

KCNH2 Gene

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1. Introduction

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.

2. Health Conditions Related to Genetic Changes

2.1. 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.

2.2. 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.

2.3. 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.

3. 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

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