CLCN7 gene

chloride voltage-gated channel 7

Normal Function

The *CLCN7* gene belongs to the CLC family of genes, which provide instructions for making chloride channels. 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. Some CLC channels regulate the flow of chloride ions across cell membranes, while others transport chloride ions within cells.

The *CLCN7* gene provides instructions for making a chloride channel called ClC-7. These channels are abundant in cells throughout the body. They are particularly important for the normal function of osteoclasts, which are specialized cells that break down bone tissue. Osteoclasts are involved in bone remodeling, a normal process in which old bone is removed and new bone is created to replace it. Bones are constantly being remodeled, and the process is carefully controlled to ensure that bones stay strong and healthy.

ClC-7 channels help regulate the relative acidity (pH) of osteoclasts. These channels transport two negatively charged chloride ions out of these cells for every positively charged hydrogen atom (hydrogen ion) that flows in. In this way, ClC-7 channels help balance the acidic environment that osteoclasts use to dissolve bone tissue. The pH inside and outside osteoclasts must be carefully controlled for these cells to break down bone effectively.

Health Conditions Related to Genetic Changes

Osteopetrosis

More than 50 mutations in the *CLCN7* gene have been identified in people with osteopetrosis. Mutations in this gene can cause several different forms of the disorder: autosomal recessive osteopetrosis (ARO), which is the most severe form; autosomal dominant osteopetrosis (ADO), which tends to be milder; and a moderate form known as intermediate autosomal osteopetrosis (IAO).

Mutations in the *CLCN7* gene impair the function of ClC-7 channels. The defective channels cannot transport chloride ions effectively, which disrupts the regulation of pH in osteoclasts. As a result, osteoclasts are unable to break down bone normally. When

old bone is not broken down as new bone is formed, bones throughout the skeleton become unusually dense. The bones are also structurally abnormal, making them prone to fracture. These problems with bone remodeling underlie all of the major forms of osteopetrosis.

Other Names for This Gene

- chloride channel 7
- chloride channel protein 7
- chloride channel, voltage-sensitive 7
- CLC-7
- CLC7
- CLCN7_HUMAN
- FLJ26686
- FLJ39644
- FLJ46423
- H(+)/Cl(-) exchange transporter 7
- OPTA2
- OPTB4
- PPP1R63

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of CLCN7 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=1186[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28CLCN7%5BTIAB%5D%29+OR+%28chloride+channel+7%5BTIAB%5D%29%29+OR+%28%28CLC-7%5BTIAB%5D%29+OR+%28CLC7%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

- CHLORIDE CHANNEL 7; CLCN7 (https://omim.org/entry/602727)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/1186)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=CLCN7[gene])

References

- Cleiren E, Benichou O, Van Hul E, Gram J, Bollerslev J, Singer FR, BeaversonK, Aledo A, Whyte MP, Yoneyama T, deVernejoul MC, Van Hul W. Albers-Schonbergdisease (autosomal dominant osteopetrosis, type II) results from mutations in theClCN7 chloride channel gene. Hum Mol Genet. 2001 Dec 1;10(25): 2861-7. doi:10.1093/hmg/10.25.2861. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/11741829)
- Del Fattore A, Peruzzi B, Rucci N, Recchia I, Cappariello A, Longo M,Fortunati D, Ballanti P, Iacobini M, Luciani M, Devito R, Pinto R, Caniglia M,Lanino E, Messina C, Cesaro S, Letizia C, Bianchini G, Fryssira H, Grabowski P,Shaw N, Bishop N, Hughes D, Kapur RP, Datta HK, Taranta A, Fornari R, MigliaccioS, Teti A. Clinical, genetic, and cellular analysis of 49 osteopetrotic patients:implications for diagnosis and treatment. J Med Genet. 2006 Apr;43(4):315-25.doi: 10.1136/jmg.2005.036673. Epub 2005 Aug 23. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16118345) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2563229/)
- Frattini A, Pangrazio A, Susani L, Sobacchi C, Mirolo M, Abinun M, Andolina M, Flanagan A, Horwitz EM, Mihci E, Notarangelo LD, Ramenghi U, Teti A, Van Hove J, Vujic D, Young T, Albertini A, Orchard PJ, Vezzoni P, Villa A. Chloride channelClCN7 mutations are responsible for severe recessive, dominant, and intermediateosteopetrosis. J Bone Miner Res. 2003 Oct;18(10):1740-7. doi:10.1359/jbmr.2003.18.10.1740. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/14584882)
- Kornak U, Kasper D, Bosl MR, Kaiser E, Schweizer M, Schulz A, Friedrich W, Delling G, Jentsch TJ. Loss of the ClC-7 chloride channel leads to osteopetrosisin mice and man. Cell. 2001 Jan 26;104(2):205-15. doi:10.1016/s0092-8674(01)00206-9. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/11207362)
- Pangrazio A, Pusch M, Caldana E, Frattini A, Lanino E, Tamhankar PM, Phadke S, Lopez AG, Orchard P, Mihci E, Abinun M, Wright M, Vettenranta K, Bariae I, MelisD, Tezcan I, Baumann C, Locatelli F, Zecca M, Horwitz E, Mansour LS, Van Roij M, Vezzoni P, Villa A, Sobacchi C. Molecular and clinical heterogeneity inCLCN7-dependent osteopetrosis: report of 20 novel mutations. Hum Mutat. 2010Jan;31(1): E1071-80. doi: 10.1002/humu.21167. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/19953639)
- Scheel O, Zdebik AA, Lourdel S, Jentsch TJ. Voltage-dependent electrogenicchloride/proton exchange by endosomal CLC proteins. Nature. 2005 Jul21;436(7049):424-7. doi: 10.1038/nature03860. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16034422)
- Sobacchi C, Villa A, Schulz A, Kornak U. CLCN7-Related Osteopetrosis.2007 Feb 12 [updated 2022 Jan 20]. 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. Availablefrom http://www.ncbi. nlm.nih.gov/books/NBK1127/ Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/ 20301306)

- Waguespack SG, Hui SL, Dimeglio LA, Econs MJ. Autosomal dominantosteopetrosis: clinical severity and natural history of 94 subjects with achloride channel 7 gene mutation. J Clin Endocrinol Metab. 2007 Mar;92(3):771-8. doi: 10.1210/jc.2006-1986. Epub 2006 Dec 12. Citation on PubMed (https://pubmed. ncbi.nlm.nih.gov/17164308)
- Waguespack SG, Koller DL, White KE, Fishburn T, Carn G, Buckwalter KA, JohnsonM, Kocisko M, Evans WE, Foroud T, Econs MJ. Chloride channel 7 (ClCN7) genemutations and autosomal dominant osteopetrosis, type II. J Bone Miner Res. 2003Aug;18(8):1513-8. doi: 10.1359/jbmr.2003.18.8.1513. Citation on PubMed (http s://pubmed.ncbi.nlm.nih.gov/12929941)

Genomic Location

The *CLCN7* gene is found on chromosome 16 (https://medlineplus.gov/genetics/chromo some/16/).

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