HSPG2 Gene

Subjects: Genetics & Heredity
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Heparan sulfate proteoglycan 2

genes

1. Introduction

The *HSPG2* gene provides instructions for making a protein called perlecan. This protein is found in the extracellular matrix, which is the intricate lattice of proteins and other molecules that forms in the spaces between cells. Specifically, it is found in part of the extracellular matrix called the basement membrane, which is a thin, sheet-like structure that separates and supports cells in many tissues. Perlecan is also found in cartilage, 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.

Perlecan is a heparan sulfate proteoglycan, which is a type of protein that interacts with many other proteins and has a variety of functions. In particular, perlecan is involved in cell signaling, the sticking (adhesion) of cells to one another, the formation of new blood vessels (angiogenesis), and the maintenance of basement membranes and cartilage throughout life. The protein also plays a critical role at the neuromuscular junction, which is the area between the ends of nerve cells and muscle cells where signals are relayed to trigger muscle contraction.

2. Health Conditions Related to Genetic Changes

2.1. Schwartz-Jampel Syndrome

More than 30 mutations in the *HSPG2* gene have been found to cause Schwartz-Jampel syndrome. This rare condition is characterized by continuous muscle contraction (myotonia) that restricts movement, as well as bone abnormalities known as chondrodysplasia. Most of the mutations reduce the amount of perlecan that is produced. Other mutations lead to a version of perlecan that is only partially functional. A reduction in the amount or function of this protein disrupts the normal development of cartilage and bone tissue, which underlies chondrodysplasia in affected individuals. A reduced amount of functional perlecan at the neuromuscular junction likely alters the balance of other molecules that signal when muscles should contract and when they should relax. As a result, muscle contraction is triggered continuously, leading to myotonia.

2.2. Other Disorders

Mutations in the *HSPG2* gene can also cause another, more severe form of chondrodysplasia called dyssegmental dysplasia, Silverman-Handmaker type. Because of the very severe abnormalities associated with this rare condition, most affected individuals die before birth, are stillborn, or live only into early infancy. At least seven *HSPG2* gene mutations have been identified in people with dyssegmental dysplasia, Silverman-Handmaker type. These mutations prevent the production or transport of any functional perlecan. A total lack of this protein significantly disrupts the development of cartilage and bone tissue, causing this very severe type of chondrodysplasia.

3. Other Names for This Gene

- endorepellin (domain V region)
- perlecan
- perlecan proteoglycan
- PLC
- PRCAN

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