CACNA1C Gene

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calcium voltage-gated channel subunit alpha1 C

genes

1. Normal Function

The *CACNA1C* gene provides instructions for making one of several calcium channels. Calcium channels, which transport positively charged calcium atoms (calcium ions) into cells, play a key role in a cell's ability to generate electrical signals. Calcium ions are important for many cellular functions, including regulating the electrical activity of cells, cell-to-cell communication, the tensing of muscle fibers (muscle contraction), and the regulation of certain genes, particularly those involved in the development of the brain and bones before birth.

The calcium channel produced from the *CACNA1C* gene is known as CaV1.2. These channels are found in many types of cells, although they appear to be particularly important for the function of heart cells (cardiomyocytes) and nerve cells (neurons) in the brain. In the heart, CaV1.2 channels open and close at specific times to control the flow of calcium ions into cardiomyocytes at each heartbeat. How long the channels are open and closed is regulated to maintain normal heart function. In the brain, CaV1.2 channels are thought to be involved in memory, the fear response, and the rapid transmission of nerve signals; however, the role of these channels in the brain and other tissues is not completely understood.

Researchers have discovered that many different versions (isoforms) of the CaV1.2 channel can be produced from the *CACNA1C* gene by a mechanism called alternative splicing. This mechanism produces different versions of the channel by cutting and rearranging the genetic instructions in different ways. Some versions of the CaV1.2 channel are more common than others in certain parts of the body. For example, in the heart and brain, about 80 percent of CaV1.2 channels are made with a particular segment known as exon 8. The other 20 percent of CaV1.2 channels contain a slightly different version of this segment, known as exon 8A. This difference becomes important when researchers are studying the effects of *CACNA1C* mutations in various tissues.

2. Health Conditions Related to Genetic Changes

2.1. Short QT Syndrome

Short QT syndrome

2.2. Timothy Syndrome

Mutations in the *CACNA1C* gene have been found to cause Timothy syndrome. This condition primarily affects the heart but can affect many other areas of the body, including the fingers and toes, teeth, nervous system, and immune system. Timothy syndrome is characterized by a heart condition called long QT syndrome, which causes the heart (cardiac) muscle to take longer than usual to recharge between beats. This abnormality in the heart's electrical system can cause severe abnormalities of the heart rhythm (arrhythmias), which can lead to sudden death.

Mutations in the *CACNA1C* gene change the structure of CaV1.2 channels throughout the body. The altered channels stay open much longer than usual, which allows calcium ions to continue flowing into cells abnormally. The resulting overload of calcium ions within cardiac muscle cells changes the way the heart beats and can cause abnormal heart muscle contraction and arrhythmia. It is thought that the altered channels and calcium ion flow also impair regulation of certain genes during development, resulting in the facial, dental, and neurological abnormalities in Timothy syndrome.

In some cases, people with *CACNA1C* gene mutations have long QT syndrome without the other features of Timothy syndrome. It is unclear why some people have only heart problems while other have additional features.

2.3. Brugada Syndrome

Brugada syndrome

2.4. Other Disorders

Mutations in the *CACNA1C* gene have also been identified in people with a condition called long QT syndrome 8. These individuals have arrhythmia that can lead to fainting (syncope) or cardiac arrest and sudden death without the other features of Timothy syndrome (described above). Research suggests that *CACNA1C* gene mutations that cause long QT syndrome 8 occur in a different part of the gene than those that cause Timothy syndrome. While these *CACNA1C* gene mutations alter CaV1.2 channels and calcium channel flow, it is unclear why they cause only heart problems.

3. Other Names for This Gene

- CAC1C_HUMAN
- CACH2
- CACN2
- CACNL1A1
- calcium channel, cardic dihydropyridine-sensitive, alpha-1 subunit
- calcium channel, L type, alpha 1 polypeptide, isoform 1, cardic muscle
- calcium channel, voltage-dependent, L type, alpha 1C subunit

- CaV1.2
- CCHL1A1
- DHPR, alpha-1 subunit
- MGC120730
- voltage-dependent L-type calcium channel alpha 1C subunit
- voltage-gated calcium channel alpha subunit Cav1.2

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