

FKTN gene

fukutin

Normal Function

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

Fukutin is involved in a protein modification process called glycosylation. Through this chemical process, sugar molecules are added to certain proteins. Fukutin works closely with other enzymes to add ribitol phosphate molecules to the chain of sugars already attached to a protein called alpha-dystroglycan. Glycosylation is critical for the normal function of alpha-dystroglycan.

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

Health Conditions Related to Genetic Changes

Fukuyama congenital muscular dystrophy

Several different variants (also called mutations) in the *FKTN* gene have been found to cause Fukuyama congenital muscular dystrophy, a condition that affects the development of the eyes, brain, and skeletal muscles. This form of congenital muscular dystrophy occurs primarily in people of Japanese ancestry.

Most people with Fukuyama congenital muscular dystrophy have at least one copy of a particular variant: an insertion of about 3,000 extra DNA building blocks (nucleotides) in the *FKTN* gene. This DNA insertion occurs in a part of the *FKTN* gene that regulates the gene's activity. Researchers believe that this DNA insertion reduces the amount of functional fukutin that is produced from the gene.

A shortage of fukutin impacts the normal glycosylation of alpha-dystroglycan. As a result, alpha-dystroglycan can no longer effectively anchor cells to the extracellular matrix.

Without enough functional alpha-dystroglycan to stabilize the muscle fibers, the fibers 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 Fukuyama congenital muscular dystrophy.

A decrease in the amount of functional alpha-dystroglycan also affects the migration of neurons during the early development of the brain. This causes a brain abnormality called cobblestone lissencephaly, in which the surface of the brain appears bumpy and irregular and lacks the normal folds and grooves. Less is known about the effects of *FKTN* gene variants in other parts of the body.

Limb-girdle muscular dystrophy

MedlinePlus Genetics provides information about Limb-girdle muscular dystrophy

Walker-Warburg syndrome

Variants in the *FKTN* gene can also cause Walker-Warburg syndrome, a severe form of congenital muscular dystrophy that affects the development of the eyes, brain, and skeletal muscles. The eye and brain abnormalities seen in those with Walker-Warburg syndrome are often more severe than those seen in people with Fukuyama congenital muscular dystrophy. Children with Walker-Warburg syndrome tend to survive only into infancy or early childhood. The *FKTN* gene variants associated with this condition prevent the production of functional fukutin protein, which leads to the severe muscle, eye, and brain problems that are characteristic of Walker-Warburg syndrome.

Other disorders

Variants in the *FKTN* gene have also been associated with another congenital muscular dystrophy called muscular dystrophy-dystroglycanopathy, type B4 (MDDGB4). People with MDDGB4 typically have muscle weakness and delayed development of motor skills.

Other Names for This Gene

- FCMD
- LGMD2M

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of *FKTN* ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=2218\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=2218[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28FKTN%5BTIAB%5D%29+OR+%28fukutin%5BTIAB%5D%29+OR+%28FCMD%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; FKTN (<https://omim.org/entry/607440>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/2218>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=FKTN\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=FKTN[gene]))

References

- Chang W, Winder TL, LeDuc CA, Simpson LL, Millar WS, Dungan J, Ginsberg N, Plaga S, Moore SA, Chung WK. Founder Fukutin mutation causes Walker-Warburgsyndrome in four Ashkenazi Jewish families. *Prenat Diagn.* 2009 Jun;29(6):560-9.doi: 10.1002/pd.2238. Citation on PubMed (<https://www.ncbi.nlm.nih.gov/pubmed/19266496>)
- Cotarelo RP, Valero MC, Prados B, Pena A, Rodriguez L, Fano O, Marco JJ, Martinez-Frias ML, Cruces J. Two new patients bearing mutations in the fukutingen confirm the relevance of this gene in Walker-Warburg syndrome. *Clin Genet.* 2008 Feb;73(2):139-45. doi: 10.1111/j.1399-0004.2007.00936.x. Epub 2007 Dec 19. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/18177472>)
- de Bernabe DB, van Bokhoven H, van Beusekom E, Van den Akker W, Kant S, DobynsWB, Cormand B, Currier S, Hamel B, Talim B, Topaloglu H, Brunner HG. A homozygousnonsense mutation in the fukutin gene causes a Walker-Warburg syndrome phenotype.*J Med Genet.* 2003 Nov;40(11):845-8. doi: 10.1136/jmg.40.11.845. No abstractavailable. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/14627679>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1735302/>)
- Gerin I, Ury B, Breloy I, Bouchet-Seraphin C, Bolsee J, Halbout M, Graff J, Vertommen D, Muccioli GG, Seta N, Cuisset JM, Dabaj I, Quijano-Roy S, Grahn A, Van Schaftingen E, Bommer GT. ISPD produces CDP-ribitol used by FKTN and FKRP totransfer ribitol phosphate onto alpha-dystroglycan. *Nat Commun.* 2016 May 19;7:11534.doi: 10.1038/ncomms11534. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/27194101>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4873967/>)
- Godfrey C, Escolar D, Brockington M, Clement EM, Mein R, Jimenez-Mallebrera C, Torelli S, Feng L, Brown SC, Sewry CA, Rutherford M, Shapira Y, Abbs S, MuntoniF. Fukutin gene mutations in steroid-responsive limb girdle muscular dystrophy.*Ann*

Neurol. 2006 Nov;60(5):603-610. doi: 10.1002/ana.21006. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/17044012>)

- Hayashi YK, Ogawa M, Tagawa K, Noguchi S, Ishihara T, Nonaka I, Arahata K. Selective deficiency of alpha-dystroglycan in Fukuyama-type congenital muscular dystrophy. *Neurology*. 2001 Jul 10;57(1):115-21. doi: 10.1212/wnl.57.1.115. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/11445638>)
- Kanagawa M, Kobayashi K, Tajiri M, Manya H, Kuga A, Yamaguchi Y, Akasaka-Manyak, Furukawa JI, Mizuno M, Kawakami H, Shinohara Y, Wada Y, Endo T, Toda T. Identification of a Post-translational Modification with Ribitol-Phosphate and Its Defect in Muscular Dystrophy. *Cell Rep*. 2016 Mar 8;14(9):2209-2223. doi:10.1016/j.celrep.2016.02.017. Epub 2016 Feb 25. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/26923585>)
- Kanagawa M, Toda T. Muscular Dystrophy with Ribitol-Phosphate Deficiency: A Novel Post-Translational Mechanism in Dystroglycanopathy. *J Neuromuscul Dis*. 2017;4(4):259-267. doi: 10.3233/JND-170255. Citation on PubMed (<https://www.ncbi.nlm.nih.gov/pubmed/29081423>)
- Kondo-Iida E, Kobayashi K, Watanabe M, Sasaki J, Kumagai T, Koide H, Saito K, Osawa M, Nakamura Y, Toda T. Novel mutations and genotype-phenotype relationships in 107 families with Fukuyama-type congenital muscular dystrophy (FCMD). *Hum Mol Genet*. 1999 Nov;8(12):2303-9. doi: 10.1093/hmg/8.12.2303. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/10545611>)
- Murakami T, Hayashi YK, Noguchi S, Ogawa M, Nonaka I, Tanabe Y, Ogino M, Takada F, Eriguchi M, Kotooka N, Campbell KP, Osawa M, Nishino I. Fukutin gene mutations cause dilated cardiomyopathy with minimal muscle weakness. *Ann Neurol*. 2006 Nov;60(5):597-602. doi: 10.1002/ana.20973. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/17036286>)
- Saito Y, Yamamoto T, Mizuguchi M, Kobayashi M, Saito K, Ohno K, Osawa M. Altered glycosylation of alpha-dystroglycan in neurons of Fukuyama congenital muscular dystrophy brains. *Brain Res*. 2006 Feb 23;1075(1):223-8. doi:10.1016/j.brainres.2005.12.108. Epub 2006 Feb 7. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16466646>)
- Toda T, Kobayashi K, Takeda S, Sasaki J, Kurahashi H, Kano H, Tachikawa M, Wang F, Nagai Y, Taniguchi K, Taniguchi M, Sunada Y, Terashima T, Endo T, Matsumura K. Fukuyama-type congenital muscular dystrophy (FCMD) and alpha-dystroglycanopathy. *Congenit Anom (Kyoto)*. 2003 Jun;43(2):97-104. doi:10.1111/j.1741-4520.2003.tb01033.x. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12893968>)
- Yis U, Uyanik G, Heck PB, Smitka M, Nobel H, Ebinger F, Dirik E, Feng L, Kurul SH, Brocke K, Unalp A, Ozer E, Cakmakci H, Sewry C, Cirak S, Muntoni F, Hehr U, Morris-Rosendahl DJ. Fukutin mutations in non-Japanese patients with congenital muscular dystrophy: less severe mutations predominate in patients with an on-Walker-Warburg phenotype. *Neuromuscul Disord*. 2011 Jan;21(1):20-30. doi: 10.1016/j.nmd.2010.08.007. Epub 2010 Oct 18. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/20961758>)

Genomic Location

The *FKTN* gene is found on chromosome 9 (<https://medlineplus.gov/genetics/chromosome/9/>).

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