

## KCNT1 gene

potassium sodium-activated channel subfamily T member 1

### Normal Function

The *KCNT1* gene belongs to a large family of genes that provide instructions for making potassium channels. These channels, which transport positively charged atoms (ions) of potassium into and out of cells, play a key role in a cell's ability to generate and transmit electrical signals.

Potassium channels are made up of several protein components (subunits). Each channel contains four alpha subunits that form the hole (pore) through which potassium ions move. Potassium channels can be made from four alpha subunits produced from the *KCNT1* gene, or they can be made from subunits produced from both the *KCNT1* gene and another gene called the *KCNT2* gene.

The specific function of a potassium channel depends on its protein components and its location in the body. Channels that are made with the KCNT1 protein are active in nerve cells (neurons) in the brain, where they transport potassium ions out of cells. This flow of ions helps generate currents that activate (excite) neurons and send signals in the brain.

Researchers have determined that a molecule called PKC can increase the activity of channels that are made with the KCNT1 protein. While these channels can generate electrical currents without PKC, the currents are stronger when PKC attaches to the channel and increases the channel's activity.

### Health Conditions Related to Genetic Changes

#### Autosomal dominant sleep-related hypermotor epilepsy

Pathogenic variants (also called mutations) in the *KCNT1* gene can cause autosomal dominant sleep related hypermotor epilepsy (ADSHE), a genetic form of epilepsy that is characterized by seizures that typically begin while a person is sleeping and involve some degree of muscle (motor) activity. The seizures may include repetitive, abnormal muscle movements; muscle stiffness; or abnormal body positioning. People with ADSHE that is caused by *KCNT1* gene variants typically have seizures that begin early in life and do not respond well to treatment. These individuals may also have intellectual disabilities and behavioral or psychiatric issues.

Most of the *KCNT1* variants that are responsible for ADSHE cause cells to produce a version of the KCNT1 protein that does not function properly. The abnormal protein increases the flow of ions through the potassium channel. Because the activity of the channel is enhanced, these variants are described as “gain-of-function variants.” The change in the flow of potassium ions likely contributes to the excitation of neurons and the seizures seen in people with ADSHE.

### Epilepsy of infancy with migrating focal seizures

Pathogenic variants in the *KCNT1* gene have been found in individuals with epilepsy of infancy with migrating focal seizures (EIMFS). This condition is typically characterized by recurrent seizures that begin before the age of 6 months. Affected individuals usually have significant developmental delays. *KCNT1* gene variants are the most common genetic cause of EIMFS.

Most of the *KCNT1* gene variants that cause EIMFS lead to the substitution of one protein building block (amino acid) for another in the KCNT1 protein. These variants are typically gain-of-function variants that increase the flow of potassium ions through the potassium channels. The change in the flow of potassium ions likely contributes to the excitation of neurons and the repeated seizures seen in people with EIMFS.

### Other disorders

Pathogenic variants in the *KCNT1* gene have also been associated with a type of developmental and epileptic encephalopathy (DEE). DEEs are a group of epileptic disorders that are characterized by developmental delays and abnormal brain function (encephalopathy) that worsens over time. Affected individuals often have seizures that are difficult to control with medication. Additional signs and symptoms seen in children with *KCNT1*-related DEE can include poor muscle tone (hypotonia), movement disorders, and a small head size (microcephaly). The *KCNT1* gene variants that are associated with DEE are typically gain-of-function variants that increase the flow of ions through the potassium channels.

### **Other Names for This Gene**

- KCa4.1
- KIAA1422
- potassium channel, sodium activated subfamily T, member 1
- potassium channel, subfamily T, member 1
- SLACK
- Slo2.2

### **Additional Information & Resources**

#### Tests Listed in the Genetic Testing Registry

- Tests of KCNT1 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=57582\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=57582[geneid]))

### Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28KCNT1%5BTIAB%5D%29+OR+%28SLACK%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5BIa%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>)

### Catalog of Genes and Diseases from OMIM

- POTASSIUM CHANNEL, SUBFAMILY T, MEMBER 1; KCNT1 (<https://omim.org/entry/608167>)

### Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/57582>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=KCNT1\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=KCNT1[gene]))

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## Genomic Location

The *KCNT1* gene is found on chromosome 9 (<https://medlineplus.gov/genetics/chromosome/9/>).

**Last updated August 1, 2025**