FE410 PRESENTATION: CHLORIDE

Presented by Öykü Yurtsever

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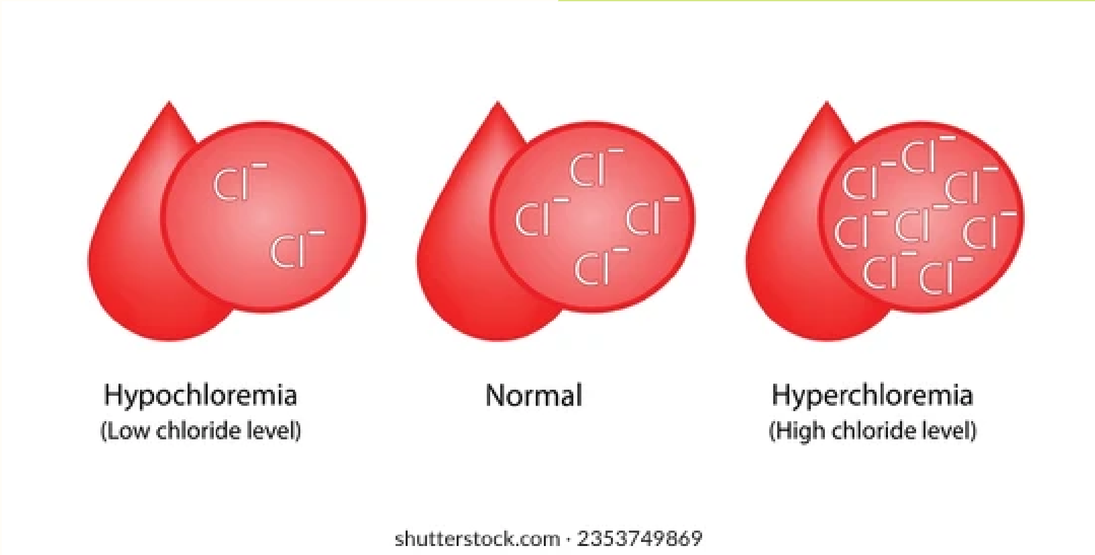
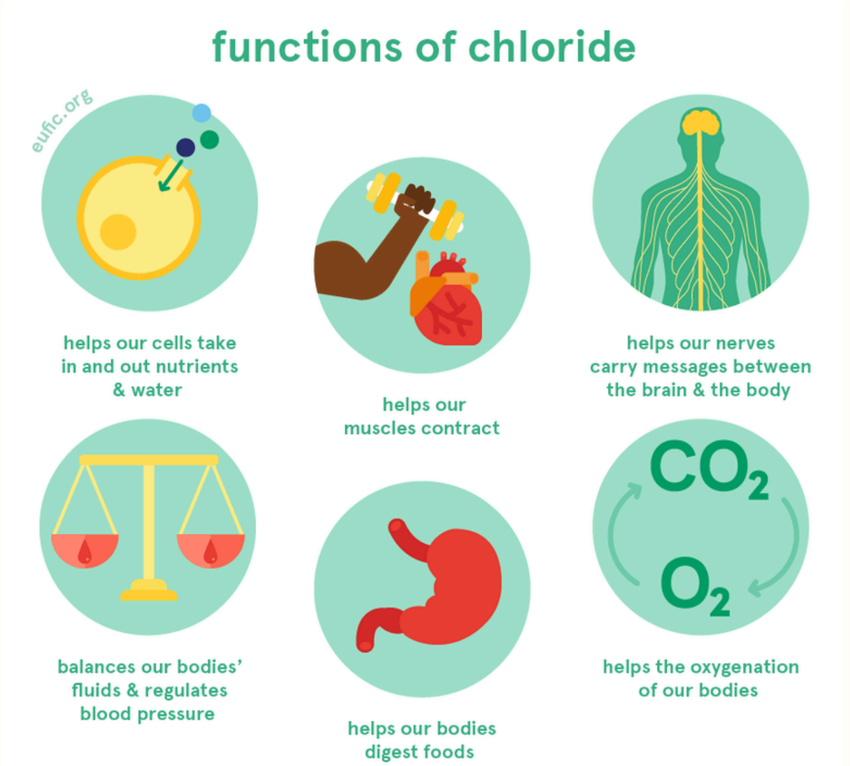
Introduction to Chloride

- Chloride is the main anion in blood and body tissues.
- It has important roles in digestion and immune defense.
- In the stomach, it forms hydrochloric acid (HCl) to help digest food.
- In immune cells, it forms hypochlorous acid, which helps kill bacteria.
- Chloride carries an electric charge, classified as an electrolye along with sodium and potassium.
- It maintains electrolyte and fluid balance.



Functions of Chloride

- It maintains osmotic pressure along with other electrolytes and regulates water balance.
- Acid-base regulation (maintains proper pH levels)-chloride shift exchange of Cl^- and HCO_3^- (bicarbonate) across red blood cell membranes to maintain blood pH.
- Cl- essential for the production of gastric HCl for the digestive process (gastric acid formation + defense against pathogens)
- Enzyme Amylase requires Chloride as a cofactor.
- It regulates the amount of fluid and types of nutrients going in and out of the cells.
- It stimulates the action of nerve and muscle cells.
- It facilitates the flow of oxygen and carbondioxide within cells.



Dietary Sources

Recommended Dietary Allowance (RDA) is established at an amount that ensures nutritional adequacy. People ages 14-50 and pregnant women is 2.3 grams daily, for ages 51-70 is 2 grams daily, and for ages 71+ is 1.8 grams daily. (chloride intake)

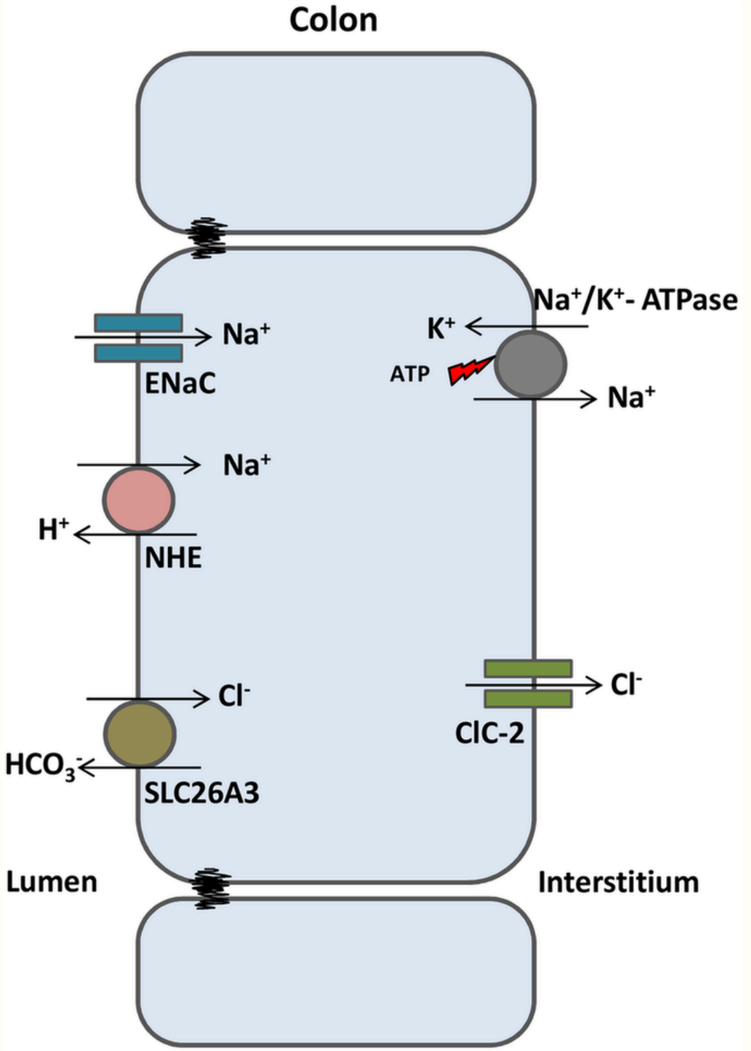
Foods such as

- Table salt, sea salt, Kosher salt
- Seaweed
- Shrimp
- High-sodium processed foods, including deli meats, hot dogs, cheese, and potato chips
- High-sodium condiments, including soy sauce, Worcestershire sauce, ketchup
- Whole grains
- Vegetables
- Eggs, milk, cheese, olives
- Processed foods

NOTE: Chloride cannot be synthesized by the human body. It is an essential mineral, it must be taken through the diet.

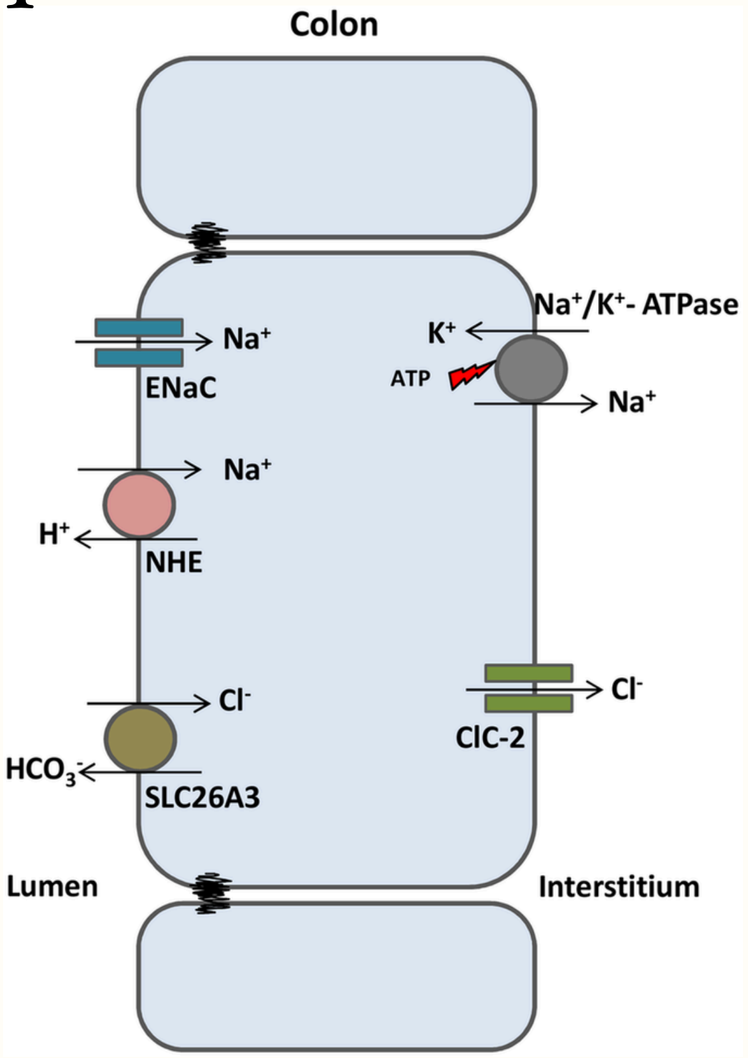
Absorption of Chloride

- Chloride is absorbed in the small intestine. (jejunum and ileum)
- Through passive diffusion and active transport mechanisms coupled with sodium absorption.
- Some reabsorption also occurs in the large intestine.
- Remains in the body's fluids and blood.
- Any excess amount is excreted in urine.
- Chloride is bound to sodium; therefore, the amount in blood tends to coincide with sodium levels.
- Absorption occurs via Na^+/Cl^- co-transporters and chloride-bicarbonate exchangers.
- In the kidney, chloride reabsorption parallels sodium reabsorption, maintaining electroneutrality and osmotic balance.
- Transport in the blood: Circulates mainly as free Cl^- ions in extracellular fluid (ECF).



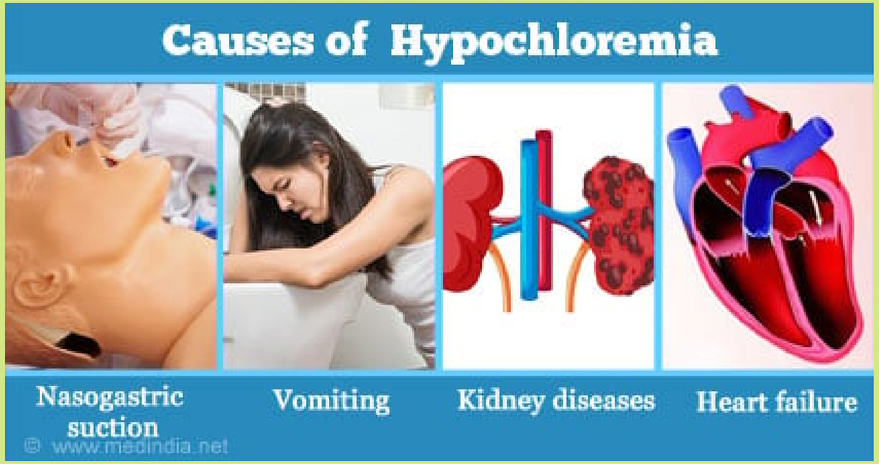
https://www.researchgate.net/figure/ClC-2-aids-in-water-absorption-in-intestinal-epithelia-In-colonic-enterocytes-chloride_fig3_315526851

Absorption of Chloride

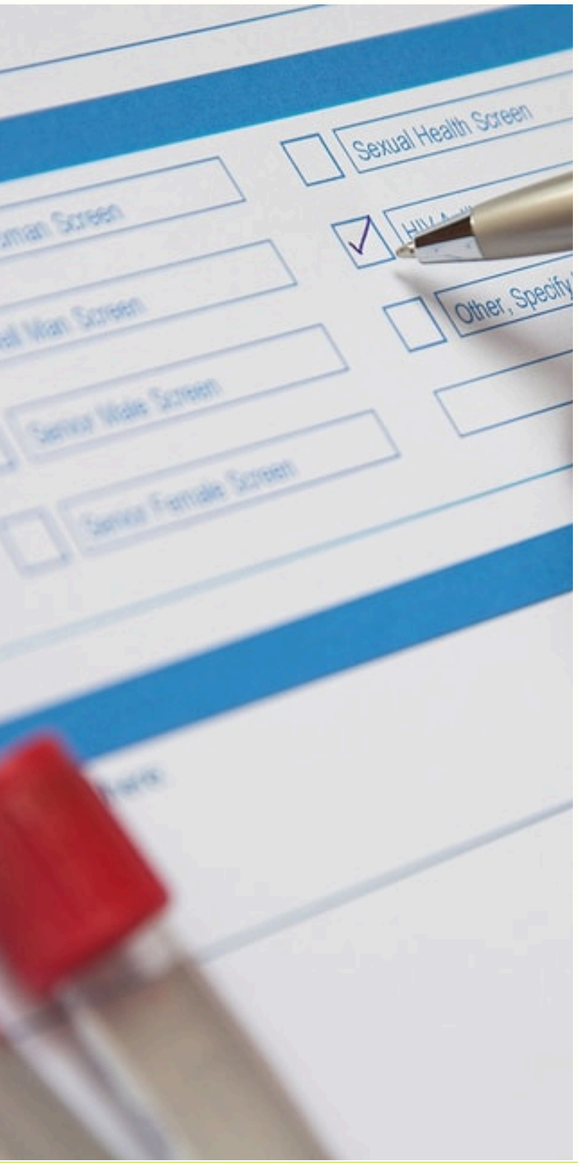


https://www.researchgate.net/figure/ClC-2-aids-in-water-absorption-in-intestinal-epithelia-In-colonic-enterocytes-chloride_fig3_315526851

Chloride Deficiency: Hypochloremia



- Chloride deficiency mostly happens due to continuous vomiting, especially in children.
- Usually, both sodium and chloride are lost together.
- This can also occur after heavy sweating and low salt intake.
- These include conditions that cause excessive fluid loss from the body, such as prolonged diarrhea.
- Diuretic medications that increase fluid excretion through the kidneys can also lead to decreased chloride levels.
- In people with diabetes, a sudden and very high level of blood glucose can cause the kidneys to remove more sodium and water from the body, which results in lower chloride levels.



Health Effects of Chloride Deficiency

Low chloride levels can cause:

Low blood pressure

Alkalosis (too much base in body fluids)

Hypokalemia (low potassium)

Lethargy and muscle weakness

Loss of cognitive and muscle control

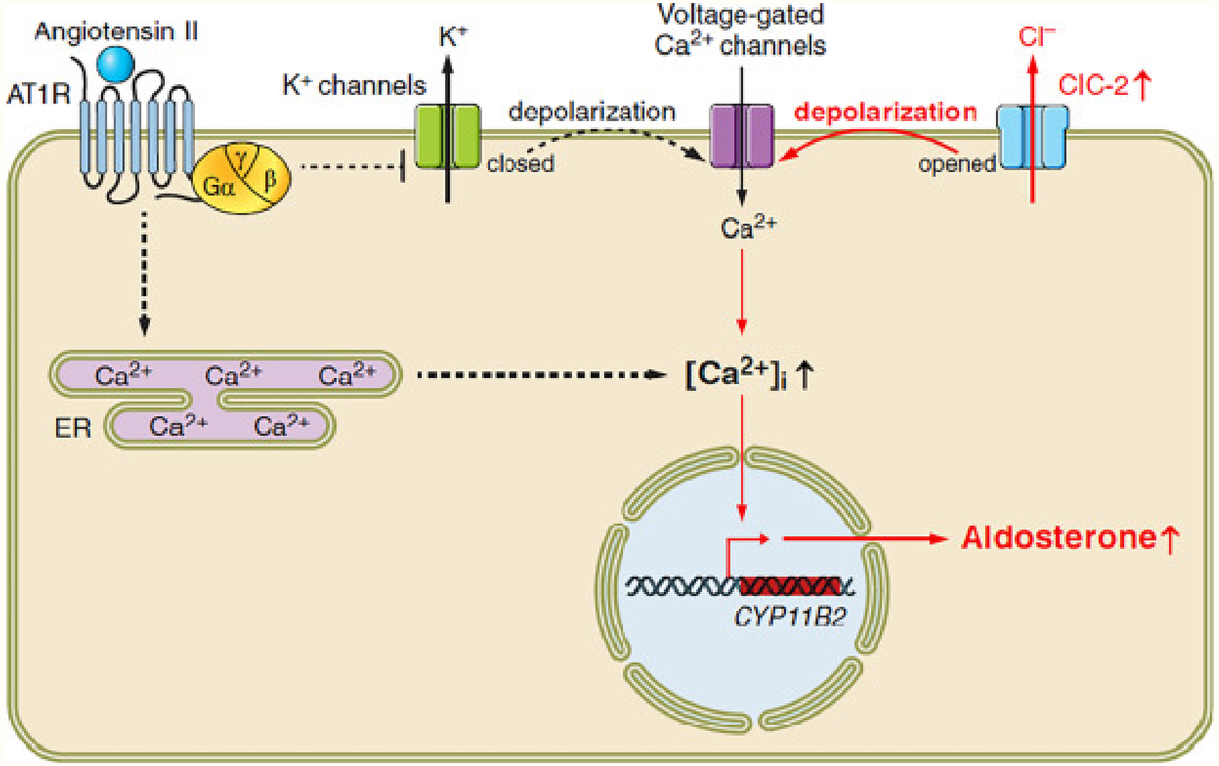
In severe cases, it can lead to death.
Also, genetic differences can make some people more vulnerable.

Toxicity of Chloride: Hyperchloremia

High levels of chloride in the blood, known as hyperchloremia, may occur due to severe dehydration, diarrhea, or metabolic problems that make the blood too acidic, such as kidney disease.

Eating too much salt can cause an excessive intake of sodium chloride, which is linked to high blood pressure.

- Symptoms of toxicity:
- Muscle weakness
- High blood pressure
- Fatigue

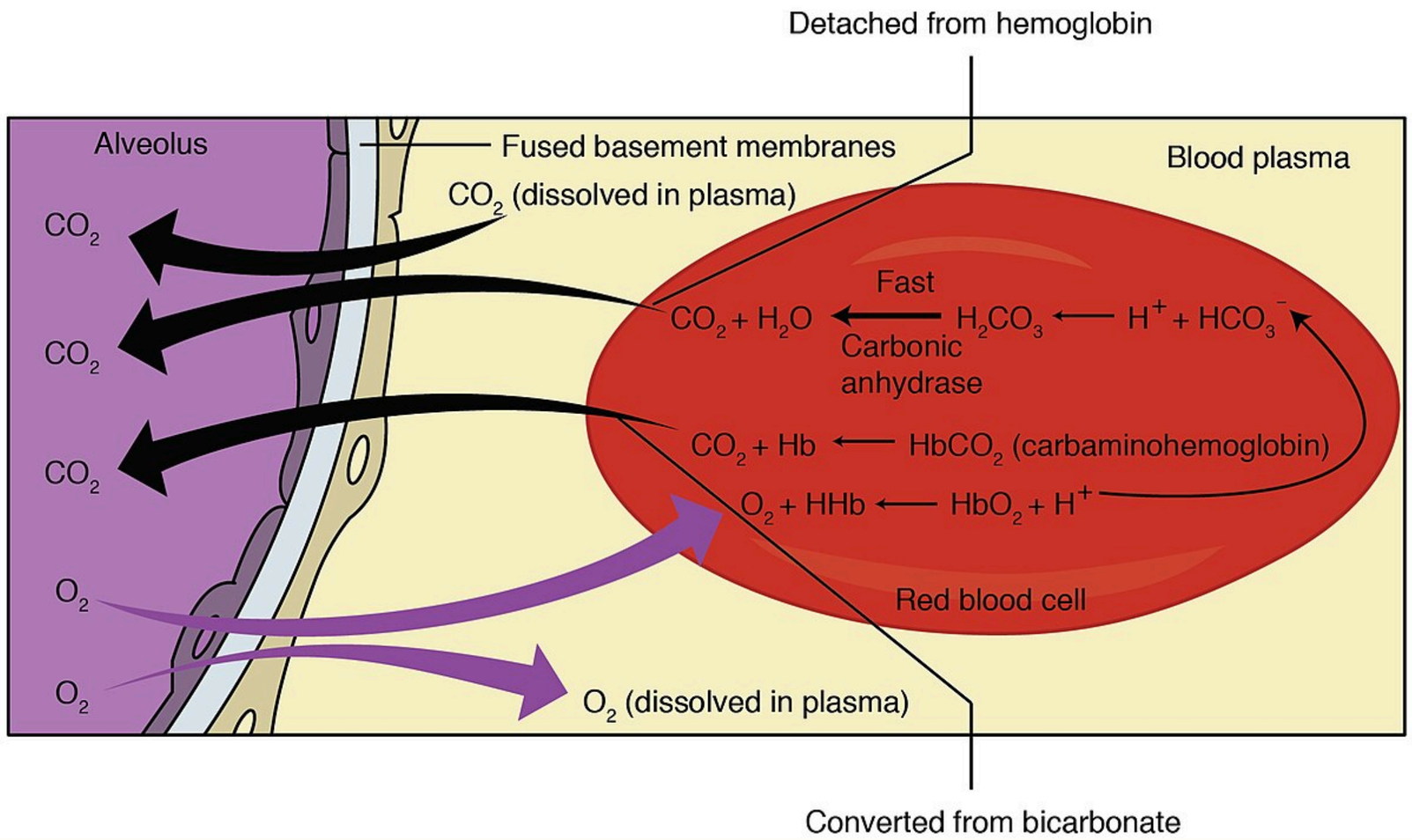


https://www.sciencedirect.com/topics/medicine-and-dentistry/chloride-transport

Chloride Transport

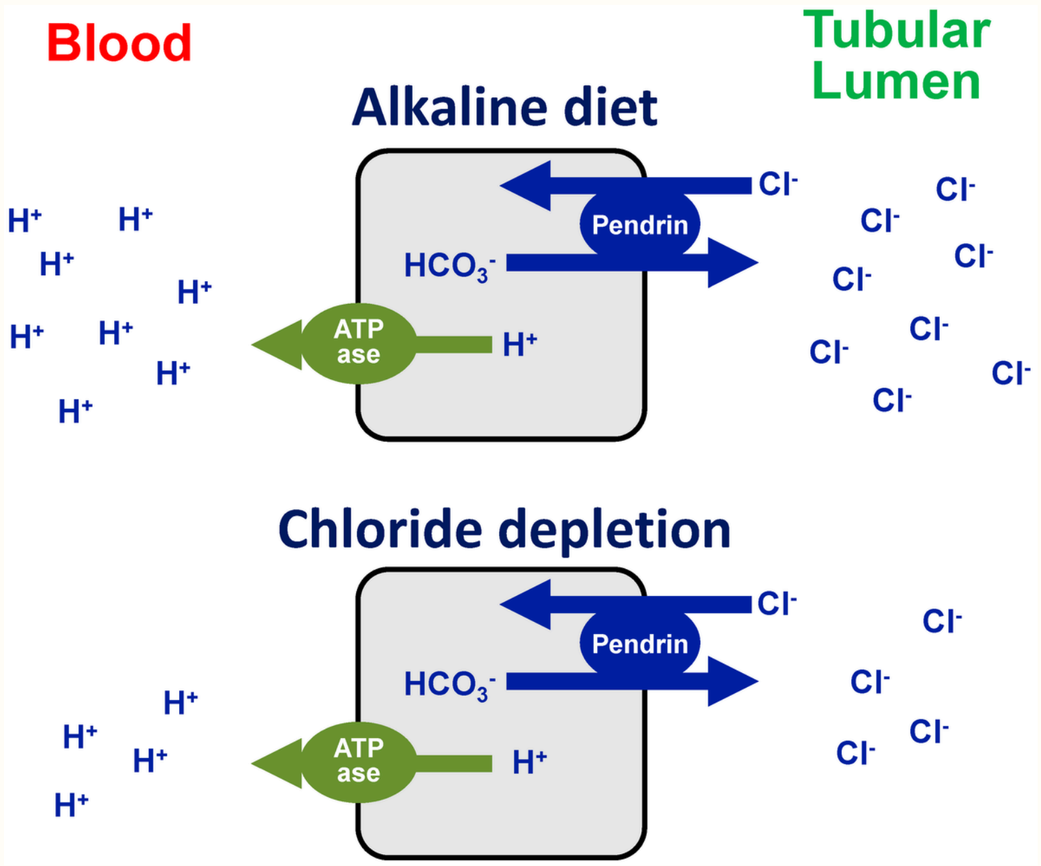
The body has many transporters and channels that control chloride absorption, distribution, and excretion.

Chloride Shift



https://en.wikipedia.org/wiki/Chloride_shift

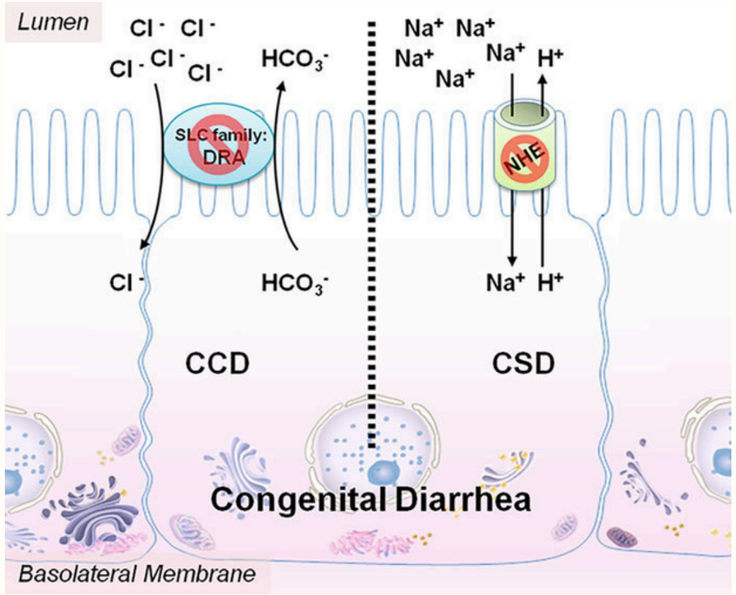
Dietary Chloride Deficiency Syndrome

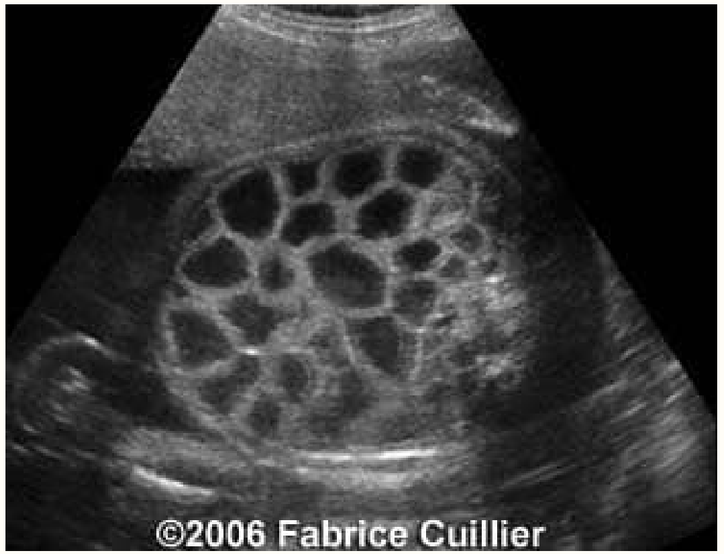


https://www.mdpi.com/2072-6643/12/11/3436

Congenital Chloride Diarrhea

- A rare condition called Congenital Chloride Diarrhea (OMIM 214700) is caused by mutations in the SLC26A3 gene.
- This mutation affects chloride transport in the ileum and colon.
- It leads to intestinal inflammation, kidney problems, and lower fertility in males.
- The body excretes watery stool containing a high amount of chloride. This leads to dehydration, low potassium levels (hypokalemia), and metabolic alkalosis.
- Increased salt intake helps improve this condition.
- CCD affects intestines.



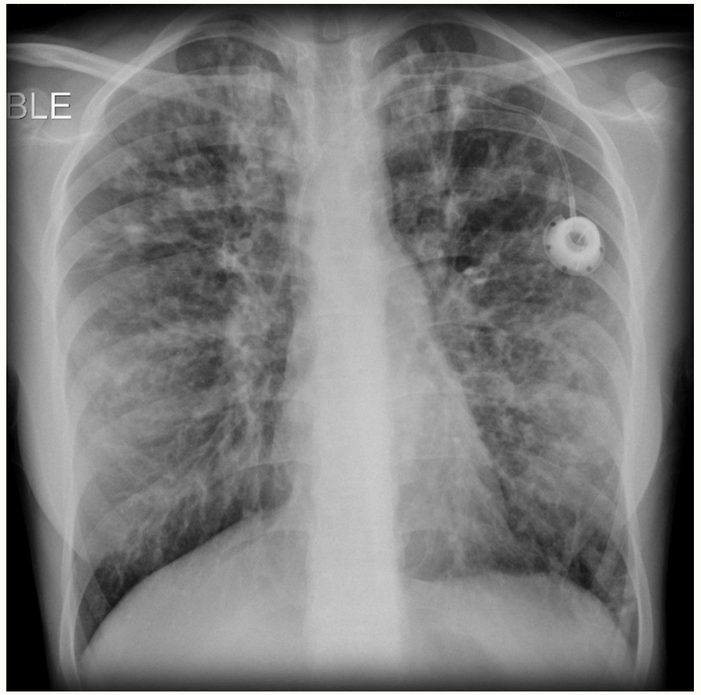


https://thefetus.net/content/congenital-chloride-diarrhea

The fetus image shows abnormal swelling in the baby's intestines.

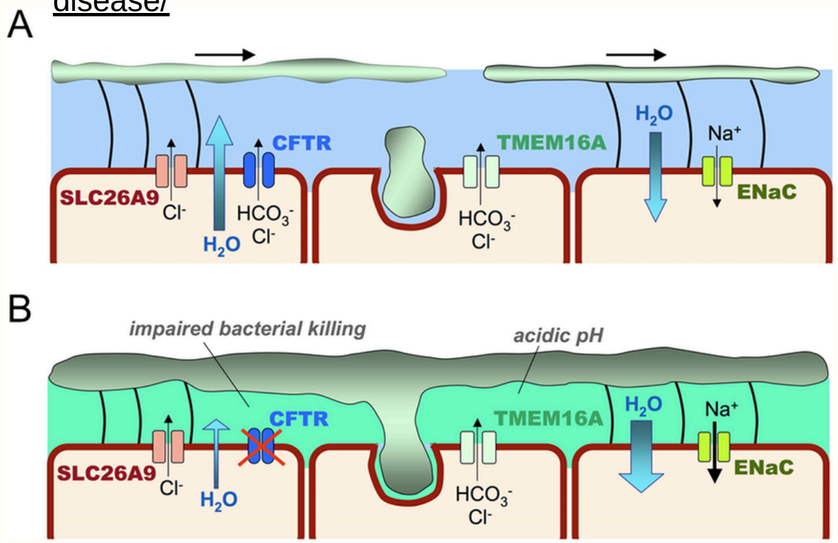
Cystic Fibrosis and CFTR

- A more common problem involves the CFTR (Cystic Fibrosis Transmembrane Conductance Regulator) gene.
- CFTR controls chloride transport and also helps regulate other ion channels for sodium and chloride.
- The exact mechanisms are still not fully understood.
- When both copies of CFTR have loss-of-function mutations, it causes Cystic Fibrosis (CF; OMIM 219700).
- Proteins help maintain the balance of salt and water on many surfaces in the body, such as the surface of the lungs. When the protein does not work properly, chloride, a component of salt, gets trapped inside the cells.
- Cystic fibrosis affects the lungs, liver, pancreas, sweat glands etc.



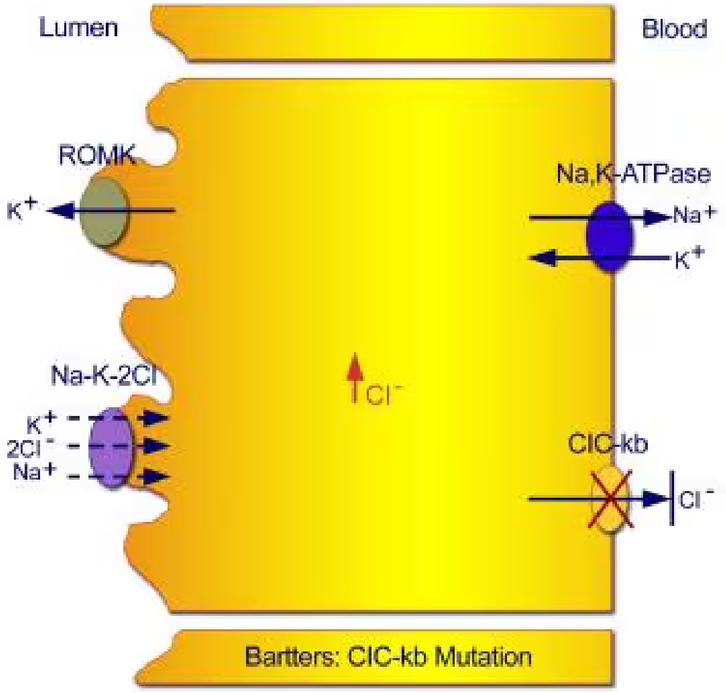
Liver Disease

https://mdsearchlight.com/genetic-disorders/cystic-fibrosis-and-liver-disease/



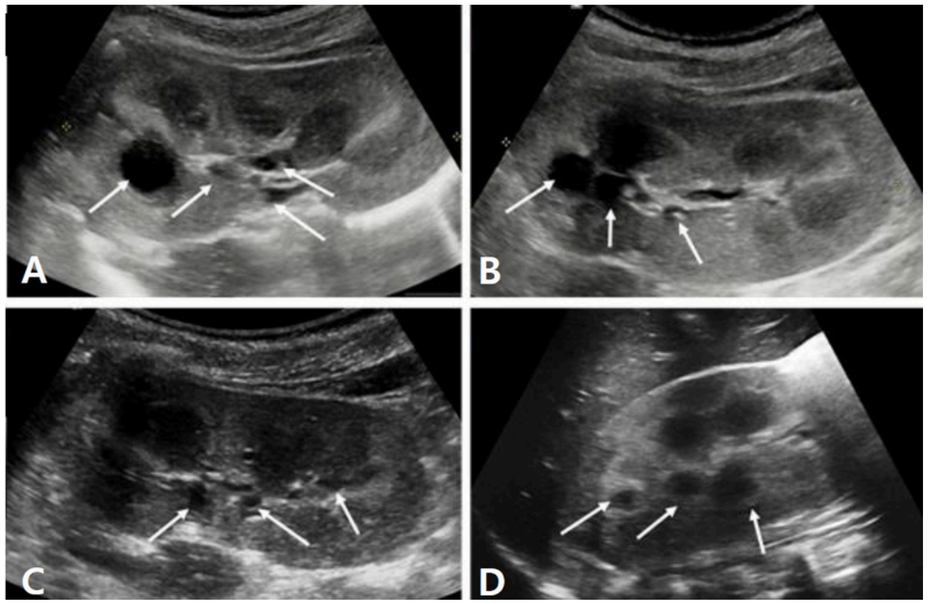
https://www.cysticfibrosisjournal.com/article/S1569-1993%2815%2900150-2/fulltext

Bartter Syndrome and Hypertension



https://emedicine.medscape.com/article/238670-overview

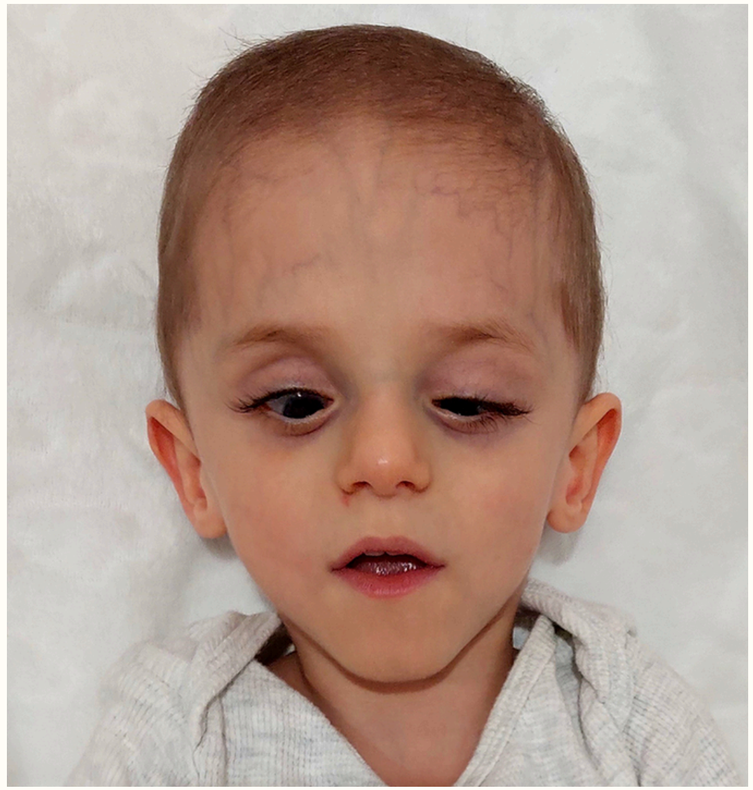
- Loss-of-function variants in the CLCNKB gene cause Bartter syndrome.
- This disorder includes excess salt loss, hypokalemia, and metabolic alkalosis.
- Another variant, where threonine at position 481 is replaced by serine, increases the gene's function.
- This variant has been linked to essential hypertension in both children and adults.

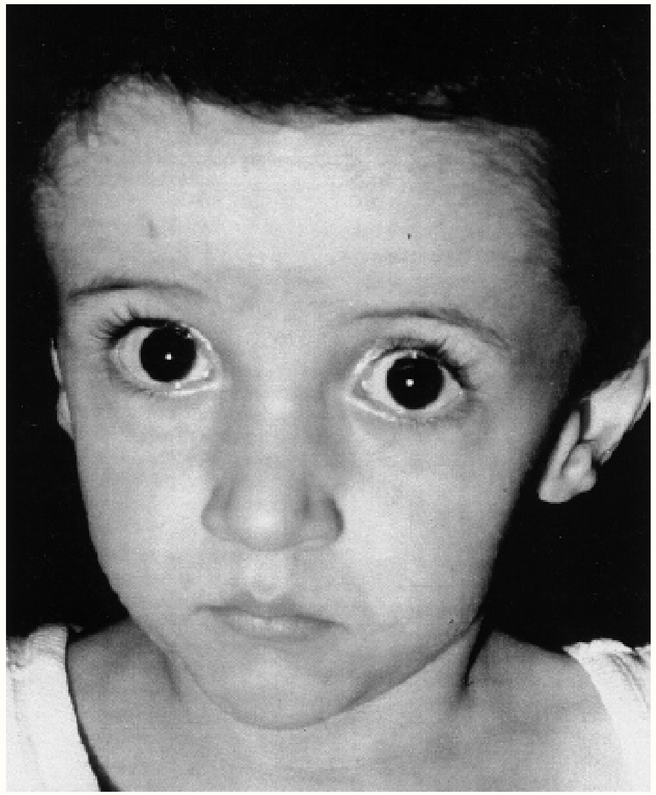


Kidney disease

https://chikd.org/journal/view.php?number=744

Bartter Syndrome





General Characteristics.
Facial Features:
Triangular-shaped face, prominent forehead, large eyes, pointed ears, "pouting" expression.

Adaptation in the Khoisan Population : Africa

- A genome study of a person with Khoisan ancestry discovered a variant in the CLCNKB gene.
- This gene controls chloride recovery in the kidney.
- The variant helps improve chloride reabsorption, an adaptation to the dry Kalahari Desert environment.

OMIM INFORMATION

Clinical features:
Chronic watery diarrhea with high chloride content from birth
Dehydration
Hypokalemia (low potassium)
Metabolic alkalosis
Molecular mechanism: Mutations in SLC26A3 impair chloride/bicarbonate exchange in intestinal epithelial cells, causing chloride to remain trapped inside cells and excessive chloride loss in stool.

ICD+

214700

DIARRHEA 1, SECRETORY CHLORIDE, CONGENITAL; DIAR1

Alternative titles; symbols

CHLORIDE DIARRHEA, CONGENITAL, FINNISH TYPE
CHLORIDORRHEA, CONGENITAL

Phenotype-Gene Relationships

Location	Phenotype	Phenotype MIM number	Inheritance	Phenotype mapping key	Gene/Locus	Gene/Locus MIM number
7q22.3-q31.1	Diarrhea 1, secretory chloride, congenital	214700	AR	3	SLC26A3	126650

https://www.omim.org/entry/214700

NCBI Information

SLC26A3 solute carrier family 26 member 3 [*Homo sapiens* (human)]

Download Datasets

Gene ID: 1811, updated on 19-Aug-2025

Summary

Official Symbol	SLC26A3 provided by HGNC
Official Full Name	solute carrier family 26 member 3 provided by HGNC
Primary source	HGNC:HGNC:3018
See related	Ensembl:ENSG00000091138 MIM:126650; AllianceGenome:HGNC:3018
Gene type	protein coding
RefSeq status	REVIEWED
Organism	Homo sapiens
Lineage	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini; Catarrhini; Hominidae; Homo
Also known as	CLD; DRA
Summary	The protein encoded by this gene is a transmembrane glycoprotein that transports chloride ions across the cell membrane in exchange for bicarbonate ions. It is localized to the mucosa of the lower intestinal tract, particularly to the apical membrane of columnar epithelium and some goblet cells. The protein is essential for intestinal chloride absorption, and mutations in this gene have been associated with congenital chloride diarrhea. [provided by RefSeq, Oct 2008]
Expression	Biased expression in colon (RPKM 709.1), duodenum (RPKM 299.0) and 1 other tissue See more
Orthologs	mouse all

NEW **Try the new Gene table**

Try the new Transcript table

https://www.ncbi.nlm.nih.gov/gene/1811

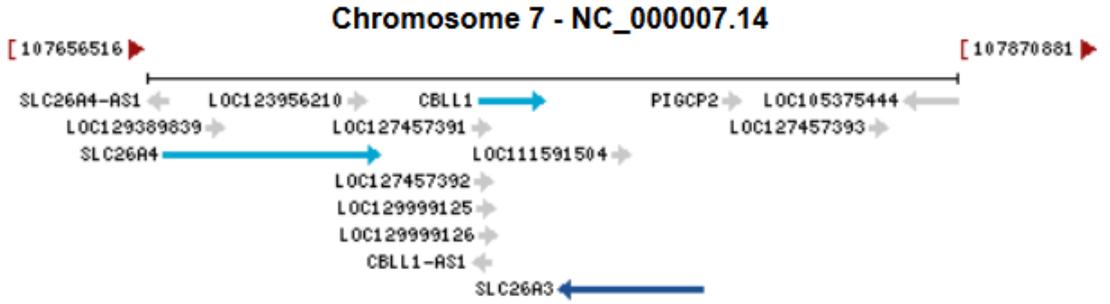
Genomic context

Location: 7q22.3-q31.1

See SLC26A3 in Genome Data Viewer

Exon count: 21

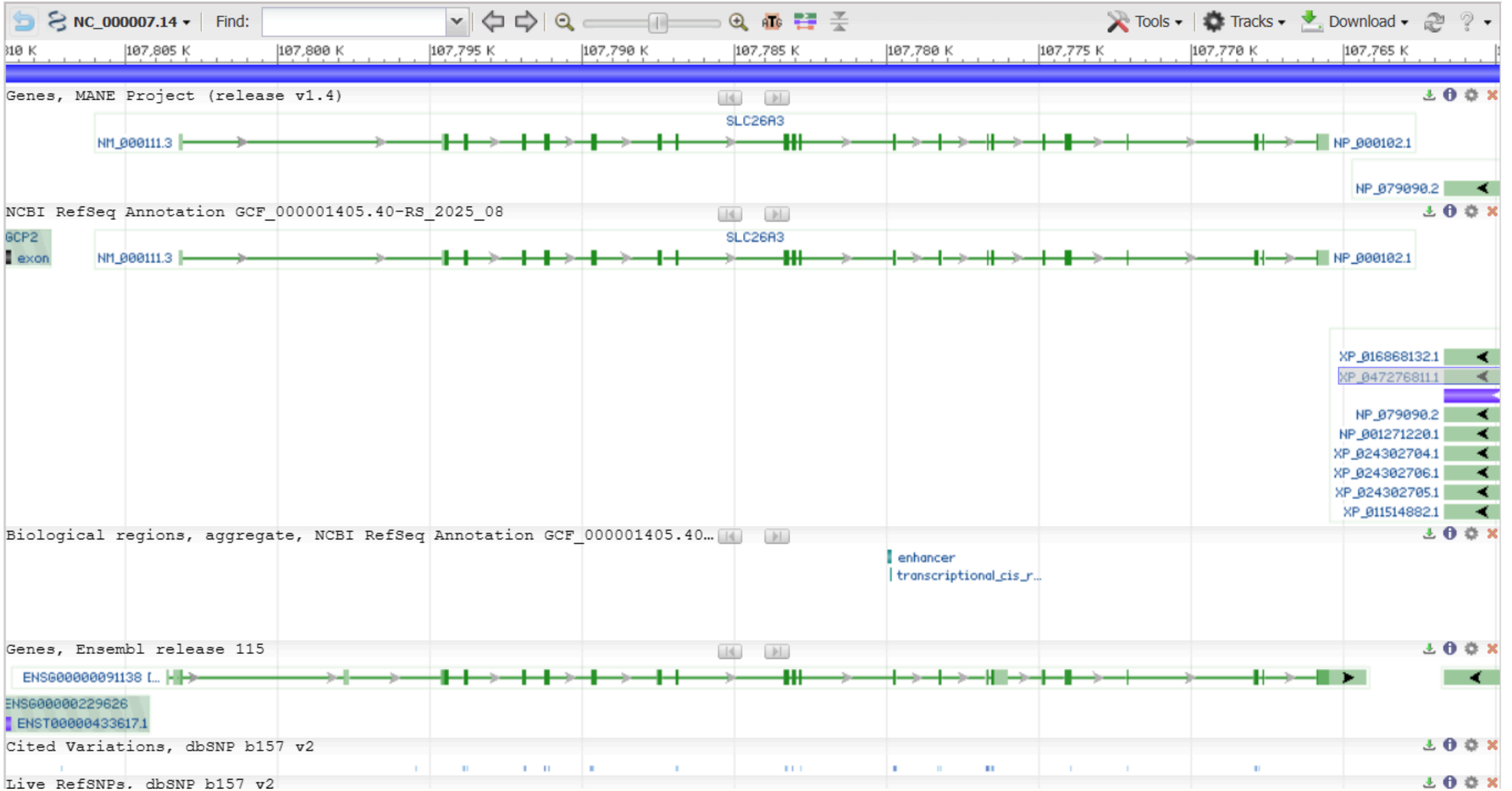
Annotation release	Status	Assembly	Chr	Location
RS_2025_08	current	GRCh38.p14 (GCF_000001405.40)	7	NC_000007.14 (107765469..107803223, complement)
RS_2025_08	current	T2T-CHM13v2.0 (GCF_009914755.1)	7	NC_060931.1 (109083905..109121574, complement)
RS_2024_09	previous assembly	GRCh37.p13 (GCF_000001405.25)	7	NC_000007.13 (107405914..107443668, complement)



Go to reference sequence details

Genomic Sequence: NC_000007.14 Chromosome 7 Reference GRCh38.p14 Primary Assembly

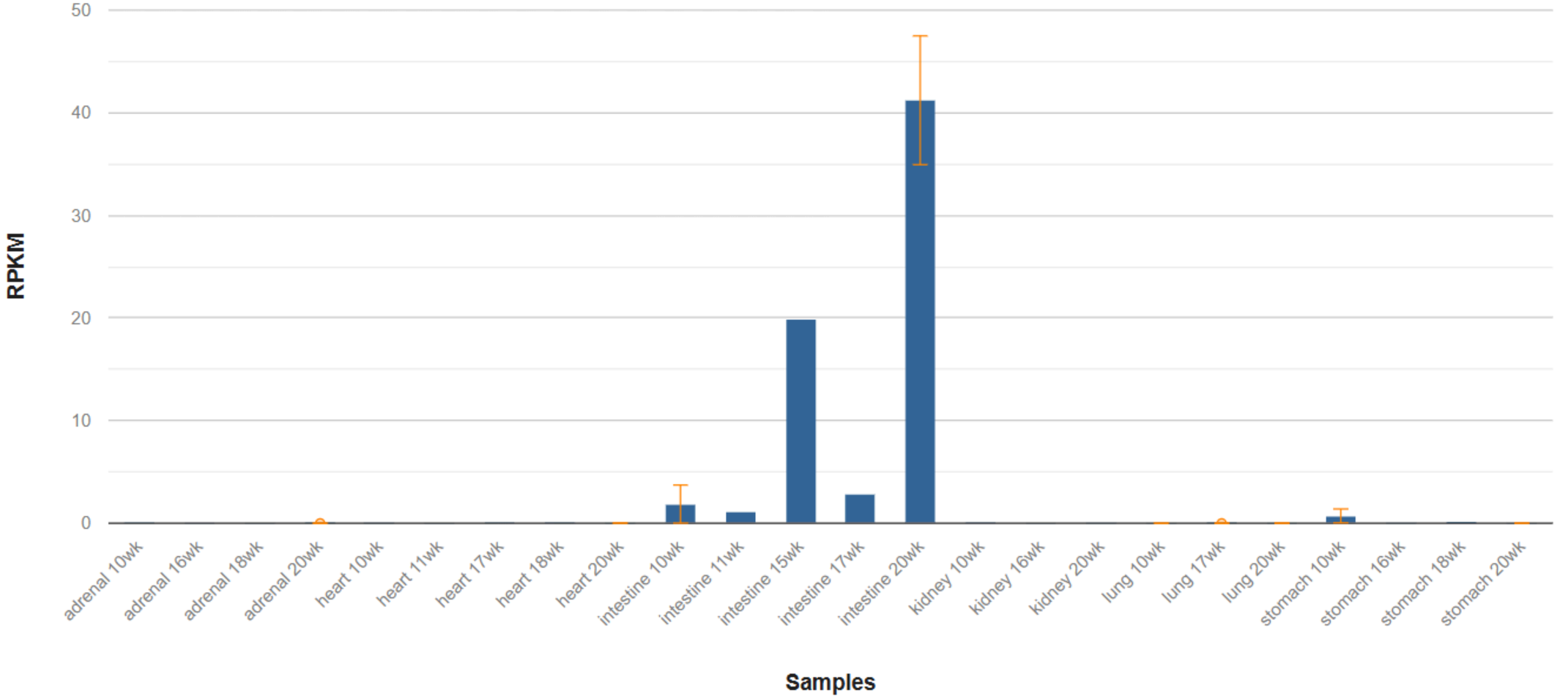
Go to nucleotide: Graphics FASTA GenBank



See details

Tissue-specific circular RNA induction during human fetal development

- Project title: Tissue-specific circular RNA induction during human fetal development
- Description: 35 human fetal samples from 6 tissues (3 - 7 replicates per tissue) collected between 10 and 20 weeks gestational time were sequenced using Illumina TruSeq Stranded Total RNA
- BioProject: PRJNA270632
- Publication: PMID 26076956
- Analysis date: Mon Apr 2 22:54:59 2018



ICD+

* 602421

CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR; CFTR

Alternative titles; symbols

ATP-BINDING CASSETTE, SUBFAMILY C, MEMBER 7; ABCC7

HGNC Approved Gene Symbol: CFTR

Cytogenetic location: 7q31.2 Genomic coordinates (GRCh38) : 7:117,480,025-117,668,665 (from NCBI)

Gene-Phenotype Relationships

Location	Phenotype View Clinical Synopses	Phenotype MIM number	Inheritance	Phenotype mapping key
7q31.2	{Bronchiectasis with or without elevated sweat chloride 1, modifier of}	211400	AD	3
	{Hypertrypsinemia, neonatal}			3
	{Pancreatitis, hereditary}	167800	AD	3
	Congenital bilateral absence of vas deferens	277180	AR	3
	Cystic fibrosis	219700	AR	3
	Sweat chloride elevation without CF			3

https://omim.org/entry/602421

CFTR CF transmembrane conductance regulator [*Homo sapiens* (human)]

Download Datasets

Gene ID: 1080, updated on 19-Aug-2025

Summary

Official Symbol	CFTR provided by HGNC
Official Full Name	CF transmembrane conductance regulator provided by HGNC
Primary source	HGNC:HGNC:1884
See related	Ensembl:ENSG00000001626 MIM:602421; AllianceGenome:HGNC:1884
Gene type	protein coding
RefSeq status	REVIEWED
Organism	Homo sapiens
Lineage	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini; Catarrhini; Hominidae; Homo
Also known as	CF; MRP7; ABC35; ABCC7; CFTR/MRP; TNR-CFTR; dJ760C5.1
Summary	This gene encodes a member of the ATP-binding cassette (ABC) transporter superfamily. The encoded protein functions as a chloride channel, making it unique among members of this protein family, and controls ion and water secretion and absorption in epithelial tissues. Channel activation is mediated by cycles of regulatory domain phosphorylation, ATP-binding by the nucleotide-binding domains, and ATP hydrolysis. Mutations in this gene cause cystic fibrosis, the most common lethal genetic disorder in populations of Northern European descent. The most frequently occurring mutation in cystic fibrosis, DeltaF508, results in impaired folding and trafficking of the encoded protein. Multiple pseudogenes have been identified in the human genome. [provided by RefSeq, Aug 2017]
Expression	Biased expression in gall bladder (RPKM 28.8), colon (RPKM 22.3) and 6 other tissues See more
Orthologs	mouse all

NEW **Try the new Gene table**
Try the new Transcript table

https://www.ncbi.nlm.nih.gov/gene/1080

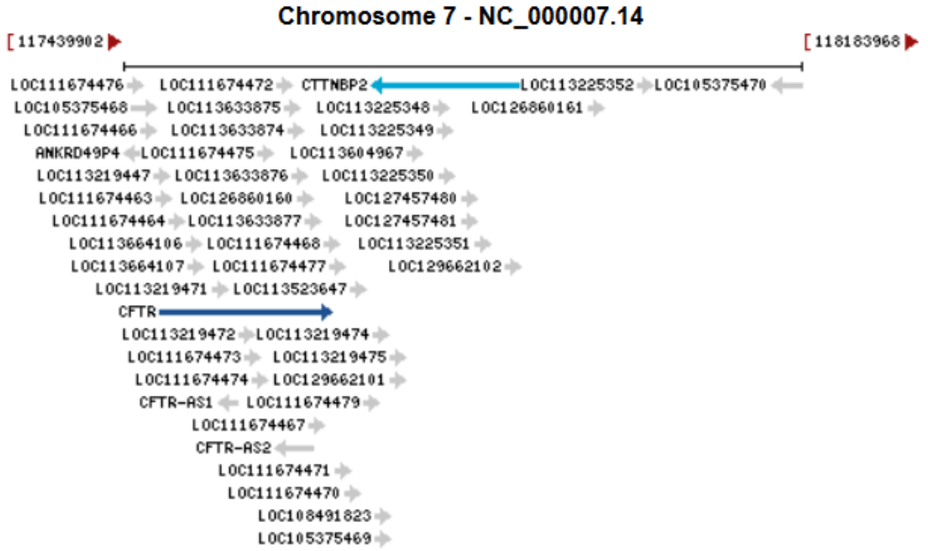
Genomic context

Location: 7q31.2

See CFTR in Genome Data Vie

Exon count: 27

Annotation release	Status	Assembly	Chr	Location
RS_2025_08	current	GRCh38.p14 (GCF_000001405.40)	7	NC_000007.14 (117480025..117668665)
RS_2025_08	current	T2T-CHM13v2.0 (GCF_009914755.1)	7	NC_060931.1 (118795361..118984026)
RS_2024_09	previous assembly	GRCh37.p13 (GCF_000001405.25)	7	NC_000007.13 (117120079..117308719)



https://www.ncbi.nlm.nih.gov/gene/1080

ICD+

* 602023

CHLORIDE CHANNEL, KIDNEY, B; CLCNKB

Alternative titles; symbols

CLCKB

HGNC Approved Gene Symbol: CLCNKB

Cytogenetic location: 1p36.13 Genomic coordinates (GRCh38) : 1:16,043,782-16,057,326 (from NCBI)

Gene-Phenotype Relationships

Location	Phenotype View Clinical Synopses	Phenotype MIM number	Inheritance	Phenotype mapping key
1p36.13	Bartter syndrome, type 3	607364	AR	3
	Bartter syndrome, type 4b, digenic	613090	DR	3

PheneGene Graphics

https://omim.org/entry/602023

CLCNKB chloride voltage-gated channel Kb [*Homo sapiens* (human)]

Download Datasets

Gene ID: 1188, updated on 19-Aug-2025

Summary

Official Symbol	CLCNKB provided by HGNC
Official Full Name	chloride voltage-gated channel Kb provided by HGNC
Primary source	HGNC:HGNC:2027
See related	Ensembl:ENSG00000184908 MIM:602023; AllianceGenome:HGNC:2027
Gene type	protein coding
RefSeq status	REVIEWED
Organism	Homo sapiens
Lineage	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini; Catarrhini; Hominidae; Homo
Also known as	CLCKB; ClC-K2; ClC-Kb
Summary	The protein encoded by this gene is a member of the family of voltage-gated chloride channels. Chloride channels have several functions, including the regulation of cell volume, membrane potential stabilization, signal transduction and transepithelial transport. This gene is expressed predominantly in the kidney and may be important for renal salt reabsorption. Mutations in this gene are associated with autosomal recessive Bartter syndrome type 3 (BS3). Alternatively spliced transcript variants encoding different isoforms have been found for this gene. [provided by RefSeq, Sep 2009]
Expression	Biased expression in kidney (RPKM 65.3), salivary gland (RPKM 9.9) and 1 other tissue See more
Orthologs	all

NEW **Try the new Gene table**
Try the new Transcript table

Genomic context

https://www.ncbi.nlm.nih.gov/gene/1188

Genomic context

Location: 1p36.13

See CLCNKB in Genome Data Viewer

Exon count: 20

Annotation release	Status	Assembly	Chr	Location
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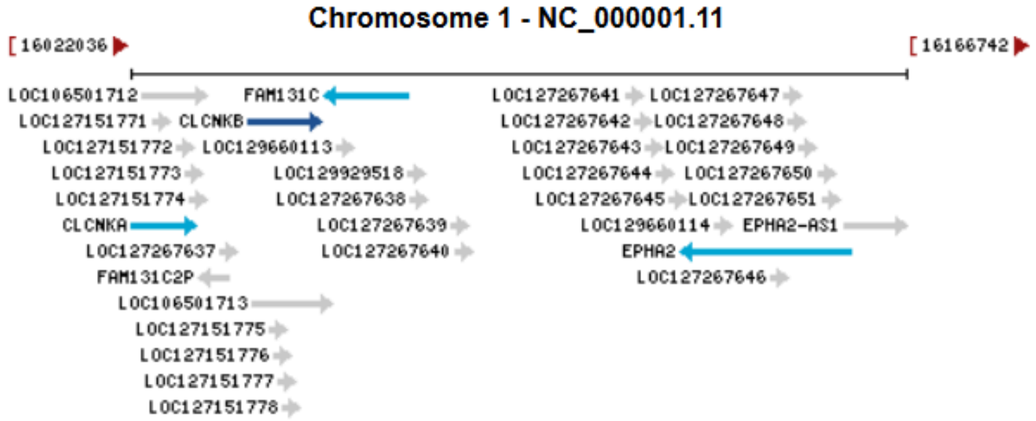
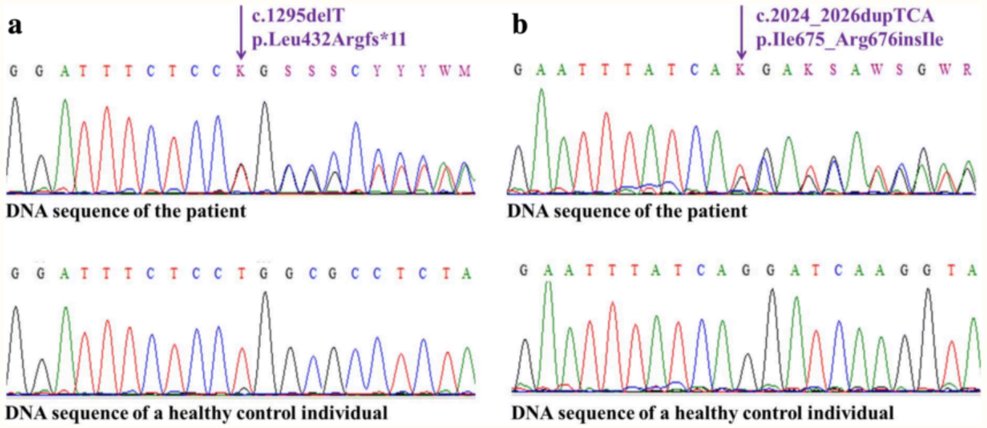
RS_2025_08	current	T2T-CHM13v2.0 (GCF_009914755.1)	1	NC_060925.1 (15485085..15498707)
RS_2024_09	previous assembly	GRCh37.p13 (GCF_000001405.25)	1	NC_000001.10 (16370277..16383821)



https://www.ncbi.nlm.nih.gov/gene/1188

Screening and Diagnosis

- Chloride blood test: A chloride blood test measures the amount of chloride in your blood.
- Genetic testing: Sequencing of SLC26A3 confirms diagnosis



Medications

- Electrolyte supplements: NaCl, KCl, Mg
- Pancreatic enzyme supplements (PERT) – for cystic fibrosis
- CFTR modulators – improve chloride channel function (cystic fibrosis)
- Prostaglandin inhibitors – reduce kidney salt loss (Bartter syndrome)
- Usually combined with diet and supplements for effective management

https://science.drinklmnt.com/did-you-know/bartter-syndrome

Conclusion & Summary

- Chloride is an essential electrolyte for fluid balance, nerve, and muscle function.
- Metabolic disorders, such as CF, CCD, Bartter, Hypochloremia etc.
- Patients need electrolyte replacement, special diets, and lifelong monitoring.
- Proper nutrition and supplementation can improve growth, health, and quality of life.
- Food Products such as Electrolyte-fortified drinks (Na^+, K^+, Cl^-, Mg^{2+}) for renal salt-wasting syndromes.

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Thank You
For Your Attention!