Defective SLC1A3 causes episodic ataxia 6 (EA6)

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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**


Reactome database release: 72

This document contains 1 pathway and 1 reaction (see Table of Contents)

https://release.reactome.org
Defective SLC1A3 causes episodic ataxia 6 (EA6)

Stable identifier: R-HSA-5619062

Diseases: episodic ataxia

There are two classes of glutamate transporters; the excitatory amino acid transporters (EAATs) which depend on an electrochemical gradient of Na+ ions and vesicular glutamate transporters (VGLUTs) which are proton-dependent. Together, these transporters uptake and release glutamate to mediate this neurotransmitter's excitatory signal and are part of the glutamate-gluatamine cycle.

The SLC1 gene family includes five high-affinity glutamate transporters encoded by SLC1, 2, 3, 6 and 7. These transporters can mediate transport of L-Glutamate (L-Glu), L-Aspartate (L-Asp) and D-Aspartate (D-Asp) with cotransport of 3 Na+ ions and H+ and antiport of a K+ ion. This mechanism allows glutamate into cells against a concentration gradient. This is a crucial factor in the protection of neurons against glutamate excitotoxicity (the excitation of nerve cells to their death) in the CNS (Zhou & Danbolt 2014).

SLC1A3 is highly expressed in the cerebellum but also found in the frontal cortex, hippocampus and basal ganglia. Defects in SLC1A3 have been shown to cause episodic ataxia type 6 (EA6; MIM:612656) where mutations in SLC1A3 can lead to decreased glutamate uptake, thus contributing to neuronal hyperexcitability to cause seizures, hemiplegia and episodic ataxia (Jen et al. 2005, de Vries et al. 2009).

Literature references


Editions

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Defective SLC1A3 does not cotransport L-Glu, L-Asp, D-Asp, H+, 3Na+ from extracellular region to cytosol

**Location:** Defective SLC1A3 causes episodic ataxia 6 (EA6)

**Stable identifier:** R-HSA-5625015