

SLC9A6 gene

solute carrier family 9 member A6

Normal Function

The *SLC9A6* gene provides instructions for making a protein called sodium/hydrogen exchanger 6 (Na⁺/H⁺ exchanger 6 or NHE6). Na⁺/H⁺ exchangers are found in the membranes that surround cells or compartments within cells. These proteins act as channels that allow positively charged sodium atoms (Na⁺ ions) into the cell or cellular compartment in exchange for positively charged hydrogen ions (H⁺, also known as protons), which are removed. The exchange of hydrogen ions helps regulate the relative acidity (pH) of the cell or cellular compartment.

The NHE6 protein is found in the membrane of compartments within the cell known as endosomes, which recycle proteins and other cellular materials. The NHE6 protein controls the pH inside endosomes, which is important for the recycling function of these compartments. The NHE6 protein may have additional functions, such as helping to move proteins to the correct location in the cell (protein trafficking).

Health Conditions Related to Genetic Changes

Christianson syndrome

Mutations in the *SLC9A6* gene lead to Christianson syndrome. This condition is characterized by neurological problems, including intellectual disabilities, seizures, and an inability to walk or speak. Mutations in the *SLC9A6* gene typically lead to an abnormally short NHE6 protein that is nonfunctional or that is broken down quickly in cells, resulting in the absence of functional NHE6 proteins. As a result, the pH in endosomes is not properly maintained. It is unclear how unregulated endosomal pH leads to neurological problems in people with Christianson syndrome. Some studies have shown that protein trafficking by endosomes is important for learning and memory, but the role of endosomal pH or the NHE6 protein in this process has not been identified.

Other Names for This Gene

- KIAA0267
- Na(+)/H(+) exchanger 6
- NHE6

- SL9A6_HUMAN
- sodium/hydrogen exchanger 6
- solute carrier family 9 (sodium/hydrogen exchanger), member 6
- solute carrier family 9 member 6
- solute carrier family 9, subfamily A (NHE6, cation proton antiporter 6), member 6

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of SLC9A6 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=10479\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=10479[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28SLC9A6%5BTIAB%5D%29+OR+%28%28KIAA0267%5BTIAB%5D%29+OR+%28NHE6%5BTIAB%5D%29+OR+%28sodium/hydrogen+exchanger+6%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%29>)

Catalog of Genes and Diseases from OMIM

- SOLUTE CARRIER FAMILY 9, MEMBER 6; SLC9A6 (<https://omim.org/entry/300231>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/10479>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=SLC9A6\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=SLC9A6[gene]))

References

- Brett CL, Wei Y, Donowitz M, Rao R. Human Na(+)/H(+) exchanger isoform 6 is found in recycling endosomes of cells, not in mitochondria. *Am J Physiol Cell Physiol*. 2002 May;282(5):C1031-41. doi: 10.1152/ajpcell.00420.2001. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/11940519>)
- Miyazaki E, Sakaguchi M, Wakabayashi S, Shigekawa M, Mihara K. NHE6 protein possesses a signal peptide destined for endoplasmic reticulum membrane and localizes in secretory organelles of the cell. *J Biol Chem*. 2001 Dec 28;276(52):49221-7. doi: 10.1074/jbc.M106267200. Epub 2001 Oct 18. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/11641397>)

- Nakamura N, Tanaka S, Teko Y, Mitsui K, Kanazawa H. Four Na⁺/H⁺ exchanger isoforms are distributed to Golgi and post-Golgi compartments and are involved in organelle pH regulation. *J Biol Chem*. 2005 Jan 14;280(2):1561-72. doi:10.1074/jbc.M410041200. Epub 2004 Nov 2. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15522866>)
- Ohgaki R, van IJzendoorn SC, Matsushita M, Hoekstra D, Kanazawa H. Organellar Na⁺/H⁺ exchangers: novel players in organelle pH regulation and their emerging functions. *Biochemistry*. 2011 Feb 1;50(4):443-50. doi: 10.1021/bi101082e. Epub 2010 Dec 30. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/21171650>)
- Park M, Salgado JM, Ostroff L, Helton TD, Robinson CG, Harris KM, Ehlers MD. Plasticity-induced growth of dendritic spines by exocytic trafficking from recycling endosomes. *Neuron*. 2006 Dec 7;52(5):817-30. doi:10.1016/j.neuron.2006.09.040. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/17145503>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1899130/>)

Genomic Location

The *SLC9A6* gene is found on the X chromosome (<https://medlineplus.gov/genetics/chromosome/x/>).

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