ABCC9 Gene

Subjects: Genetics & Heredity
Contributor: Bruce Ren

ATP binding cassette subfamily C member 9

Keywords: genes

1. Normal Function

The *ABCC9* gene provides instructions for making the sulfonylurea receptor 2 (SUR2) protein. This protein forms one part (subunit) of a channel that transports charged atoms of potassium (potassium ions) across cell membranes. Each of these channels consists of eight subunits: four SUR2 proteins and four proteins produced from either the *KCNJ8* or *KCNJ11* gene. The SUR2 subunits regulate the activity of the channel, determining whether it is open or closed.

Channels made with the SUR2 protein are known as ATP-sensitive potassium (K-ATP) channels. The channels open and close in response to the amount of ATP, the cell's main energy source, inside the cell. The resulting transport of potassium ions is part of a complex network of signals that relay chemical messages into and out of cells.

Although K-ATP channels are present in cells and tissues throughout the body, the highest levels of SUR2-containing channels are found in skeletal and heart (cardiac) muscle. These channels indirectly help regulate the concentration of calcium ions in cells. This regulation is essential for normal heart function. The function of these channels in other tissues is unclear.

2. Health Conditions Related to Genetic Changes

2.1 Cantú syndrome

At least 14 mutations in the *ABCC9* gene have been found to cause Cantú syndrome, a rare condition characterized by excess hair growth (hypertrichosis), a distinctive facial appearance, and heart defects. Each of the mutations changes a single protein building block (amino acid) in the SUR2 protein. These changes likely alter the structure of the protein and its ability to regulate the activity of K-ATP channels. Studies suggest that the abnormal channels are open when they should be closed. However, it is unknown how this problem with potassium channel function leads to excess hair growth, heart defects, and the other features of Cantú syndrome.

2.2 Familial atrial fibrillation

MedlinePlus Genetics provides information about Familial atrial fibrillation

2.3 Familial dilated cardiomyopathy

MedlinePlus Genetics provides information about Familial dilated cardiomyopathy

2.4 Other disorders

At least two mutations in the *ABCC9* gene have been identified in people with dilated cardiomyopathy, a form of heart disease that enlarges and weakens the cardiac muscle, preventing the heart from pumping blood efficiently. Signs and symptoms of this condition can include an irregular heartbeat (arrhythmia), shortness of breath, extreme tiredness (fatigue), and swelling of the legs and feet. Research suggests that each mutation changes the structure of the SUR2 protein and disrupts the regulation of the K-ATP channel. Although K-ATP channels appear to play an important role in cardiac muscle, little is known about how malfunctioning channels are related to dilated cardiomyopathy.

3. Other Names for This Gene

- ABC37
- ABCC9_HUMAN
- ATFB12
- ATP-binding cassette sub-family C member 9
- ATP-binding cassette sub-family C member 9 isoform SUR2A
- ATP-binding cassette sub-family C member 9 isoform SUR2B
- ATP-binding cassette transporter sub-family C member 9
- ATP-binding cassette, sub-family C (CFTR/MRP), member 9
- CANTU
- CMD1O
- sulfonylurea receptor 2
- SUR2

References

1. Bienengraeber M, Olson TM, Selivanov VA, Kathmann EC, O'Cochlain F, Gao F,Karger AB, Ballew JD, Hodgson DM, Zingman LV, Pang YP, Alekseev AE, Terzic A.ABCC9 mutations identified in human dilated cardiomyopathy disrupt catalytic KATPchannel gating. Nat Genet. 2004 Apr;36(4):382-7.
2. Bryan J, Muñoz A, Zhang X, Düfer M, Drews G, Krippeit-Drews P, Aguilar-BryanL. ABCC8 and ABCC9: ABC transporters that regulate K+ channels. Pflugers Arch.2007 Feb;453(5):703-18.
3. Harakalova M, van Harssel JJ, Terhal PA, van Lieshout S, Duran K, Renkens I,Amor DJ, Wilson LC, Kirk EP, Turner CL, Shears D, Garcia-Minaur S, Lees MM, Ross A, Venselaar H, Vriend G, Takanari H, Rook MB, van der Heyden MA, Asselbergs FW, Breur HM, Swinkels ME, Scurr IJ, Smithson SF, Knoers NV, van der Smagt JJ, NijmanIJ, Kloosterman WP, van Haelst MM, van Haaften G, Cuppen E. Dominant missensemutations in ABCC9 cause Cantú syndrome. Nat Genet. 2012 May 18;44(7):793-6. doi:10.1038/ng.2324.
4. Solbach TF, König J, Fromm MF, Zolk O. ATP-binding cassette transporters inthe heart. Trends Cardiovasc Med. 2006 Jan;16(1):7-15. Review.
5. van Bon BW, Gilissen C, Grange DK, Hennekam RC, Kayserili H, Engels H, ReutterH, Ostergaard JR, Morava E, Tsiakas K, Isidor B, Le Merrer M, Eser M, Wieskamp N,de Vries P, Steehouwer M, Veltman JA, Robertson SP, Brunner HG, de Vries BB,Hoischen A. Cantú syndrome is caused by mutations in ABCC9. Am J Hum Genet. 2012 Jun 8;90(6):1094-101. doi: 10.1016/j.ajhg.2012.04.014.