COMP Gene

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cartilage oligomeric matrix protein

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1. Normal Function

The *COMP* gene provides the instructions for making the COMP protein. This protein is found in the extracellular matrix, which is an intricate lattice of proteins and other molecules that forms in the spaces between cells. Specifically, the COMP protein is located in the extracellular matrix surrounding the cells that make up ligaments and tendons, and near cartilage-forming cells (chondrocytes). Chondrocytes play an important role in bone formation (osteogenesis). In the bones of the spine, hips, and limbs, the process of osteogenesis starts with the formation of cartilage, which is then converted into bone.

The normal function of the COMP protein is not fully known. It is believed to play a role in cell growth and division (proliferation) and the self-destruction of cells (apoptosis), as well as in the regulation of cell movement and attachment. Research has also shown that the COMP protein binds strongly to calcium.

2. Health Conditions Related to Genetic Changes

2.1. Multiple Epiphyseal Dysplasia

More than 20 mutations in the *COMP* gene that cause dominant multiple epiphyseal dysplasia have been identified. This disorder can also be caused by mutations in four other genes; however, the majority of individuals have mutations in the *COMP* gene.

Mutations in the *COMP* gene that cause dominant multiple epiphyseal dysplasia change one protein building block (amino acid) or result in small additions or deletions of amino acids in the COMP protein. All identified mutations have occurred in two regions of the COMP protein, which are referred to as the type III and C-terminal domains. *COMP* mutations lead to the improper folding of the COMP protein in the endoplasmic reticulum, a structure in the cell involved in protein processing and transport. The abnormal COMP protein is unable to leave the endoplasmic reticulum, which causes this cellular structure to enlarge. The endoplasmic reticulum eventually becomes so large that it is no longer able to function normally, and the chondrocyte dies. The premature death of chondrocytes results in diminished growth of the long bones and short stature.

Researchers believe that the lack of COMP protein in the spaces between the chondrocytes leads to the formation of abnormal cartilage. This abnormal cartilage probably breaks down easily, which results in early-onset osteoarthritis.

2. Pseudoachondroplasia

About 60 mutations in the *COMP* gene have been identified in individuals with pseudoachondroplasia. One particular mutation is found in approximately 30 percent of affected individuals. This mutation results in the deletion of a single amino acid, called aspartic acid, in the COMP protein. This gene mutation is usually written as 469delD or D469del. Most other *COMP* gene mutations involve the substitution of one amino acid for another amino acid in the COMP protein.

Mutations in the *COMP* gene that cause pseudoachondroplasia also result in the buildup of COMP protein in the endoplasmic reticulum and eventual chondrocyte death. It is not clear why some mutations in the *COMP* gene cause pseudoachondroplasia and other mutations cause dominant multiple epiphyseal dysplasia.

3. Other Names for This Gene

- cartilage oligomeric matrix protein (pseudoachondroplasia, epiphyseal dysplasia 1, multiple)
- COMP_HUMAN
- EDM1
- EPD1
- MED
- PSACH
- pseudoachondroplasia (epiphyseal dysplasia 1, multiple)
- THBS5
- thrombospondin-5

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