KCNQ1 Gene

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Potassium voltage-gated channel subfamily Q member 1

genes

1. Introduction

The *KCNQ1* 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 KCNQ1 proteins are primarily found in the inner ear and in heart (cardiac) muscle. In the inner ear, these channels help maintain the proper ion balance needed for normal hearing. In the heart, the channels are involved in recharging the cardiac muscle after each heartbeat to maintain a regular rhythm. The KCNQ1 protein is also produced in the kidney, lung, stomach, and intestine.

The KCNQ1 protein interacts with proteins in the KCNE family (such as the KCNE1 protein) to form functional potassium channels. Four alpha subunits made from KCNQ1 proteins form the structure of each channel. One beta subunit, made from a KCNE protein, attaches (binds) to the channel and regulates its activity.

2. Health Conditions Related to Genetic Changes

2.1. Familial Atrial Fibrillation

Changes in the *KCNQ1* gene are an uncommon cause of familial atrial fibrillation, a disruption of the heart's normal rhythm (arrhythmia) characterized by uncoordinated electrical activity in the heart's upper chambers (the atria). Several mutations have been found to cause the condition; these genetic changes alter single protein building blocks (amino acids) in the KCNQ1 protein. In cardiac muscle cells, the mutations appear to increase the flow of potassium ions through the channel formed with the KCNQ1 protein. The enhanced ion transport can disrupt the heart's normal rhythm, resulting in atrial fibrillation.

2.2. Jervell and Lange-Nielsen Syndrome

More than 30 *KCNQ1* gene mutations have been found to cause Jervell and Lange-Nielsen syndrome, a condition that causes arrhythmia and profound hearing loss from birth. About 90 percent of cases are caused by mutations in this gene. These mutations are typically present in both copies of the *KCNQ1* gene in each cell. Most of these changes lead to the production of an abnormally short, nonfunctional version of the KCNQ1 protein that cannot be used to build potassium channels. Other mutations change a small number of amino acids in this protein, which alters the normal structure and function of the channels. An inability of these channels to properly transport potassium ions in the inner ear and cardiac muscle leads to the hearing loss and arrhythmia characteristic of Jervell and Lange-Nielsen syndrome.

2.3. Romano-Ward Syndrome

Mutations in the *KCNQ1* gene are thought to be the most common cause of Romano-Ward syndrome, accounting for approximately one-third of cases. This condition is a form of arrhythmia called long QT syndrome. In people with Romano-Ward syndrome, the heart muscle takes longer than usual to recharge between beats.

More than 600 *KCNQ1* gene mutations that cause Romano-Ward syndrome have been identified. The mutations that cause Romano-Ward syndrome are typically present in only one copy of the *KCNQ1* gene in each cell. Most of these mutations change single amino acids in the KCNQ1 protein or insert or delete a small number of amino acids. These changes allow the protein to form channels but reduce the channels' ability to transport potassium ions out of 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.

2.4. Short QT Syndrome

At least two mutations in the *KCNQ1* gene can 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.

The *KCNQ1* gene mutations associated with short QT syndrome change single amino acids in the KCNQ1 protein. The mutations alter the function of ion channels made with the KCNQ1 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.

2.5. Other Disorders

Mutations in the *KCNQ1* gene have been associated with several other conditions related to heart rhythm abnormalities, including sudden infant death syndrome (SIDS) and acquired long QT syndrome.

SIDS is a major cause of death in babies younger than one year. It is characterized by sudden and unexplained death, usually during sleep. Although the cause of SIDS is often unknown, researchers have identified mutations in

the *KCNQ1* gene in a few cases of this condition. Other genetic and environmental factors, many of which have not been identified, also play a part in determining the risk of SIDS.

Certain drugs, including medications used to treat arrhythmias, infections, seizures, and psychotic disorders, 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 *KCNQ1* gene.

3. Other Names for This Gene

- ATFB1
- IKs producing slow voltage-gated potassium channel alpha subunit KvLQT1
- JLNS1
- KCNA8
- KCNA9
- KCNQ1_HUMAN
- KQT-like 1
- Kv1.9
- Kv7.1
- KVLQT1
- LQT1
- potassium channel, voltage gated KQT-like subfamily Q, member 1
- potassium voltage-gated channel, KQT-like subfamily, member 1

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