Kuskokwim Syndrome

Subjects: Genetics & Heredity

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Kuskokwim syndrome is characterized by joint deformities called contractures that restrict the movement of affected joints.

genetic conditions

1. Introduction

Kuskokwim syndrome has been found only in a population of Alaska Natives known as Yup'ik Eskimos, who live in and around a region of southwest Alaska known as the Kuskokwim River Delta.

In Kuskokwim syndrome, contractures most commonly affect the knees, ankles, and elbows, although other joints, particularly of the lower body, can be affected. The contractures are usually present at birth and worsen during childhood. They tend to stabilize after childhood, and they remain throughout life.

Some individuals with this condition have other bone abnormalities, most commonly affecting the spine, pelvis, and feet. Affected individuals can develop an inward curve of the lower back (lordosis), a spine that curves to the side (scoliosis), wedge-shaped spinal bones, or an abnormality of the collarbones (clavicles) described as clubbing. Affected individuals are typically shorter than their peers and they may have an abnormally large head (macrocephaly).

2. Frequency

Kuskokwim syndrome is extremely rare. It affects a small number of people from the Yup'ik Eskimo population in southwest Alaska.

3. Causes

Kuskokwim syndrome is caused by mutations in the *FKBP10* gene, which provides instructions for making the FKBP10 protein (formerly known as FKBP65). This protein is important for the correct processing of complex molecules called collagens, which provide structure and strength to connective tissues that support the body's bones, joints, and organs. Collagen molecules are cross-linked to one another to form long, thin fibrils, which are found in the spaces around cells (the extracellular matrix). The formation of cross-links results in very strong collagen fibrils. The FKBP10 protein attaches to collagens and plays a role in their cross-linking.

A mutation in the *FKBP10* gene alters the FKBP10 protein, making it unstable and easily broken down. As a result, people with Kuskokwim syndrome have only about 5 percent of the normal amount of FKBP10 protein. This reduction in protein levels impairs collagen cross-linking and leads to a disorganized network of collagen molecules. It is unclear how these changes in the collagen matrix are involved in the development of joint contractures and other abnormalities in people with Kuskokwim syndrome.

3.1. The gene associated with Kuskokwim syndrome

- FKBP10

4. Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

5. Other Names for This Condition

- arthrogryposis-like syndrome
- Bruck syndrome 1
- Kuskokwim disease

References

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