PHKA2 gene
phosphorylase kinase regulatory subunit alpha 2

Normal Function

The PHKA2 gene provides instructions for making one piece, the alpha subunit, of the phosphorylase b kinase enzyme. This enzyme is made up of 16 subunits, four each of the alpha, beta, gamma, and delta subunits. (Each subunit is produced from a different gene.) The alpha subunit helps regulate the activity of phosphorylase b kinase. This enzyme is found in various tissues, although it is most abundant in the liver and muscles. One version of the enzyme is found in liver cells and another in muscle cells. The alpha-2 subunit produced from the PHKA2 gene is part of the enzyme found in the liver.

Phosphorylase b kinase plays an important role in providing energy for cells. The main source of cellular energy is a simple sugar called glucose. Glucose is stored in muscle and liver cells in a form called glycogen. Glycogen can be broken down rapidly when glucose is needed, for instance to maintain normal levels of glucose in the blood between meals. Phosphorylase b kinase turns on (activates) another enzyme called glycogen phosphorylase b by converting it to the more active form, glycogen phosphorylase a. When active, this enzyme breaks down glycogen.

Health Conditions Related to Genetic Changes

Glycogen storage disease type IX

At least 90 mutations in the PHKA2 gene are known to cause a form of glycogen storage disease type IX (GSD IX) called GSD IXa or X-linked liver glycogenosis (XLG). This is the most common form of GSD IX, accounting for approximately 75 percent of cases. GSD IXa affects liver function, and its characteristic features include an enlarged liver (hepatomegaly), slow growth, and periods of low blood sugar (hypoglycemia). These features usually improve over time. However, some affected individuals have a buildup of scar tissue (fibrosis) in the liver, which can rarely progress to irreversible liver disease (cirrhosis).

Mutations in the PHKA2 gene reduce the activity of phosphorylase b kinase in liver cells, although the mechanism is unknown. Reduction of this enzyme's function impairs glycogen breakdown. As a result, glycogen builds up in cells, and glucose is not available for energy. Glycogen accumulation in the liver leads to hepatomegaly and can damage the organ. The inability to break down glycogen for energy contributes to hypoglycemia and the other features of GSD IXa.

There are two subtypes of GSD IXa, known as XLG1 and XLG2, which are classified by the activity of phosphorylase b kinase in various tissues. In XLG1, the more
common subtype, enzyme activity is decreased in the liver and in red blood cells. In contrast, in XLG2, the enzyme's activity appears low or normal in the liver and normal or high in red blood cells when measured by laboratory tests. The subtypes are indistinguishable based on symptoms.

Chromosomental Location

Cytogenetic Location: Xp22.13, which is the short (p) arm of the X chromosome at position 22.13

Molecular Location: base pairs 18,892,298 to 18,984,114 on the X chromosome (Homo sapiens Updated Annotation Release 109.20190607, GRCh38.p13) (NCBI)

Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- GSD9A
- KP2B_HUMAN
- PHK
- phosphorylase b kinase regulatory subunit alpha, liver isoform
- phosphorylase kinase alpha L subunit
- phosphorylase kinase alpha-subunit
- phosphorylase kinase, alpha 2 (liver)
- PYK
- PYKL
- XLG

Additional Information & Resources

Educational Resources

- Biochemistry (fifth edition, 2002): Glycogen Metabolism
  https://www.ncbi.nlm.nih.gov/books/NBK21190/
Clinical Information from GeneReviews

- Phosphorylase Kinase Deficiency
  https://www.ncbi.nlm.nih.gov/books/NBK55061

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28PHKA2%5BTIAB%5D%29+OR+%28%28phosphorylase+kinase+alpha-subunit%5BTIAB%5D%29+OR+%28PYK%5BTIAB%5D%29+OR+%284XLG%5BTIAB%5D%29+AND+%28%28Genes%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

- PHOSPHORYLASE KINASE, LIVER, ALPHA-2 SUBUNIT
  http://omim.org/entry/300798

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_PHKA2.html
- ClinVar
- HGNC Gene Symbol Report
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:5256
- NCBI Gene
- UniProt
  https://www.uniprot.org/uniprot/P46019

Sources for This Summary

- Brushia RJ, Walsh DA. Phosphorylase kinase: the complexity of its regulation is reflected in the complexity of its structure. Front Biosci. 1999 Sep 15;4:D618-41. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10487978
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/9600238
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/8733134

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10330341
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1377897/

• OMIM: PHOSPHORYLASE KINASE, LIVER, ALPHA-2 SUBUNIT
  http://omim.org/entry/300798

Reprinted from Genetics Home Reference:

Reviewed: August 2015
Published: September 10, 2019

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services