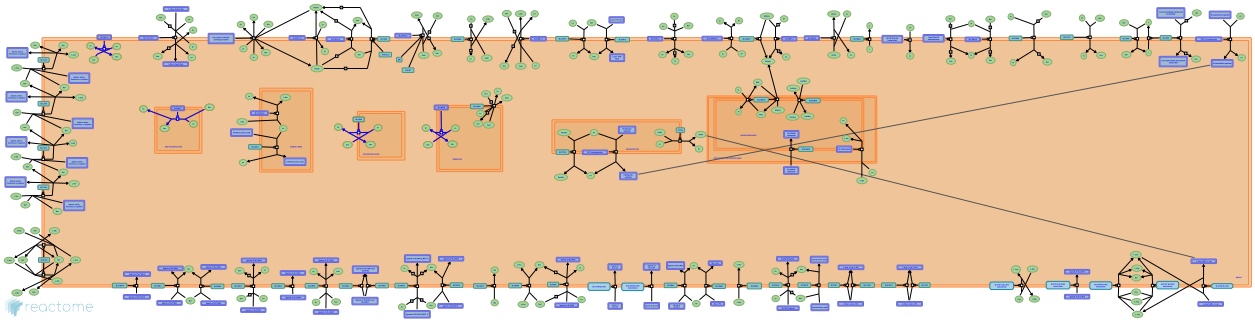
Sodium/Proton exchangers



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Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

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Literature references

Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics, 18*, 142. ↗

Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

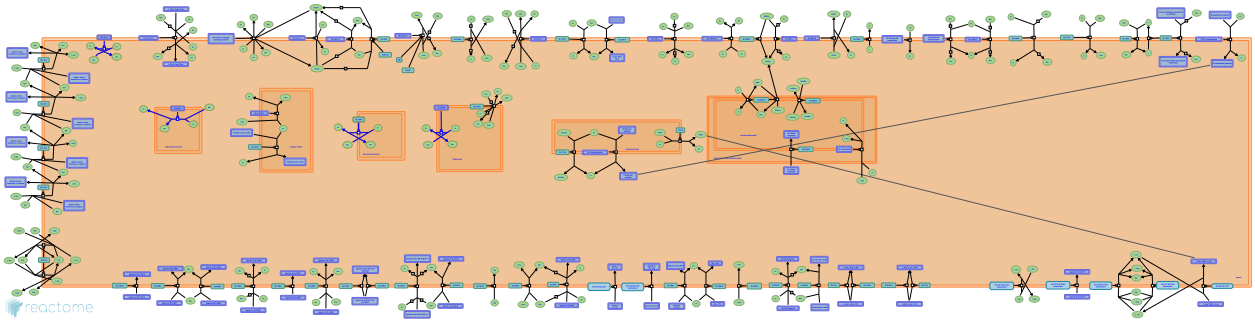
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

Sodium/Proton exchangers ↗

Stable identifier: R-HSA-425986

Compartments: plasma membrane



The SLC9 gene family encode proteins (sodium/proton exchangers, NHE or NHX) which exchange sodium (influx) for protons (efflux) electroneutrally. This mechanism is important because many metabolic processes generate acids which need to be removed to maintain pH. This is the major proton extruding system in cells, driven by the inward sodium ion chemical gradient. To date, there are eleven NHE genes, NHE1-11. NHE1-5 exchange cations at the cell membrane. NHE6-9 exchange cations at endosomal membranes or the trans-golgi network membranes.

Literature references

Orlowski, J., Grinstein, S. (2004). Diversity of the mammalian sodium/proton exchanger SLC9 gene family. *Pflugers Arch, 447*, 549-65. ↗

Nakamura, N., Tanaka, S., Teko, Y., Mitsui, K., Kanazawa, H. (2005). Four Na+/H+ exchanger isoforms are distributed to Golgi and post-Golgi compartments and are involved in organelle pH regulation. *J Biol Chem, 280*, 1561-72. ↗

Numata, M., Orlowski, J. (2001). Molecular cloning and characterization of a novel (Na+,K+)/H+ exchanger localized to the trans-Golgi network. *J Biol Chem, 276*, 17387-94. ↗

Editions

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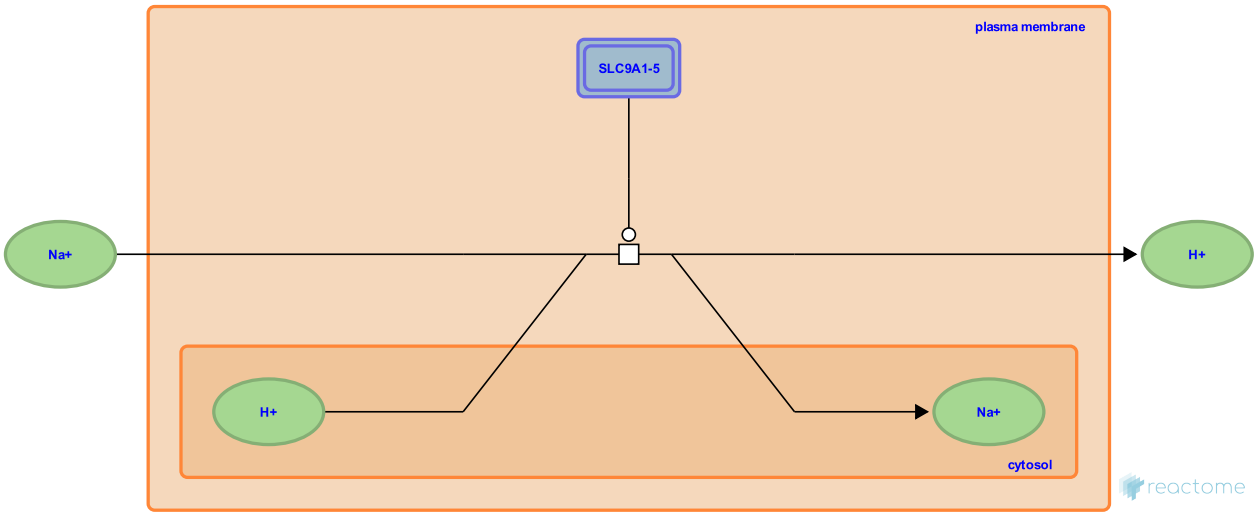
Na+/H+ exchanger transport (at cell membrane) ↗

Location: Sodium/Proton exchangers

Stable identifier: R-HSA-425994

Type: transition

Compartments: plasma membrane



NHE1 (SLC9A1) is present in most cells and is the most extensively characterized member of this family (Sardet C et al, 1989). NHE2-4 (SLC9A2-4) (Malakooti J et al, 1999; Brant SR et al, 1995) are expressed mainly in the kidney and GI tract. NHE5 (SLC9A5) (Baird NR et al, 1999) is highly expressed in neuronal-enriched areas of the CNS.

Literature references

Sardet, C., Franchi, A., Pouysségur, J. (1989). Molecular cloning, primary structure, and expression of the human growth factor-activatable Na+/H+ antiporter. *Cell, 56*, 271-80. ↗

Malakooti, J., Dahdal, RY., Schmidt, L., Layden, TJ., Dudeja, PK., Ramaswamy, K. (1999). Molecular cloning, tissue distribution, and functional expression of the human Na(+)/H(+) exchanger NHE2. *Am J Physiol, 277*, G383-90. ↗

Brant, SR., Yun, CH., Donowitz, M., Tse, CM. (1995). Cloning, tissue distribution, and functional analysis of the human Na+/N+ exchanger isoform, NHE3. *Am J Physiol, 269*, C198-206. ↗

Baird, NR., Orlowski, J., Szabó, EZ., Zaun, HC., Schultheis, PJ., Menon, AG. et al. (1999). Molecular cloning, genomic organization, and functional expression of Na+/H+ exchanger isoform 5 (NHE5) from human brain. *J Biol Chem, 274*, 4377-82. ↗

Editions

2009-06-11	Authored, Edited	Jassal, B.
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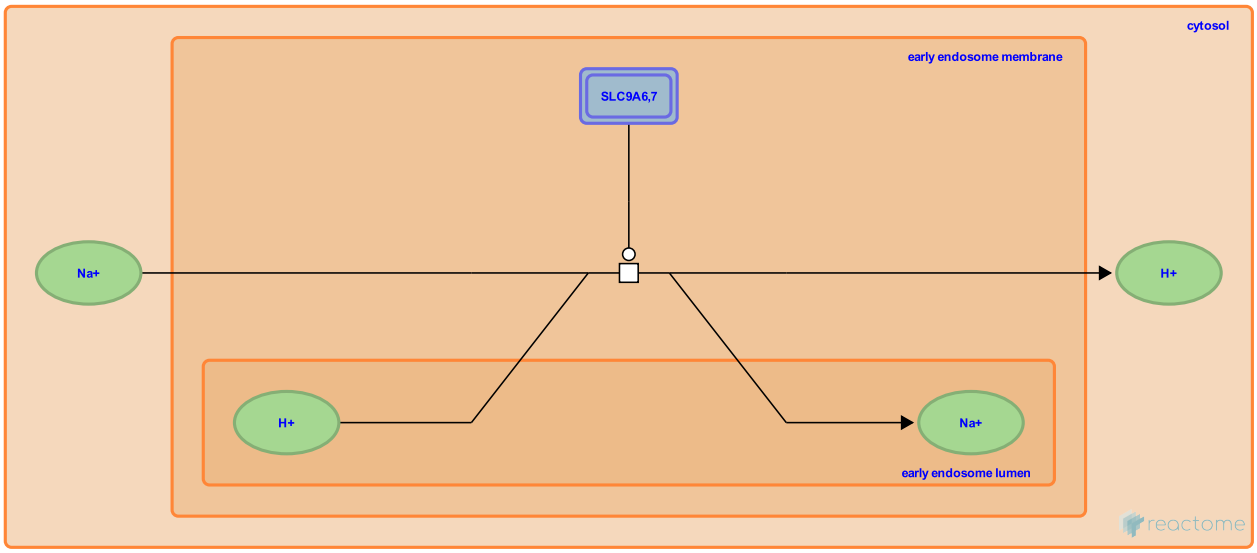
SLC9A6,7 exchange Na+ for H+ across the early endosome membrane ↗

Location: Sodium/Proton exchangers

Stable identifier: R-HSA-425983

Type: transition

Compartments: early endosome membrane



NHE6 (SLC9A6) (Brett CL et al, 2002; Nakamura N et al, 2005) is expressed ubiquitously and thought to play a housekeeping role in pH homeostasis in early endosomes.

Literature references

Brett, CL., Wei, Y., Donowitz, M., Rao, R. (2002). Human Na(+)/H(+) exchanger isoform 6 is found in recycling endosomes of cells, not in mitochondria. *Am J Physiol Cell Physiol, 282*, C1031-41. ↗

Nakamura, N., Tanaka, S., Teko, Y., Mitsui, K., Kanazawa, H. (2005). Four Na+/H+ exchanger isoforms are distributed to Golgi and post-Golgi compartments and are involved in organelle pH regulation. *J Biol Chem, 280*, 1561-72. ↗

Editions

2009-06-11	Authored, Edited	Jassal, B.
2009-08-24	Reviewed	He, L.

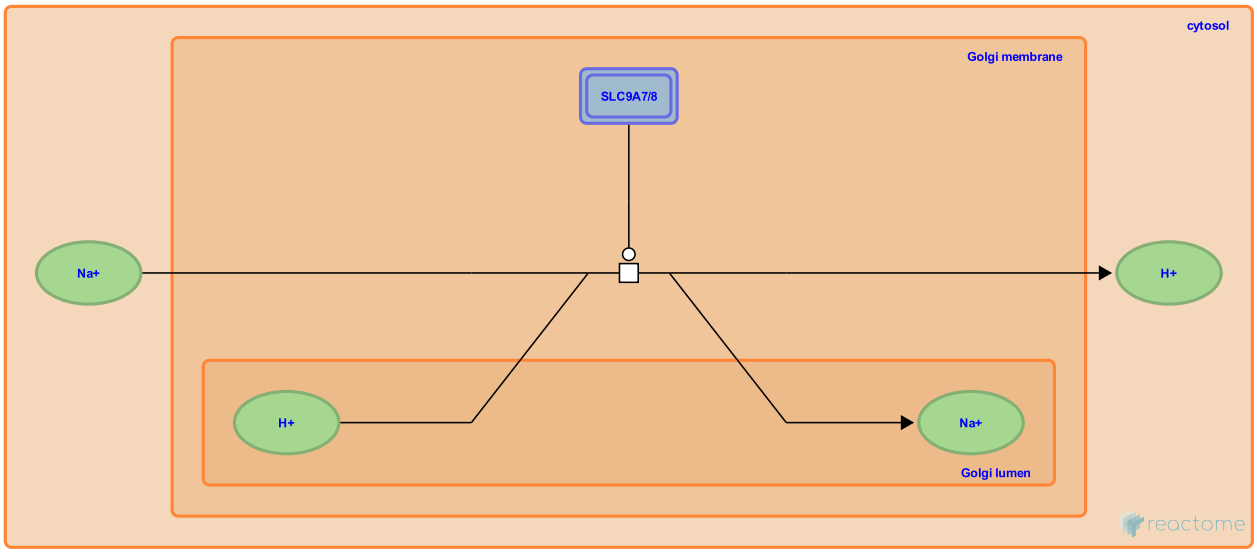
Na+/H+ exchanger transport (at trans-golgi membrane) ↗

Location: Sodium/Proton exchangers

Stable identifier: R-HSA-426015

Type: transition

Compartments: Golgi membrane



NHE7 and 8 (SLC9A7,8) (Nakamura N et al, 2005) are expressed ubiquitously and thought to play a house-keeping role in pH homeostasis in the trans-golgi network.

Literature references

Nakamura, N., Tanaka, S., Teko, Y., Mitsui, K., Kanazawa, H. (2005). Four Na+/H+ exchanger isoforms are distributed to Golgi and post-Golgi compartments and are involved in organelle pH regulation. *J Biol Chem, 280*, 1561-72. ↗

Numata, M., Orlowski, J. (2001). Molecular cloning and characterization of a novel (Na+,K+)/H+ exchanger localized to the trans-Golgi network. *J Biol Chem, 276*, 17387-94. ↗

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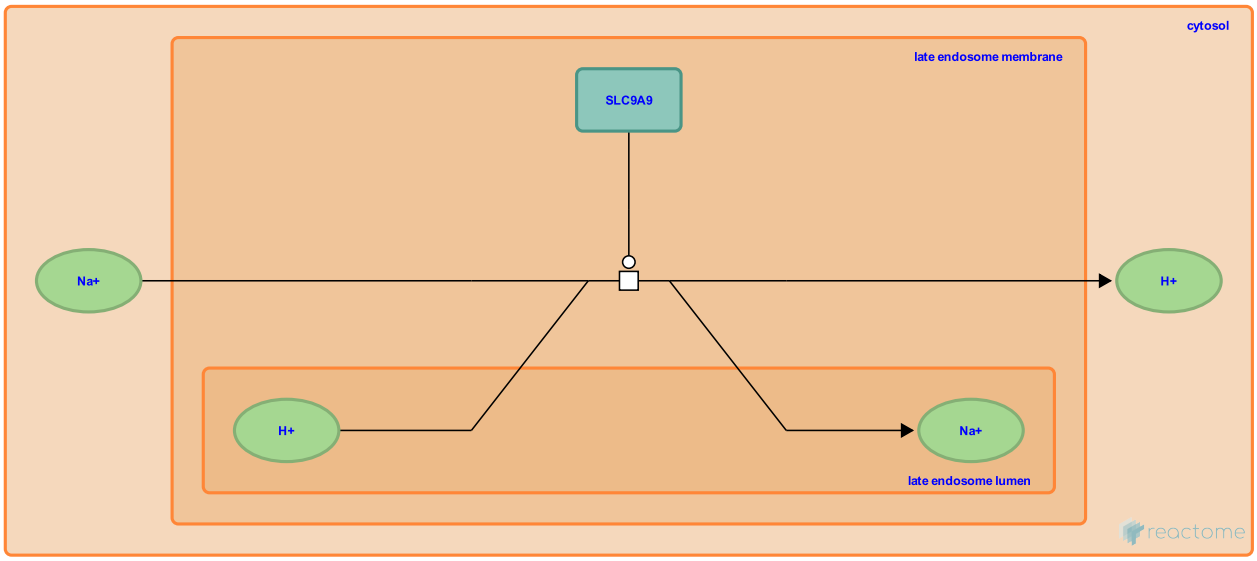
SLC9A9 exchanges Na+ for H+ across the late endosome membrane ↗

Location: Sodium/Proton exchangers

Stable identifier: R-HSA-425965

Type: transition

Compartments: late endosome membrane



NHE9 (SLC9A9) (Nakamura al. 2005) is expressed ubiquitously and thought to play a housekeeping role in pH homeostasis in the late endosome membrane.

Literature references

Nakamura, N., Tanaka, S., Teko, Y., Mitsui, K., Kanazawa, H. (2005). Four Na+/H+ exchanger isoforms are distributed to Golgi and post-Golgi compartments and are involved in organelle pH regulation. *J Biol Chem, 280*, 1561-72. ↗

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