KCNJ2 Gene

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1. Introduction

The *KCNJ2* gene belongs to a large family of genes that provide instructions for making potassium channels. These channels, which transport positively charged potassium ions 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 the KCNJ2 protein are active in muscles used for movement (skeletal muscles) and in heart (cardiac) muscle. In skeletal muscle, these channels play an important role in the pattern of muscle tensing (contraction) and relaxation that allows the body to move. In the heart, the channels are involved in recharging the cardiac muscle after each heartbeat to maintain a regular rhythm. Channels formed with the KCNJ2 protein may also be involved in bone development, but their role in this process is unclear.

Researchers have determined that a molecule called PIP2 must attach (bind) to channels made with the KCNJ2 protein for the channels to function normally. PIP2 activates the ion channel and helps it stay open, which allows ions to flow across the cell membrane.

2. Health Conditions Related to Genetic Changes

2.1. Andersen-Tawil Syndrome

More than 60 mutations in the *KCNJ2* gene have been found to cause Andersen-Tawil syndrome, a disorder characterized by episodes of muscle weakness (periodic paralysis), changes in heart rhythm (arrhythmia), and physical abnormalities affecting the face, other parts of the head, and the limbs. Most of the mutations change a single protein building block (amino acid) in the KCNJ2 protein.

Mutations in the *KCNJ2* gene lead to the production of a nonfunctional potassium channel. Some mutations change the shape of the channel so it cannot transport potassium ions, while other mutations prevent the channels from being inserted correctly into the cell membrane. Many *KCNJ2* mutations prevent PIP2 from effectively binding to and activating potassium channels. If the KCNJ2 protein is unable to bind to PIP2, the channels remain closed and potassium ions are unable to flow across the cell membrane. Researchers believe that problems with PIP2 binding are a major cause of Andersen-Tawil syndrome.

A loss of this channel's function in skeletal and cardiac muscle cells disrupts the normal flow of potassium ions out of these cells, resulting in periodic paralysis and an irregular heart rhythm. It is not known how mutations in the *KCNJ2* gene contribute to the physical abnormalities often found in Andersen-Tawil syndrome.

2.2. Short QT Syndrome

Mutations in the *KCNJ2* gene can also cause a heart condition called short QT syndrome, which is a type of arrhythmia. In people with this condition, the cardiac muscle takes less time than usual to recharge between beats. This change increases the risk of abnormal heart rhythm that can cause fainting or sudden death.

At least two mutations in the *KCNJ2* gene have been found to cause short QT syndrome in a small number of affected families. These mutations change single amino acids in the KCNJ2 protein, which increases the activity of channels made with this protein. 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.

3. Other Names for This Gene

- cardiac inward rectifier potassium channel
- HHBIRK1
- HHIRK1
- HIRK1
- inward rectifier K+ channel KIR2.1
- IRK1
- IRK2_HUMAN
- KIR2.1
- LQT7
- potassium channel, inwardly rectifying subfamily J, member 2
- potassium inwardly-rectifying channel J2
- potassium inwardly-rectifying channel, subfamily J, member 2

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