



### What is Familial Hyperinsulinism, *ABCC8*-related?

Familial hyperinsulinism (FHI) is an inherited disease characterized by hypoglycemia due to unregulated release of insulin from cells in the pancreas.<sup>1</sup> Symptoms are the result of increased levels of insulin in the blood, which causes decreased blood sugar levels (or hypoglycemia). FHI is also known as congenital hyperinsulinism (CHI).

### What are the symptoms of Familial Hyperinsulinism, *ABCC8*-related and what treatment is available?

Familial hyperinsulinism, *ABCC8*-related is a disease that varies in severity and age at presentation, even within families. The disease can involve the entire pancreas (diffuse form) or can be limited to confined areas of the pancreas (focal form); however the symptoms are similar. (GT)

Severe FHI that is diagnosed soon after birth is characterized by<sup>1</sup>:

- Increased birth weight
- Very low blood sugar (hypoglycemia) that may be difficult to manage
- Seizures
- Poor feeding
- Low muscle tone (hypotonia)
- Difficulty breathing (apnea)

If untreated, these complications may lead to irreversible brain damage and can be fatal.<sup>2</sup>

Individuals who are diagnosed in childhood or early adulthood usually have a milder form of the disease with varying degrees of low blood sugar.

Treatments include medications and diet control to help normalize blood sugar and prevent brain damage. For individuals with the focal forms of FHI, partial removal of the pancreas may be curative, whereas a near total removal of the pancreas may improve symptoms for individuals with the diffuse forms of FHI.<sup>1</sup>

### How is Familial Hyperinsulinism, *ABCC8*-related inherited?

FHI is a disease that is associated with mutations in at least five known genes. The most common gene involved is the *ABCC8* gene, previously known as *SUR*.<sup>1</sup>

Most often, *ABCC8*-related FHI is inherited as an autosomal-recessive disease.<sup>1</sup> In these cases, an individual who inherits one copy of an *ABCC8* gene mutation is a “carrier” and is not expected to have related health problems.<sup>3</sup> An individual who inherits two mutations in this gene, one from each parent, is expected to be affected with the diffuse form of FHI. If both members of a couple are carriers, the risk for an affected child is 25% in each pregnancy; therefore, it is especially important that the reproductive partner of a carrier be offered testing.

However, in rare cases, an individual who inherits an *ABCC8* mutation only from one’s father can be affected with focal FHI.<sup>1</sup> Symptoms are usually relatively mild and may not appear until as late as early adulthood. If only the male in a couple is a carrier, there appears to be a 1-2% chance for an affected child in each pregnancy.<sup>1</sup>





### **Who is at risk for Familial Hyperinsulinism, *ABCC8*?**

FHI can occur in individuals of virtually all races and ethnicities. In the Ashkenazi Jewish population, the incidence of *ABCC8*-related FHI is approximately 1 in 10,800 (for Diffuse-CHI) , and the carrier frequency is 1 in 52.<sup>2</sup>

If there is no family history, the risk for an individual to be a carrier depends on an individual's ethnic background.

### **What does a positive test result mean?**

If a gene mutation is identified, an individual should speak to a physician or genetics health professional about the implications of the result and appropriate testing for the reproductive partner and at-risk family members.

### **What does a negative test result mean?**

A negative result reduces, but does not eliminate, the possibility that an individual carries a gene mutation. The likelihood of being a carrier is also influenced by family history, medical symptoms, and other relevant test results.

### **Where can I get more information?**

- NIH Office of Rare Diseases Research – Genetic and Rare Diseases (GARD) Information Center: [http://www.rarediseases.info.nih.gov/GARD/Condition/3947/Familial\\_hyperinsulinism.aspx](http://www.rarediseases.info.nih.gov/GARD/Condition/3947/Familial_hyperinsulinism.aspx)

### **References**

1. Glaser B. Familial hyperinsulinism. *GeneReviews*. Available at <http://www.ncbi.nlm.nih.gov/books/NBK1375/>. Accessed: January 20, 2012.
2. Glaser B *et al*. *ABCC8* mutation allele frequency in the Ashkenazi Jewish population and risk of focal hyperinsulinemic hypoglycemia. *Genet Med*. 2011; 13(10): 891-894.

