CLCN5 gene

chloride voltage-gated channel 5

Normal Function

The *CLCN5* gene provides instructions for making a protein called ClC-5 that transports charged atoms (ions) across cell membranes. Specifically, ClC-5 exchanges negatively charged atoms of chlorine (chloride ions) for positively charged atoms of hydrogen (protons or hydrogen ions). Based on this function, ClC-5 is known as a H^+/Cl^- exchanger.

ClC-5 is found primarily in the kidneys, particularly in structures called proximal tubules. These structures help to reabsorb nutrients, water, and other materials that have been filtered from the bloodstream. The kidneys reabsorb needed materials into the blood and excrete everything else into the urine.

Within proximal tubule cells, ClC-5 is embedded in specialized compartments called endosomes. Endosomes are formed at the cell surface to carry proteins and other molecules to their destinations within the cell. ClC-5 transports hydrogen ions into endosomes and chloride ions out, which helps these compartments maintain the proper acidity level (pH). Endosomal pH levels must be tightly regulated for proximal tubule cells to function properly.

Health Conditions Related to Genetic Changes

Dent disease

About 150 mutations in the *CLCN5* gene have been found to cause Dent disease 1, a chronic kidney disorder that can cause kidney failure. Most of the mutations lead to the production of an abnormally short, nonfunctional version of ClC-5 or prevent cells from producing any of this protein. A loss of ClC-5 alters the regulation of endosomal pH, which disrupts the overall function of proximal tubule cells and prevents them from reabsorbing proteins and other materials into the bloodstream. As a result, proteins are lost through the urine (tubular proteinuria). A failure to reabsorb calcium and other nutrients into the bloodstream can cause bone defects, kidney stones, and related health problems in people with Dent disease 1. Abnormal proximal tubule function ultimately leads to kidney failure in most affected individuals.

Hereditary hypophosphatemic rickets

MedlinePlus Genetics provides information about Hereditary hypophosphatemic rickets

Other Names for This Gene

- chloride channel 5
- chloride channel protein 5
- chloride channel, voltage-sensitive 5
- chloride transporter ClC-5
- clC-5
- CLC5
- CLCK2
- CLCN5_HUMAN
- DENTS
- H(+)/Cl(-) exchange transporter 5
- hCIC-K2
- hClC-K2
- NPHL1
- NPHL2
- XLRH
- XRN

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of CLCN5 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=1184[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28CLCN5%5BTIAB%5D%29+OR+%28CLC-5%5BTIAB%5D%29+OR+%28CLC5%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 5; CLCN5 (https://omim.org/entry/300008)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/1184)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=CLCN5[gene])

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Genomic Location

The *CLCN5* gene is found on the X chromosome (https://medlineplus.gov/genetics/chromosome/x/).

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