CACNA1C Timothy syndrome

https://medlineplus.gov/genetics/gene/cacna1c/

You Are Here:

Home

→

Genetics

→

Genes

→

CACNA1C gene

CACNA1C gene

calcium voltage-gated channel subunit alpha1 C

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.

Health Conditions Related to Genetic Changes

Short QT syndrome

MedlinePlus Genetics provides information about Short QT syndrome

More About This Health Condition

Timothy syndrome

Variants (also known as 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.Variants 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 variants 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.

More About This Health Condition

Brugada syndrome

MedlinePlus Genetics provides information about Brugada syndrome

More About This Health Condition

Other disorders

Variants 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 variants that cause long QT syndrome 8 occur in a different part of the gene than those that cause Timothy syndrome. While these CACNA1C gene variants alter CaV1.2 channels and calcium channel flow, it is unclear why they cause only heart problems.Other variants in the CACNA1C gene have been found in individuals with a condition known as CACNA1C-related disorder. People with this condition have some but not all of the features of Timothy syndrome. These features can include seizures, intellectual disability, autism spectrum disorder, anxiety, and walking difficulty. Individuals with this condition can also experience delayed speech, language or motor skills. Some affected individuals have heart problems separate from long QT syndrome. The severity of CACNA1C-related disorder varies greatly; some people with the condition are mildly affected with only a few features whereas others have many features and are severely affected.

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

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

Tests of CACNA1C

Scientific Articles on PubMed

PubMed

Catalog of Genes and Diseases from OMIM

CALCIUM CHANNEL, VOLTAGE-DEPENDENT, L TYPE, ALPHA-1C SUBUNIT; CACNA1C

LONG QT SYNDROME 8; LQT8

Gene and Variant Databases

NCBI Gene

ClinVar

References

Bozarth X, Dines JN, Cong Q, Mirzaa GM, Foss K, Lawrence Merritt J 2nd, Thies J, Mefford HC, Novotny E. Expanding clinical phenotype in CACNA1C related disorders: From neonatal onset severe epileptic encephalopathy to late-onset epilepsy. Am J Med Genet A. 2018 Dec;176(12):2733-2739. doi: 10.1002/ajmg.a.40657. Epub 2018 Dec 4. Citation on PubMed

Fukuyama M, Wang Q, Kato K, Ohno S, Ding WG, Toyoda F, Itoh H, Kimura H, Makiyama T, Ito M, Matsuura H, Horie M. Long QT syndrome type 8: novel CACNA1C mutations causing QT prolongation and variant phenotypes. Europace. 2014 Dec;16(12):1828-37. doi: 10.1093/europace/euu063. Epub 2014 Apr 12. Citation on PubMed

Gardner RJM, Crozier IG, Binfield AL, Love DR, Lehnert K, Gibson K, Lintott CJ, Snell RG, Jacobsen JC, Jones PP, Waddell-Smith KE, Kennedy MA, Skinner JR. Penetrance and expressivity of the R858H CACNA1C variant in a five-generation

pedigree segregating an arrhythmogenic channelopathy. Mol Genet Genomic Med. 2019 Jan;7(1):e00476. doi: 10.1002/mgg3.476. Epub 2018 Oct 21. Citation on PubMed or Free article on PubMed Central

Liao P, Yong TF, Liang MC, Yue DT, Soong TW. Splicing for alternative structures of Cav1.2 Ca2+ channels in cardiac and smooth muscles. Cardiovasc Res. 2005 Nov 1;68(2):197-203. doi: 10.1016/j.cardiores.2005.06.024. Epub 2005 Jul 27. Citation on PubMed

Napolitano C, Antzelevitch C. Phenotypical manifestations of mutations in the genes encoding subunits of the cardiac voltage-dependent L-type calcium channel. Circ Res. 2011 Mar 4;108(5):607-18. doi: 10.1161/CIRCRESAHA.110.224279. Citation on PubMed or Free article on PubMed Central

Napolitano C, Timothy KW, Bloise R, Priori SG. CACNA1C-Related Disorders. 2006 Feb 15 [updated 2021 Feb 11]. In: Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE, Bean LJH, Gripp KW, Amemiya A, editors. GeneReviews(R) [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. Available from http://www.ncbi.nlm.nih.gov/books/NBK1403/ Citation on PubMed

Paar V, Jirak P, Larbig R, Zagidullin NS, Brandt MC, Lichtenauer M, Hoppe UC, Motloch LJ. Pathophysiology of Calcium Mediated Ventricular Arrhythmias and Novel Therapeutic Options with Focus on Gene Therapy. Int J Mol Sci. 2019 Oct 24;20(21):5304. doi: 10.3390/ijms20215304. Citation on PubMed or Free article on PubMed Central

Rodan LH, Spillmann RC, Kurata HT, Lamothe SM, Maghera J, Jamra RA, Alkelai A, Antonarakis SE, Atallah I, Bar-Yosef O, Bilan F, Bjorgo K, Blanc X, Van Bogaert P, Bolkier Y, Burrage LC, Christ BU, Granadillo JL, Dickson P, Donald KA, Dubourg C, Eliyahu A, Emrick L, Engleman K, Gonfiantini MV, Good JM, Kalser J, Kloeckner C, Lachmeijer G, Macchiaiolo M, Nicita F, Odent S, O'Heir E, Ortiz-Gonzalez X, Pacio-Miguez M, Palomares-Bralo M, Pena L, Platzer K, Quinodoz M, Ranza E,

Rosenfeld JA, Roulet-Perez E, Santani A, Santos-Simarro F, Pode-Shakked B, Skraban C, Slaugh R, Superti-Furga A, Thiffault I, van Jaabrsveld RH, Vincent M, Wang HG, Zacher P; Undiagnosed Diseases Network; Rush E, Pitt GS, Au PYB, Shashi V. Phenotypic expansion of CACNA1C-associated disorders to include isolated neurological manifestations. Genet Med. 2021 Oct;23(10):1922-1932. doi: 10.1038/s41436-021-01232-8. Epub 2021 Jun 23. Erratum In: Genet Med. 2021 Sep 14;: Citation on PubMed

Splawski I, Timothy KW, Decher N, Kumar P, Sachse FB, Beggs AH, Sanguinetti MC, Keating MT. Severe arrhythmia disorder caused by cardiac L-type calcium channel mutations. Proc Natl Acad Sci U S A. 2005 Jun 7;102(23):8089-96; discussion 8086-8. doi: 10.1073/pnas.0502506102. Epub 2005 Apr 29. Citation on PubMed or Free article on PubMed Central

Splawski I, Timothy KW, Sharpe LM, Decher N, Kumar P, Bloise R, Napolitano C, Schwartz PJ, Joseph RM, Condouris K, Tager-Flusberg H, Priori SG, Sanguinetti MC, Keating MT. Ca(V)1.2 calcium channel dysfunction causes a multisystem disorder including arrhythmia and autism. Cell. 2004 Oct 1;119(1):19-31. doi: 10.1016/j.cell.2004.09.011. Citation on PubMed

Wemhoner K, Friedrich C, Stallmeyer B, Coffey AJ, Grace A, Zumhagen S, Seebohm G, Ortiz-Bonnin B, Rinne S, Sachse FB, Schulze-Bahr E, Decher N. Gain-of-function mutations in the calcium channel CACNA1C (Cav1.2) cause non-syndromic long-QT but not Timothy syndrome. J Mol Cell Cardiol. 2015 Mar;80:186-95. doi: 10.1016/j.yjmcc.2015.01.002. Epub 2015 Jan 26. Citation on PubMed

Yamakage M, Namiki A. Calcium channels--basic aspects of their structure, function and gene encoding; anesthetic action on the channels--a review. Can J Anaesth. 2002 Feb;49(2):151-64. doi: 10.1007/BF03020488. Citation on PubMed

Genomic LocationThe CACNA1C gene is found on chromosome 12.

Related Health Topics

Genes and Gene Therapy

Genetic Disorders

MEDICAL ENCYCLOPEDIA

Genes

Genetics

Understanding Genetics

What is DNA?

What is a gene?

What is a gene variant and how do variants occur?

Disclaimers

MedlinePlus links to health information from the National Institutes of Health and other federal

government agencies. MedlinePlus also links to health information from non-government Web sites. See our disclaimer about external links and our quality guidelines.

The information on this site should not be used as a substitute for professional medical care or advice. Contact a health care provider if you have questions about your health.

Learn how to cite this page