ABCC8 Gene

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ATP binding cassette subfamily C member 8

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1. Normal Function

The *ABCC8* gene provides instructions for making the sulfonylurea receptor 1 (SUR1) protein. The SUR1 protein is one part (subunit) of the ATP-sensitive potassium (K-ATP) channel that is found across cell membranes in the beta cells of the pancreas. Beta cells secrete insulin, which is a hormone that helps control blood sugar levels. Insulin controls how much sugar (in the form of glucose) is passed from the bloodstream into cells to be used as energy. The K-ATP channel controls the secretion of insulin out of beta cells and into the bloodstream. These channels open and close in response to the amount of glucose in the bloodstream, which helps regulate insulin secretion and control blood sugar levels. The closing of the channels results in a process that triggers insulin secretion by beta cells.

2. Health Conditions Related to Genetic Changes

2.1 Congenital hyperinsulinism

More than 300 mutations in the *ABCC8* gene have been found to cause congenital hyperinsulinism. This condition causes frequent episodes of low blood sugar (hypoglycemia), decreased energy, and irritability. Most of these mutations change single protein building blocks (amino acids) in the SUR1 protein.

Some *ABCC8* mutations prevent the SUR1 protein from reaching the cell membrane, interfering with the proper formation of the K-ATP channel. Other mutations interfere with the K-ATP channel's function or its responses to outside molecules. Defective K-ATP channels lead to the constant release of insulin from beta cells. As a result, glucose is rapidly removed from the bloodstream. Without treatment, the hypoglycemia caused by congenital hyperinsulinism may result in serious complications such as intellectual disability and seizures.

2.2 Permanent neonatal diabetes mellitus

At least 14 mutations in the *ABCC8* gene have been identified in people with permanent neonatal diabetes mellitus. Individuals with this condition often have a low birth weight and develop increased blood sugar (hyperglycemia) within the first 6 months of life.

ABCC8 gene mutations that cause permanent neonatal diabetes mellitus change single amino acids in the protein sequence. These mutations result in K-ATP channels that do not close, leading to reduced insulin secretion from beta cells and impaired blood sugar control.

2.3 Maturity-onset diabetes of the young

MedlinePlus Genetics provides information about Maturity-onset diabetes of the young

2.4 Other disorders

Other *ABCC8* gene mutations that have a relatively mild effect on K-ATP channel function as compared to that seen in permanent neonatal diabetes mellitus (see above) cause a condition called transient neonatal diabetes mellitus. Infants with this condition have hyperglycemia during the first 6 months of life, but their blood sugar returns to normal by age 18 months. However, affected individuals usually develop hyperglycemia again during adolescence or early adulthood. As in permanent neonatal diabetes mellitus, *ABCC8* gene mutations that cause transient neonatal diabetes mellitus interfere with K-ATP channel closure and lead to a reduction in insulin secretion.

Some studies suggest that normal variations (polymorphisms) in the *ABCC8* gene are associated with an increased risk of type 2 diabetes, the most common form of diabetes. Other studies, however, have not found an association between *ABCC8* gene variants and type 2 diabetes. People with this disease have hyperglycemia because the body does not respond correctly to the insulin secreted from beta cells. Although changes in the *ABCC8* gene may be associated with type 2 diabetes, a combination of lifestyle, genetic, and environmental factors all play a part in determining the risk of this complex disorder.

3. Other Names for This Gene

- ABC36
- ABCC8_HUMAN
- ATP-binding cassette, sub-family C (CFTR/MRP), member 8
- ATP-binding cassette, sub-family C, member 8
- MRP8
- SUR
- SUR1
- TNDM2

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