

KCNJ2 gene

potassium inwardly rectifying channel subfamily J member 2

Normal Function

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.

Health Conditions Related to Genetic Changes

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.

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.

Familial atrial fibrillation

MedlinePlus Genetics provides information about Familial atrial fibrillation

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

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of KCNJ2 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=3759\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=3759[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28KCNJ2%5BTI%5D%29+OR+%28%28KIR2.1%5BTI%5D%29+OR+%28LQT7%5BTI%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D>)

Catalog of Genes and Diseases from OMIM

- POTASSIUM CHANNEL, INWARDLY RECTIFYING, SUBFAMILY J, MEMBER 2; KCNJ2 (<https://omim.org/entry/600681>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/3759>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=KCNJ2\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=KCNJ2[gene]))

References

- Bendahhou S, Donaldson MR, Plaster NM, Tristani-Firouzi M, Fu YH, Ptacek LJ. Defective potassium channel Kir2.1 trafficking underlies Andersen-Tawil syndrome. *J Biol Chem*. 2003 Dec 19;278(51):51779-85. doi: 10.1074/jbc.M310278200. Epub 2003 Oct 1. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/14522976>)
- Casini S, Postma AV. Decreased inward rectification of Kir2.1 channels is a novel mechanism underlying the short QT syndrome. *Cardiovasc Res*. 2012 Mar 15;93(4):535-6. doi: 10.1093/cvr/cvs084. Epub 2012 Feb 5. No abstract available. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/22311718>)
- Chun TU, Epstein MR, Dick M 2nd, Andelfinger G, Ballester L, Vanoye CG, George AL Jr, Benson DW. Polymorphic ventricular tachycardia and KCNJ2 mutations. *Heart Rhythm*. 2004 Jul;1(2):235-41. doi: 10.1016/j.hrthm.2004.02.017. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15851159>)
- Donaldson MR, Jensen JL, Tristani-Firouzi M, Tawil R, Bendahhou S, Suarez WA, Cobo AM, Poza JJ, Behr E, Wagstaff J, Szepietowski P, Pereira S, Mozaffar T, Escolar DM, Fu YH, Ptacek LJ. PIP2 binding residues of Kir2.1 are common targets of mutations causing Andersen syndrome. *Neurology*. 2003 Jun 10;60(11):1811-6. doi: 10.1212/01.wnl.0000072261.14060.47. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12796536>)
- Hattori T, Makiyama T, Akao M, Ehara E, Ohno S, Iguchi M, Nishio Y, Sasaki K, Itoh H, Yokode M, Kita T, Horie M, Kimura T. A novel gain-of-function KCNJ2 mutation associated with short-QT syndrome impairs inward rectification of Kir2.1 currents. *Cardiovasc Res*. 2012 Mar 15;93(4):666-73. doi: 10.1093/cvr/cvr329. Epub 2011 Dec

8. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/22155372>)

- Kimura H, Zhou J, Kawamura M, Itoh H, Mizusawa Y, Ding WG, Wu J, Ohno S, Makiyama T, Miyamoto A, Naiki N, Wang Q, Xie Y, Suzuki T, Tateno S, Nakamura Y, Zang WJ, Ito M, Matsuura H, Horie M. Phenotype variability in patients carrying KCNJ2 mutations. *Circ Cardiovasc Genet*. 2012 Jun;5(3):344-53. doi:10.1161/CIRCGENETICS.111.962316. Epub 2012 May 15. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/22589293>)
- Nguyen HL, Pieper GH, Wilders R. Andersen-Tawil syndrome: clinical and molecular aspects. *Int J Cardiol*. 2013 Dec 5;170(1):1-16. doi:10.1016/j.ijcard.2013.10.010. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/24383070>)
- Plaster NM, Tawil R, Tristani-Firouzi M, Canun S, Bendahhou S, Tsunoda A, Donaldson MR, Iannaccone ST, Brunt E, Barohn R, Clark J, Deymeer F, George AL Jr, Fish FA, Hahn A, Nitu A, Ozdemir C, Serdaroglu P, Subramony SH, Wolfe G, Fu YH, Ptacek LJ. Mutations in Kir2.1 cause the developmental and episodic electrical phenotypes of Andersen's syndrome. *Cell*. 2001 May 18;105(4):511-9. doi:10.1016/s0092-8674(01)00342-7. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/11371347>)
- Priori SG, Pandit SV, Rivolta I, Berenfeld O, Ronchetti E, Dhamoon A, Napolitano C, Anumonwo J, di Barletta MR, Gudapakkam S, Bosi G, Stramba-Badiale M, Jalife J. A novel form of short QT syndrome (SQT3) is caused by a mutation in the KCNJ2 gene. *Circ Res*. 2005 Apr 15;96(7):800-7. doi:10.1161/01.RES.0000162101.76263.8c. Epub 2005 Mar 10. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15761194>)
- Schulze-Bahr E. Short QT syndrome or Andersen syndrome: Yin and Yang of Kir2.1 channel dysfunction. *Circ Res*. 2005 Apr 15;96(7):703-4. doi:10.1161/01.RES.0000164186.86838.09. No abstract available. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15831819>)
- Tristani-Firouzi M, Jensen JL, Donaldson MR, Sansone V, Meola G, Hahn A, Bendahhou S, Kwiecinski H, Fidzianska A, Plaster N, Fu YH, Ptacek LJ, Tawil R. Functional and clinical characterization of KCNJ2 mutations associated with LQT7 (Andersen syndrome). *J Clin Invest*. 2002 Aug;110(3):381-8. doi: 10.1172/JCI15183. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12163457>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC151085/>)
- Veerapandiyani A, Statland JM, Tawil R. Andersen-Tawil Syndrome. 2004 Nov 22 [updated 2018 Jun 7]. 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/NBK1264/> Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/20301441>)

Genomic Location

The *KCNJ2* gene is found on chromosome 17 (<https://medlineplus.gov/genetics/chromosome/17/>).

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