SLC12A6 gene

solute carrier family 12 member 6

Normal Function

The *SLC12A6* gene provides instructions for making a protein called KCC3, a K-Cl co-transporter present in several organs. This protein is involved in moving charged atoms (ions) of potassium (K) and chlorine (Cl) across the cell membrane. The positively charged potassium ions and negatively charged chlorine ions are moved together (co-transported), so that the charges inside and outside the cell membrane are unchanged (electroneutral).

Electroneutral co-transport of ions across cell membranes is involved in many functions of the body. While the specific function of the KCC3 protein is unknown, it seems to be critical for the development and maintenance of nerve tissue and axons, which are specialized extensions of neurons that transmit nerve impulses throughout the nervous system. KCC3 may be involved in regulating the amounts of potassium, chlorine, or water in cells and intercellular spaces. The KCC3 protein may also help regulate the activity of other proteins that are sensitive to ion concentrations.

Health Conditions Related to Genetic Changes

Andermann syndrome

Several *SLC12A6* gene variants (mutations) have been identified in people with Andermann syndrome. This condition damages the nerves used for muscle movement and sensation (motor and sensory neuropathy). Almost all affected individuals of French-Canadian descent have the same variant in both copies of the *SLC12A6* gene, in which the DNA building block (nucleotide) guanine is deleted at position 2436 (written as 2436delG). This variant is common in the populations of the Saguenay-Lac-St.-Jean and Charlevoix regions of northeastern Quebec. Most *SLC12A6* gene variants that cause Andermann syndrome result in a KCC3 protein that is shortened and nonfunctional.

The lack of functional protein produced from the *SLC12A6* gene is believed to interfere with the development of the left and right halves of the brain (corpus callosum) and maintenance of the nerves that transmit signals needed for movement and sensation, resulting in the signs and symptoms of Andermann syndrome.

Charcot-Marie-Tooth disease

MedlinePlus Genetics provides information about Charcot-Marie-Tooth disease

Other Names for This Gene

- ACCPN
- DKFZP434D2135
- KCC3
- KCC3A
- KCC3B
- potassium chloride cotransporter 3
- potassium chloride cotransporter KCC3a-S3
- S12A6_HUMAN
- solute carrier family 12 (potassium/chloride transporter), member 6
- solute carrier family 12 (potassium/chloride transporters), member 6
- solute carrier family 12, member 6

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of SLC12A6 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=9990[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28SLC12A6%5BTIAB%5D%29+OR+%28%28KCC3%5BTIAB%5D%29+OR+%28ACCPN%5BTIAB%5D%29+OR+%28KCC3A%5BTIAB%5D%29+OR+%28KCC3B%5BTIAB%5D%29+OR+%28potassium+chloride+cotransporter+3%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- SOLUTE CARRIER FAMILY 12 (POTASSIUM/CHLORIDE TRANSPORTER), MEMBER 6; SLC12A6 (https://omim.org/entry/604878)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/9990)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=SLC12A6[gene])

References

- Ando M, Higuchi Y, Yuan J, Yoshimura A, Taniguchi T, Takei J, Takeuchi M, Hiramatsu Y, Shimizu F, Kubota M, Takeshima A, Ueda T, Koh K, Nagaoka U, Tokashiki T, Sawai S, Sakiyama Y, Hashiguchi A, Sato R, Kanda T, Okamoto Y, Takashima H. Novel heterozygous variants of SLC12A6 in Japanese families withCharcot-Marie-Tooth disease. Ann Clin Transl Neurol. 2022 Jul;9(7):902-911. doi:10.1002/acn3.51603. Epub 2022 Jun 22. Citation on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/35733399)
- Dupre N, Howard HC, Mathieu J, Karpati G, Vanasse M, Bouchard JP, Carpenter S, Rouleau GA. Hereditary motor and sensory neuropathy with agenesis of the corpuscallosum. Ann Neurol. 2003 Jul;54(1):9-18. doi: 10.1002/ana.77777. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/12838516)
- Gauvreau C, Brisson JD, Dupre N. Hereditary Motor and Sensory Neuropathy withAgenesis of the Corpus Callosum. 2006 Feb 2 [updated 2020 Sep 17]. In: Adam MP,Feldman J, Mirzaa GM, Pagon RA, Wallace SE, Bean LJH, Gripp KW, Amemiya A,editors. GeneReviews(R) [Internet]. Seattle (WA): University ofWashington, Seattle; 1993-2024. Available fromhttp://www.ncbi.nlm.nih.gov/books/NBK1372/ Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20301546)
- Hebert SC, Mount DB, Gamba G. Molecular physiology of cation-coupled Cl- cotransport: the SLC12 family. Pflugers Arch. 2004 Feb;447(5):580-93. doi:10.1007/s00424-003-1066-3. Epub 2003 May 9. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/12739168)
- Howard HC, Mount DB, Rochefort D, Byun N, Dupre N, Lu J, Fan X, Song L,Riviere JB, Prevost C, Horst J, Simonati A, Lemcke B, Welch R, England R, ZhanFQ, Mercado A, Siesser WB, George AL Jr, McDonald MP, Bouchard JP, Mathieu J, Delpire E, Rouleau GA. The K-Cl cotransporter KCC3 is mutant in a severeperipheral neuropathy associated with agenesis of the corpus callosum. Nat Genet.2002 Nov;32(3):384-92. doi: 10.1038/ng1002. Epub 2002 Oct 7. Erratum In: NatGenet 2002 Dec;32(4):681. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/12368912)
- Kahle KT, Flores B, Bharucha-Goebel D, Zhang J, Donkervoort S, Hegde M, Hussain G, Duran D, Liang B, Sun D, Bonnemann CG, Delpire E. Peripheral motorneuropathy is associated with defective kinase regulation of the KCC3cotransporter. Sci Signal. 2016 Aug 2;9(439):ra77. doi:10.1126/scisignal.aae0546. Citation on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/27485015)
- Meyer J, Johannssen K, Freitag CM, Schraut K, Teuber I, Hahner A, Mainhardt C, Mossner R, Volz HP, Wienker TF, McKeane D, Stephan DA, Rouleau G, Reif A, LeschKP. Rare variants of the gene encoding the potassium chloride co-transporter 3are associated with bipolar disorder. Int J Neuropsychopharmacol. 2005Dec;8(4):495-504. doi: 10.1017/S1461145705005821. Epub 2005 Aug 5. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16098236)
- Race JE, Makhlouf FN, Logue PJ, Wilson FH, Dunham PB, Holtzman EJ. Molecularcloning and functional characterization of KCC3, a new K-Cl cotransporter. Am JPhysiol. 1999 Dec;277(6):C1210-9. doi: 10.1152/ajpcell.1999.277.6.C1210. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/10600773)

- Salin-Cantegrel A, Riviere JB, Dupre N, Charron FM, Shekarabi M, Karemera L, Gaspar C, Horst J, Tekin M, Deda G, Krause A, Lippert MM, Willemsen MA, Jarrar R, Lapointe JY, Rouleau GA. Distal truncation of KCC3 in non-French CanadianHMSN/ACC families. Neurology. 2007 Sep 25;69(13):1350-5. doi:10.1212/01.wnl.0000291779.35643.15. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17893295)
- Uyanik G, Elcioglu N, Penzien J, Gross C, Yilmaz Y, Olmez A, Demir E, Wahl D, Scheglmann K, Winner B, Bogdahn U, Topaloglu H, Hehr U, Winkler J. Noveltruncating and missense mutations of the KCC3 gene associated with Andermannsyndrome. Neurology. 2006 Apr 11;66(7):1044-8. doi:10.1212/01.wnl.0000204181.31175.8b. Erratum In: Neurology. 2006 Oct24;67(8):1528. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16606917)

Genomic Location

The *SLC12A6* gene is found on chromosome 15 (https://medlineplus.gov/genetics/chromosome/15/).

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