PHKA2 Gene

Subjects: Genetics
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Definition

phosphorylase kinase regulatory subunit alpha 2

1. Introduction

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.

2. Health Conditions Related to Genetic Changes

2.1. 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.

3. Other Names for This Gene

- GSD9A
- KPB2_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

References

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Keywords

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