PFKM gene

phosphofructokinase, muscle

Normal Function

The *PFKM* gene provides instructions for making one piece (the PFKM subunit) of an enzyme called phosphofructokinase. This enzyme plays a role in the breakdown of a complex sugar called glycogen, which is a major source of stored energy in the body. The phosphofructokinase enzyme is made up of four subunits and is found in a variety of tissues. Different combinations of subunits are found in different tissues. In muscles used for movement (skeletal muscles), the phosphofructokinase enzyme is composed solely of subunits produced from the *PFKM* gene.

The cells' main source of energy is stored as glycogen. Glycogen can be broken down rapidly into the simple sugar glucose when energy is needed, for instance to maintain normal blood glucose levels between meals or for energy during exercise. Phosphofructokinase composed of PFKM subunits is involved in the sequence of events that breaks down glycogen to provide energy to muscle cells. Specifically, the enzyme converts a molecule called fructose-6-phosphate to a molecule called fructose 1,6-bisphosphate.

Health Conditions Related to Genetic Changes

Glycogen storage disease type VII

At least 20 mutations in the *PFKM* gene have been found to cause glycogen storage disease type VII (GSDVII). This condition is characterized by an inability to break down glycogen in muscle cells, resulting in muscle cramps and weakness that can vary in severity among affected individuals. *PFKM* gene mutations that cause GSDVII result in the production of PFKM subunits that have little or no function. One *PFKM* gene mutation accounts for most cases of GSDVII in people with Ashkenazi Jewish ancestry. This mutation (written as IVS5+1G>A) results in a small deletion of genetic material within the gene, which alters the way the gene's instructions are pieced together and causes a nonfunctional subunit to be produced.

Without functional PFKM subunits, no functional phosphofructokinase is formed in skeletal muscles and glycogen cannot be completely broken down. Partially broken down glycogen builds up in muscle cells. Muscles that do not have access to glycogen as an energy source become weakened and cramped following moderate strain, such

as exercise, and in some cases, begin to break down. In other tissues, other subunits that make up the phosphofructokinase enzyme likely compensate for the lack of PFKM subunits, and the enzyme is able to retain some function. This compensation may help explain why other tissues are not affected by *PFKM* gene mutations. It is unclear why some individuals with GSDVII are more severely affected than others.

Other Names for This Gene

- 6-phosphofructo-1-kinase
- 6-phosphofructokinase, muscle type
- K6PF_HUMAN
- PFK-1
- PFK-A
- PFK1
- PFKA
- PFKX
- phosphofructo-1-kinase isozyme A
- phosphofructokinase 1
- phosphofructokinase, polypeptide X
- phosphofructokinase-M
- phosphohexokinase

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of PFKM (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=5213[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28PFKM%5BTIAB%5D%29+OR+%28muscle+phosphofructokinase%5BTIAB%5D%29%29+OR+%286-phosphofructo-1-kinase%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- PHOSPHOFRUCTOKINASE, MUSCLE TYPE; PFKM (https://omim.org/entry/610681)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/5213)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=PFKM[gene])

References

- Bruser A, Kirchberger J, Kloos M, Strater N, Schoneberg T. Functional linkageof adenine nucleotide binding sites in mammalian muscle 6-phosphofructokinase. JBiol Chem. 2012 May 18;287(21):17546-17553. doi: 10.1074/jbc.M112.347153. Epub2012 Apr 3. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/22474333) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3366854/)
- Schoneberg T, Kloos M, Bruser A, Kirchberger J, Strater N. Structure andallosteric regulation of eukaryotic 6-phosphofructokinases. Biol Chem. 2013Aug;394(8):977-93. doi: 10.1515/hsz-2013-0130. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/23729568)
- Vives-Corrons JL, Koralkova P, Grau JM, Manu Pereira Mdel M, Van Wijk R. Firstdescription of phosphofructokinase deficiency in spain: identification of a novelhomozygous missense mutation in the PFKM gene. Front Physiol. 2013 Dec 30;4:393.doi: 10.3389/fphys.2013.00393. eCollection 2013. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/24427140) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3875906/)

Genomic Location

The *PFKM* gene is found on chromosome 12 (https://medlineplus.gov/genetics/chromosome/12/).

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