producing any normal pro-α2(I) chains. As a result, type I collagen fibrils in the skin and other tissues cannot be assembled correctly. The abnormal collagen weakens connective tissues, which causes the signs and symptoms of this condition.

2.2. Osteogenesis Imperfecta

Most *COL1A2* gene mutations cause severe forms of osteogenesis imperfecta, including types II, III, and IV. People with these conditions have bones that break easily, often from mild trauma or with no apparent cause. Mutations in the *COL1A2* gene occasionally cause osteogenesis imperfecta type I, the mildest form of this disorder.

Some *COL1A2* mutations delete pieces of the gene, which leads to a pro-α2(I) chain that is missing critical regions. Other genetic changes alter the sequence of protein building blocks (amino acids) in the pro-α2(I) chain, usually replacing the amino acid glycine with a different amino acid. In some cases, amino acid substitutions alter one end of the protein chain

(called the C-terminus), which interferes with the assembly of collagen molecules. These *COL1A2* mutations prevent the normal production of type I collagen. When abnormal collagen is incorporated into developing bones and other connective tissues, it causes the serious medical problems associated with severe forms of osteogenesis imperfecta.

2.3. Other Disorders

People with certain *COL1A2* mutations exhibit the signs and symptoms of both osteogenesis imperfecta and Ehlers-Danlos syndrome (described above). These mutations include duplications of a large part of the gene, deletions of an important segment of the pro-α2(I) chain, and genetic changes that result in an abnormally shortened version of the pro-α2(I) chain. Mutations in the *COL1A2* gene alter the structure of type I collagen fibrils, which weakens connective tissue and leads to the characteristic features of these two conditions.

3. Other Names for This Gene

- alpha 2 collagen type I
- CO1A2_HUMAN
- collagen I, alpha-2 polypeptide
- collagen of skin, tendon and bone, alpha-2 chain
- collagen type I alpha 2
- collagen, type I, alpha 2

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