

CLCN1 Gene

Subjects: Genetics

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Definition

chloride voltage-gated channel 1

1. Normal Function

The *CLCN1* gene provides instructions for making a type of protein called a chloride channel. These channels, which transport negatively charged chlorine atoms (chloride ions), play a key role in a cell's ability to generate and transmit electrical signals.

The *CLCN1* gene provides instructions for making a chloride channel called CIC-1. These channels are found only in muscles used for movement (skeletal muscles). For the body to move normally, skeletal muscles must tense (contract) and relax in a coordinated way. Muscle contraction and relaxation are controlled by the flow of certain ions into and out of muscle cells. CIC-1 channels, which span the cell membrane, control the flow of chloride ions into these cells. This influx stabilizes the cells' electrical charge, which prevents muscles from contracting abnormally.

CIC-1 channels are made of two identical protein subunits, each produced from the *CLCN1* gene. Although each subunit forms a separate opening (pore) that allows chloride ions to pass through, the two proteins work together to regulate the flow of chloride ions into skeletal muscle cells.

2. Health Conditions Related to Genetic Changes

Myotonia congenita

More than 150 mutations in the *CLCN1* gene have been identified in people with myotonia congenita. Most of these mutations cause the autosomal recessive form of the disorder, which is known as Becker disease. Autosomal recessive inheritance means two copies of the gene in each cell are altered. Becker disease results when *CLCN1* mutations change the structure or function of both protein subunits that make up the CIC-1 channel. The altered channels greatly reduce the flow of chloride ions into skeletal muscle cells, which triggers prolonged muscle contractions. Abnormally sustained muscle contractions are the hallmark of myotonia.

CLCN1 mutations also cause the autosomal dominant form of myotonia congenita, which is known as Thomsen disease. Autosomal dominant inheritance means one copy of the altered gene in each cell is sufficient to cause the disorder. Studies suggest that the *CLCN1* mutations responsible for Thomsen disease change one of the two protein subunits that make up the CIC-1 channel. The altered protein takes on new, but harmful, properties that disrupt the ability of both subunits to regulate chloride ion flow. Reduced movement of chloride ions into skeletal muscle cells leads to myotonia, which underlies the stiffness and other muscle problems in people with myotonia congenita.

Because several *CLCN1* mutations can cause either Becker disease or Thomsen disease, doctors usually rely on characteristic signs and symptoms to distinguish the two forms of myotonia congenita.

3. Other Names for This Gene

- chloride channel 1, skeletal muscle
- Chloride channel protein 1
- Chloride channel protein, skeletal muscle
- chloride channel, voltage-sensitive 1

- CIC-1
- CLC1
- CLCN1_HUMAN
- MGC138361
- MGC142055
- skeletal muscle chloride channel 1

References

1. Colding-Jørgensen E. Phenotypic variability in myotonia congenita. *MuscleNerve*. 2005 Jul;32(1):19-34. Review.
2. Dunø M, Colding-Jørgensen E, Grunnet M, Jespersen T, Vissing J, Schwartz M. Difference in allelic expression of the CLCN1 gene and the possible influence on the myotonia congenita phenotype. *Eur J Hum Genet*. 2004 Sep;12(9):738-43.
3. Dunø M, Colding-Jørgensen E. Myotonia Congenita. 2005 Aug 3 [updated 2015 Aug 6]. In: Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH, Stephens K, Amemiya A, editors. *GeneReviews*® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2020. Available from <http://www.ncbi.nlm.nih.gov/books/NBK1355/>
4. Grunnet M, Jespersen T, Colding-Jørgensen E, Schwartz M, Klaerke DA, Vissing J, Olesen SP, Dunø M. Characterization of two new dominant CIC-1 channel mutations associated with myotonia. *Muscle Nerve*. 2003 Dec;28(6):722-32.
5. Imbrici P, Altamura C, Pessia M, Mantegazza R, Desaphy JF, Camerino DC. CIC-1 chloride channels: state-of-the-art research and future challenges. *Front Cell Neurosci*. 2015 Apr 27;9:156. doi: 10.3389/fncel.2015.00156. Review.
6. Jentsch TJ, Stein V, Weinreich F, Zdebik AA. Molecular structure and physiological function of chloride channels. *Physiol Rev*. 2002 Apr;82(2):503-68. Review. Erratum in: *Physiol Rev*. 2003 Apr;83(2):following table of contents.
7. Pusch M. Myotonia caused by mutations in the muscle chloride channel gene CLCN1. *Hum Mutat*. 2002 Apr;19(4):423-34. Review.
8. Zhang J, Bendahhou S, Sanguinetti MC, Ptáček LJ. Functional consequences of chloride channel gene (CLCN1) mutations causing myotonia congenita. *Neurology*. 2000 Feb 22;54(4):937-42.
9. Zhang J, George AL Jr, Griggs RC, Fouad GT, Roberts J, Kwieciński H, Connolly AM, Ptáček LJ. Mutations in the human skeletal muscle chloride channel gene (CLCN1) associated with dominant and recessive myotonia congenita. *Neurology*. 1996 Oct;47(4):993-8.

Keywords

genes