KCNJ5 gene

potassium inwardly rectifying channel subfamily J member 5

Normal Function

The *KCNJ5* gene provides instructions for making a protein that functions as a potassium channel, which means that it transports positively charged atoms (ions) of potassium (K^+) into and out of cells. Potassium channels produced from the *KCNJ5* gene are found in several tissues, including the adrenal glands, which are small hormone-producing glands located on top of each kidney. In these glands, the flow of ions creates an electrical charge across the cell membrane, which affects the triggering of certain biochemical processes that regulate aldosterone production. Aldosterone helps control blood pressure by maintaining proper salt and fluid levels in the body.

Health Conditions Related to Genetic Changes

Aldosterone-producing adenoma

Mutations in the *KCNJ5* gene cause about 40 percent of aldosterone-producing adenomas, which are noncancerous (benign) tumors that form in the adrenal glands. The genetic changes involved in these tumors, called somatic mutations, are acquired during a person's lifetime and are present only in adrenal gland cells that give rise to the tumor.

KCNJ5 gene mutations associated with this condition change single protein building blocks (amino acids) in the potassium channel. The altered potassium channels are less selective, allowing other ions, particularly sodium, to pass through. The flow of sodium ions into adrenal gland cells affects the electrical charge across the cell membrane, activating another type of channel that allows calcium ions to enter. The influx of calcium ions overactivates a process called the calcium/calmodulin pathway that increases aldosterone production, resulting in excess aldosterone and leading to high blood pressure (hypertension) and an increased risk of heart attack and stroke. Overactivation of the calcium/calmodulin pathway in the adrenal glands also increases cell growth and division (proliferation), which promotes adenoma formation.

Familial hyperaldosteronism

Inherited *KCNJ5* gene mutations have been identified in people with familial hyperaldosteronism type III. These mutations, known as germline mutations, are found

in every cell of the body. Familial hyperaldosteronism causes hypertension, and some affected individuals have abnormally large adrenal glands (adrenal hyperplasia). As in aldosterone-producing adenomas (described above), *KCNJ5* gene mutations result in production of less-selective potassium channels. The abnormal flow of ions through these channels leads to increased aldosterone production, causing hypertension.

Andersen-Tawil syndrome

MedlinePlus Genetics provides information about Andersen-Tawil syndrome

Romano-Ward syndrome

MedlinePlus Genetics provides information about Romano-Ward syndrome

Other Names for This Gene

- cardiac ATP-sensitive potassium channel
- CIR
- G protein-activated inward rectifier potassium channel 4
- GIRK4
- heart KATP channel
- inward rectifier K+ channel KIR3.4
- IRK-4
- KATP1
- KIR3.4
- LQT13
- potassium channel, inwardly rectifying subfamily J, member 5
- potassium inwardly-rectifying channel, subfamily J, member 5

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of KCNJ5 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=3762[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28KCNJ5%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+1800+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- POTASSIUM CHANNEL, INWARDLY RECTIFYING, SUBFAMILY J, MEMBER 5; KCNJ5 (https://omim.org/entry/600734)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/3762)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=KCNJ5[gene])

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Genomic Location

The *KCNJ5* gene is found on chromosome 11 (https://medlineplus.gov/genetics/chromosome/11/).

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