FKBP10 gene

FKBP prolyl isomerase 10

Normal Function

The *FKBP10* gene provides instructions for making a protein that is found in a cell structure called the endoplasmic reticulum, which is involved in protein production, processing, and transport. The FKBP10 protein (formerly known as FKBP65) is important for the correct processing of complex molecules called collagen and elastin, which are part of the intricate lattice of proteins and other molecules that forms in the spaces between cells (the extracellular matrix). This matrix provides structure and strength to connective tissues that support the body's joints and organs.

In the extracellular matrix, collagen molecules are cross-linked to one another to form long, thin fibrils. The formation of cross-links results in very strong collagen fibrils. The FKBP10 protein attaches to collagen molecules and plays a role in their cross-linking. It is thought to be involved in a reaction called hydroxylation that modifies a particular region of the collagen molecule and is necessary for cross-linking of the molecules.

The FKBP10 protein is also involved in the formation of elastin. In particular, FKBP10 helps with the proper folding of a protein called tropoelastin. Multiple copies of tropoelastin attach to one another to make elastin. Elastin is the major component of elastic fibers, which provide strength and elasticity to connective tissues as part of the extracellular matrix.

Health Conditions Related to Genetic Changes

Kuskokwim syndrome

At least one mutation in the *FKBP10* gene causes Kuskokwim syndrome, a rare condition that affects a small number of people from the Yup'ik Eskimo population in southwest Alaska. This condition is characterized by joint deformities called contractures, particularly in the knees, ankles, and elbows. The contractures restrict the movement of affected joints.

The *FKBP10* gene mutation involved in Kuskokwim syndrome deletes a single protein building block (amino acid) from the FKBP10 protein. The mutation, written as Tyr293del, removes the amino acid tyrosine at position 293. This genetic change leads to production of a protein that is unstable and easily broken down. As a result, people

with Kuskokwim syndrome have only about 5 percent of the normal amount of FKBP10 protein. Although the mechanism is unclear, the reduction of FKBP10 protein leads to a severe decrease in collagen hydroxylation, which interferes with collagen cross-linking. The network of collagen molecules in affected individuals is disorganized. It is unclear how changes in the collagen matrix are involved in the development of joint contractures in people with Kuskokwim syndrome. It is unknown whether elastin abnormalities also contribute to the features of this disorder.

Osteogenesis imperfecta

MedlinePlus Genetics provides information about Osteogenesis imperfecta

Other disorders

Mutations in the *FKBP10* gene are also associated with another connective tissue disorder known as Bruck syndrome 1. This condition has features similar to both osteogenesis imperfecta type XI and Kuskokwim syndrome (described above): affected individuals have fragile bones as well as joint contractures that typically affect the knees, ankles, and elbows.

The mutations that cause Bruck syndrome 1 lead to the production of little to no FKBP10 protein. While people with Kuskokwim syndrome have some residual collagen hydroxylation, it is nearly absent in people with osteogenesis imperfecta type XI and Bruck syndrome 1. As a result, collagen cross-linking is severely impaired: there are very few collagen fibrils in the extracellular matrix, and the network is sparse and disorganized. How these changes in collagen lead to the signs and symptoms of osteogenesis imperfecta type XI and Bruck syndrome 1 is unclear. In addition, it is unknown whether abnormalities in elastin are also involved in development of these conditions. Researchers are unsure why some people with these more severe gene mutations have joint deformities in addition to fragile bones and others do not.

Other Names for This Gene

- 65 kDa FK506-binding protein
- 65 kDa FKBP
- FK506 binding protein 10
- FK506 binding protein 10, 65 kDa
- FK506-binding protein 10
- FKB10_HUMAN
- FKBP-10
- FKBP-65
- FKBP6
- FKBP65
- FLJ20683
- FLJ22041

- FLJ23833
- hFKBP65
- immunophilin FKBP65
- OI11
- OI6
- peptidyl-prolyl cis-trans isomerase FKBP10
- peptidyl-prolyl cis-trans isomerase FKBP10 precursor
- PPIASE
- PPIase FKBP10
- rotamase

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of FKBP10 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=60681[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28FKBP10%5BTIAB%5D%29+OR+%28%28OI6%5BTIAB%5D%29+OR+%28OI11%5BTIAB%5D%29+OR+%28FKBP65%5BTIAB%5D%29+OR+%28PPIASE%5BTIAB%5D%29+OR+%28hFKBP65%5BTIAB%5D%29+OR+%28FKBP-65%5BTIAB%5D%29+OR+%28rotamase%5BTIAB%5D%29+OR+%28FK506-binding+protein+10%5BTIAB%5D%29+OR+%28FKBP6%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- BRUCK SYNDROME 1; BRKS1 (https://omim.org/entry/259450)
- FK506-BINDING PROTEIN 10; FKBP10 (https://omim.org/entry/607063)
- OSTEOGENESIS IMPERFECTA, TYPE XI; OI11 (https://omim.org/entry/610968)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/60681)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=FKBP10[gene])

References

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Genomic Location

The *FKBP10* gene is found on chromosome 17 (https://medlineplus.gov/genetics/chromosome/17/).

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