

FKRP gene

fukutin related protein

Normal Function

The *FKRP* gene provides instructions for making a protein called fukutin-related protein (FKRP). This protein is present in many of the body's tissues but is particularly abundant in the brain, heart (cardiac) muscle, and muscles used for movement (skeletal muscles). Within cells, FKRP is found in a specialized structure called the Golgi apparatus, where newly produced proteins are modified.

FKRP is involved in a process called glycosylation. Through this chemical process, sugar molecules are added to certain proteins. In particular, FKRP adds a molecule called ribitol 5-phosphate to the chain of sugars attached to a protein called alpha (α)-dystroglycan. Glycosylation is critical for the normal function of α -dystroglycan.

The α -dystroglycan protein helps anchor the structural framework inside each cell (cytoskeleton) to the lattice of proteins and other molecules outside the cell (extracellular matrix). In skeletal muscles, glycosylated α -dystroglycan helps stabilize and protect muscle fibers. In the brain, it helps direct the movement (migration) of nerve cells (neurons) during early development.

Health Conditions Related to Genetic Changes

Walker-Warburg syndrome

At least five mutations in the *FKRP* gene have been found to cause Walker-Warburg syndrome. This condition is the most severe form of a group of disorders known as congenital muscular dystrophies. Walker-Warburg syndrome causes skeletal muscle weakness and abnormalities of the brain and eyes. Because of the severity of the problems caused by this condition, affected individuals usually do not survive past early childhood.

Many *FKRP* gene mutations involved in Walker-Warburg syndrome change single protein building blocks (amino acids) in FKRP. The altered protein cannot reach the Golgi apparatus and is instead broken down, reducing the amount of functional FKRP.

A shortage of FKRP prevents the normal glycosylation of α -dystroglycan. As a result, α -dystroglycan can no longer effectively anchor cells to the proteins and other molecules

that surround them. Without functional α -dystroglycan to stabilize the muscle fibers, they become damaged as they repeatedly contract and relax with use. The damaged fibers weaken and die over time, which affects the development, structure, and function of skeletal muscles in people with Walker-Warburg syndrome.

Defective α -dystroglycan also affects the migration of neurons during the early development of the brain. Instead of stopping when they reach their intended destinations, some neurons migrate past the surface of the brain into the fluid-filled space that surrounds it. Researchers believe that this problem with neuronal migration causes a brain abnormality called cobblestone lissencephaly, in which the surface of the brain lacks the normal folds and grooves and instead appears bumpy and irregular. Less is known about the effects of *FKRP* gene mutations in other parts of the body.

Limb-girdle muscular dystrophy

MedlinePlus Genetics provides information about Limb-girdle muscular dystrophy

Other disorders

Mutations in the *FKRP* gene have been found in a small number of people with congenital muscular dystrophy type 1C (MDC1C), which causes muscle weakness, brain abnormalities, and intellectual disability but usually does not affect the eyes. Rarely, mutations in the *FKRP* gene are associated with muscle eye brain disease, which causes muscle weakness, eye problems, and intellectual disability. The signs and symptoms of muscle eye brain disease are less severe than those of Walker-Warburg syndrome (described above). It is unclear how mutations in the *FKRP* gene cause several different muscular dystrophies.

Other Names for This Gene

- FKRP_HUMAN
- LGMD2I
- MDC1C
- MDDGA5
- MDDGB5
- MDDGC5

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of FKRP ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=79147\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=79147[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28FKRP%5BTIAB%5D%29+OR+%28fukutin+related+protein%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+1800+days%22%5Bdp%5D>)

Catalog of Genes and Diseases from OMIM

- FUKUTIN-RELATED PROTEIN; FKRP (<https://omim.org/entry/606596>)
- MUSCULAR DYSTROPHY-DYSTROGLYCANOPATHY (CONGENITAL WITH OR WITHOUT IMPAIRED INTELLECTUAL DEVELOPMENT), TYPE B, 5; MDDGB5 (<https://omim.org/entry/606612>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/79147>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=FKRP\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=FKRP[gene]))

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Genomic Location

The *FKRP* gene is found on chromosome 19 (<https://medlineplus.gov/genetics/chromosome/19/>).

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