CLCN2 gene

chloride voltage-gated channel 2

Normal Function

The *CLCN2* 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 chloride channels regulate the flow of chloride ions across cell membranes, while others transport chloride ions within cells.

The *CLCN2* gene provides instructions for making a chloride channel called ClC-2. These channels are embedded within the outer membrane of most cells, and they transport chloride ions in and out of cells. The channel's function is thought to be particularly important in nerve cells (neurons) in the brain. The ClC-2 channel regulates the size (volume) of neurons by playing a role in the intake and release of water as well as maintaining a normal balance of ions in cells.

Health Conditions Related to Genetic Changes

CLCN2-related leukoencephalopathy

At least 18 mutations in the *CLCN2* gene have been found to cause *CLCN2*-related leukoencephalopathy. This condition is characterized primarily by problems with coordination and balance (ataxia) but can also cause learning disabilities, frequent headaches, and vision problems.

Some *CLCN2* gene mutations change single protein building blocks (amino acids) in the ClC-2 channel, impairing the stability of the channel and reducing channel function. Other *CLCN2* gene mutations result in a complete loss of channel function, typically by leading to the production of an abnormally short channel protein. A shortened protein is either trapped inside the cell and cannot get to the cell membrane or is quickly broken down.

As a result of this reduction in ClC-2 channel activity, certain brain cells and the myelin that surrounds neurons become filled with too much water and cannot function properly. Fluid-filled myelin cannot transmit nerve impulses effectively, resulting in neurological problems such as ataxia and the other signs and symptoms of *CLCN2*-related leukoencephalopathy.

Juvenile myoclonic epilepsy

MedlinePlus Genetics provides information about Juvenile myoclonic epilepsy

Other Names for This Gene

- chloride channel 2
- chloride channel, voltage-sensitive 2
- ClC-2
- clC-2
- CLC2
- ECA2
- ECA3
- EGI11
- EGI3
- EGMA
- EJM6
- EJM8
- LKPAT

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of CLCN2 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=1181[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28CLCN2%5BTIAB%5D%29+OR+%28chloride+voltage-gated+channel+2%5BTIAB%5D%29%29+OR+%28%28CLC-2%5BTIAB%5D%29+OR+%28LKPAT%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+1800+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- CHLORIDE CHANNEL 2; CLCN2 (https://omim.org/entry/600570)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/1181)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=CLCN2[gene])

References

- Gaitan-Penas H, Apaja PM, Arnedo T, Castellanos A, Elorza-Vidal X, Soto D,Gasull X, Lukacs GL, Estevez R. Leukoencephalopathy-causing CLCN2 mutations areassociated with impaired Cl- channel function and trafficking. JPhysiol. 2017 Nov 15;595(22):6993-7008. doi: 10.1113/JP275087. Epub 2017 Oct 9. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/28905383) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5685823/)
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- Wang H, Xu M, Kong Q, Sun P, Yan F, Tian W, Wang X. Research and progress onClC-2 (Review). Mol Med Rep. 2017 Jul;16(1):11-22. doi: 10.3892/mmr.2017.6600.Epub 2017 May 18. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/28534947) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5482133/)

Genomic Location

The *CLCN2* gene is found on chromosome 3 (https://medlineplus.gov/genetics/chromosome/3/).

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