KCNJ11 gene

potassium inwardly rectifying channel subfamily J member 11

Normal Function

The *KCNJ11* gene provides instructions for making parts (subunits) of the ATP-sensitive potassium (K-ATP) channel. Each K-ATP channel consists of eight subunits. Four subunits are produced from the *KCNJ11* gene, and four are produced from another gene called *ABCC8*.

K-ATP channels are found in beta cells, which are cells in the pancreas that secrete the hormone insulin. The K-ATP channels are embedded in cell membranes, where they open and close in response to the amount of glucose in the bloodstream. Glucose is a simple sugar and the primary energy source for most cells in the body. Closure of the K-ATP channels in response to increased glucose triggers the release of insulin out of beta cells and into the bloodstream, which helps control blood glucose levels.

Health Conditions Related to Genetic Changes

Congenital hyperinsulinism

More than 30 mutations in the *KCNJ11* gene have been found to cause congenital hyperinsulinism. This condition causes frequent episodes of low blood glucose (hypoglycemia), decreased energy, and irritability. Most of these mutations change single protein building blocks (amino acids) in the protein sequence, reducing or preventing activity of the K-ATP channels. Loss of K-ATP channel function leads 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.

Permanent neonatal diabetes mellitus

At least 30 mutations in the *KCNJ11* 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 glucose (hyperglycemia) within the first 6 months of life.

KCNJ11 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 glucose control.

Gestational diabetes

MedlinePlus Genetics provides information about Gestational diabetes

Maturity-onset diabetes of the young

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

Other disorders

Other *KCNJ11* 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 glucose 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, *KCNJ11* gene mutations that cause transient neonatal diabetes mellitus also interfere with K-ATP channel closure and lead to a reduction in insulin secretion.

A normal variation (polymorphism) in the *KCNJ11* gene is associated with an increased risk of type 2 diabetes, the most common form of diabetes. This variant leads to a change in the K-ATP channel, replacing the amino acid glutamic acid with the amino acid lysine at position 23, written as Glu23Lys or E23K. People with type 2 diabetes have hyperglycemia because the body does not respond correctly to the insulin secreted from beta cells. The same variant has also been associated with changes in the heart's response to stress, leading to an increased risk of heart failure. Although changes in the *KCNJ11* gene can be associated with type 2 diabetes and heart failure, a combination of lifestyle, genetic, and environmental factors all play a part in determining the risk of these complex disorders.

Other Names for This Gene

- ATP-sensitive inward rectifier potassium channel 11
- beta-cell inward rectifier subunit
- BIR
- HHF2
- IKATP
- inward rectifier K(+) channel Kir6.2
- inwardly rectifying potassium channel KIR6.2
- KIR6.2
- MGC133230
- potassium channel, inwardly rectifying subfamily J member 11

- potassium channel, inwardly rectifying subfamily J, member 11
- potassium inwardly-rectifying channel, subfamily J, member 11
- TNDM3

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of KCNJ11 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=3767[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28KCNJ11%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+360+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- TYPE 2 DIABETES MELLITUS; T2D (https://omim.org/entry/125853)
- POTASSIUM CHANNEL, INWARDLY RECTIFYING, SUBFAMILY J, MEMBER 11; KCNJ11 (https://omim.org/entry/600937)
- DIABETES MELLITUS, TRANSIENT NEONATAL, 3; TNDM3 (https://omim.org/entry/610582)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/3767)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=KCNJ11[gene])

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Genomic Location

The *KCNJ11* gene is found on chromosome 11 (https://medlineplus.gov/genetics/chrom osome/11/).

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