KCNH2 gene

potassium voltage-gated channel subfamily H member 2

Normal Function

The *KCNH2* gene belongs to a large family of genes that provide instructions for making potassium channels. These channels, which transport positively charged atoms (ions) of potassium out of cells, play key roles in a cell's ability to generate and transmit electrical signals.

The specific function of a potassium channel depends on its protein components and its location in the body. Channels made with KCNH2 proteins (also known as hERG1) are active in heart (cardiac) muscle. They are involved in recharging the cardiac muscle after each heartbeat to maintain a regular rhythm. The KCNH2 protein is also produced in nerve cells and certain immune cells (microglia) in the brain and spinal cord (central nervous system).

The proteins produced from the *KCNH2* gene and another gene, *KCNE2*, interact to form a functional potassium channel. Four alpha subunits, each produced from the *KCNH2* gene, form the structure of each channel. One beta subunit, produced from the *KCNE2* gene, attaches (binds) to the channel and regulates its activity.

Health Conditions Related to Genetic Changes

Romano-Ward syndrome

Mutations in the *KCNH2* gene can cause Romano-Ward syndrome, which is the most common form of a heart condition called long QT syndrome. Mutations in this gene account for approximately 25 percent of cases of Romano-Ward syndrome. In individuals with this condition, the heart muscle takes longer than usual to recharge between beats, which can lead to an abnormal heart rhythm (arrhythmia).

More than 900 *KCNH2* gene mutations that cause Romano-Ward syndrome have been identified. Some of these mutations change single protein building blocks (amino acids) in the KCNH2 protein, while other mutations delete several amino acids from the protein. These changes prevent the protein from assembling into ion channels or alter the channels' structure or function. As a result, the channels cannot properly regulate the flow of potassium ions in cardiac muscle cells. The reduced ion transport alters the transmission of electrical signals in the heart, increasing the risk of an irregular

heartbeat that can cause fainting (syncope) or sudden death.

Short QT syndrome

Mutations in the *KCNH2* gene can also cause a heart condition called short QT syndrome. In people with this condition, the cardiac muscle takes less time than usual to recharge between beats. This change increases the risk of an abnormal heart rhythm that can cause syncope or sudden death.

At least eight mutations in the *KCNH2* gene have been found to cause short QT syndrome in a small number of affected families. These mutations change single amino acids in the KCNH2 protein. The genetic changes alter the function of ion channels made with the KCNH2 protein, increasing the channels' activity. As a result, more potassium ions flow out of cardiac muscle cells at a critical time during the heartbeat, which can lead to an irregular heart rhythm.

Familial atrial fibrillation

MedlinePlus Genetics provides information about Familial atrial fibrillation

Other disorders

Certain drugs, including medications used to treat arrhythmias, infections, seizures, psychiatric disorders, and other problems can lead to an abnormal heart rhythm in some people. This drug-induced heart condition, which is known as acquired long QT syndrome, increases the risk of cardiac arrest and sudden death. A small percentage of cases of acquired long QT syndrome occur in people who have an underlying variation in the *KCNH2* gene.

Other Names for This Gene

- ERG1
- ether-a-go-go related gene potassium channel 1
- H-ERG
- HERG
- HERG1
- human ether a-go-go-related gene
- KCNH2_HUMAN
- Kv11.1
- LQT2
- potassium channel, voltage gated eag related subfamily H, member 2
- potassium voltage-gated channel, subfamily H (eag-related), member 2

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of KCNH2 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=3757[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28KCNH2%5BTI%5D%29+OR+%28hERG1%5BTI%5D%29%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, VOLTAGE-GATED, SUBFAMILY H, MEMBER 2; KCNH2 (https://omim.org/entry/152427)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/3757)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=KCNH2[gene])

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Genomic Location

The *KCNH2* gene is found on chromosome 7 (https://medlineplus.gov/genetics/chromosome/7/).

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