

LGI1 gene

leucine rich glioma inactivated 1

Normal Function

The *LGI1* gene provides instructions for making a protein called leucine-rich glioma inactivated 1 (Lgi1) or epitempin. This protein is found primarily in nerve cells (neurons) in the brain, including a part of the brain called the temporal lobe. The temporal lobe is involved in hearing, speech, memory, and emotion.

Although researchers have proposed several functions for epitempin, its precise role in the brain remains uncertain. This protein is probably involved in normal brain development.

Some studies have suggested that epitempin plays a role in the normal function of potassium channels in neurons. These channels are embedded in the cell membrane, and they transport charged potassium atoms (potassium ions) out of neurons. Potassium channels are critical for normal electrical signaling in these cells. Other studies have found that epitempin is transported out of neurons. The function of this protein outside cells is unclear.

Epitempin may also help regulate communication between neurons. Researchers have determined that epitempin attaches (binds) to a receptor protein called ADAM22 on the surface of neurons. Together, these proteins help control the release of certain brain chemicals called neurotransmitters. These chemicals allow neighboring neurons to communicate with each other, which is how signals are relayed throughout the brain.

Health Conditions Related to Genetic Changes

Autosomal dominant epilepsy with auditory features

Many variants (also called mutations) in the *LGI1* gene have been identified in people with autosomal dominant epilepsy with auditory features (ADEAF). People with this rare form of epilepsy typically hear sounds, like buzzing or humming, during seizures. Some of the variants associated with this condition change a single protein building block (amino acid) in the epitempin protein, which alters the protein's structure. Other variants lead to the production of an abnormally short, nonfunctional version of the protein. Researchers suspect that the altered protein is unable to be secreted, which would leave it trapped inside cells and unable to perform its usual functions. Changes to

epitempin may alter communication between neurons, which can lead to seizure activity in the brain.

Cancers

When the *LG1* gene was first described, researchers believed that it might play a role in the growth and progression of brain tumors called gliomas. Epitempin was thought to act as a tumor suppressor, which is a protein that keeps cells from growing and dividing too fast or in an uncontrolled way. More recent studies, however, have called into question the role of epitempin in cancerous tumors. Because no *LG1* variants have been identified in gliomas and people with ADEAF do not appear to have a significantly increased risk of these tumors, it now appears unlikely that epitempin functions as a tumor suppressor.

Other Names for This Gene

- EPITEMPIN
- Epitempin 1
- EPT
- ETL1
- IB1099
- Leucine-Rich Glioma-Inactivated Protein 1
- leucine-rich, glioma inactivated 1
- LGI1_HUMAN

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of LGI1 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=9211\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=9211[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28LGI1%5BTIAB%5D%29+OR+%28epitempin%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+1800+days%22%5Bdp%5D>)

Catalog of Genes and Diseases from OMIM

- LEUCINE-RICH GENE, GLIOMA-INACTIVATED, 1; LGI1 (<https://omim.org/entry/604619>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/9211>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=LGI1\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=LGI1[gene]))

References

- Chernova OB, Somerville RP, Cowell JK. A novel gene, LGI1, from 10q24 is rearranged and downregulated in malignant brain tumors. *Oncogene*. 1998 Dec3; 17(22):2873-81. doi: 10.1038/sj.onc.1202481. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/9879993>)
- Fels E, Muniz-Castrillo S, Vogrig A, Joubert B, Honnorat J, Pascual O. Role of LGI1 protein in synaptic transmission: From physiology to pathology. *Neurobiol Dis*. 2021 Dec;160:105537. doi: 10.1016/j.nbd.2021.105537. Epub 2021 Oct 22. Citation on PubMed (<https://www.ncbi.nlm.nih.gov/pubmed/34695575>)
- Fukata Y, Adesnik H, Iwanaga T, Bredt DS, Nicoll RA, Fukata M. Epilepsy-related ligand/receptor complex LGI1 and ADAM22 regulate synaptic transmission. *Science*. 2006 Sep 22;313(5794):1792-5. doi:10.1126/science.1129947. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16990550>)
- Furlan S, Roncaroli F, Forner F, Vitiello L, Calabria E, Piquer-Sirerol S, Valle G, Perez-Tur J, Michelucci R, Nobile C. The LGI1/epitempin gene encodes two protein isoforms differentially expressed in human brain. *J Neurochem*. 2006 Aug;98(3):985-91. doi: 10.1111/j.1471-4159.2006.03939.x. Epub 2006 Jun 19. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16787412>)
- Gu W, Brodtkorb E, Piepoli T, Finocchiaro G, Steinlein OK. LGI1: a gene involved in epileptogenesis and glioma progression? *Neurogenetics*. 2005 May;6(2):59-66. doi: 10.1007/s10048-005-0216-5. Epub 2005 Apr 13. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15827762>)
- Gu W, Brodtkorb E, Steinlein OK. LGI1 is mutated in familial temporal lobe epilepsy characterized by aphasic seizures. *Ann Neurol*. 2002 Sep;52(3):364-7. doi: 10.1002/ana.10280. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12205652>)
- Kalachikov S, Evgrafov O, Ross B, Winawer M, Barker-Cummings C, Martinelli-Boneschi F, Choi C, Morozov P, Das K, Teplitskaya E, Yu A, Cayanis E, Penchaszadeh G, Kottmann AH, Pedley TA, Hauser WA, Ottman R, Gilliam TC. Mutations in LGI1 cause autosomal-dominant partial epilepsy with auditory features. *Nat Genet*. 2002 Mar;30(3):335-41. doi: 10.1038/ng832. Epub 2002 Jan 28. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/11810107>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2606053/>)
- Morante-Redolat JM, Gorostidi-Pagola A, Piquer-Sirerol S, Saenz A, Poza JJ, Galan J, Gesk S, Sarafidou T, Mautner VF, Binelli S, Staub E, Hinzmann B, French L, Prud'homme JF, Passarelli D, Scannapieco P, Tassinari CA, Avanzini G, Marti-Masso JF, Kluwe L, Deloukas P, Moschonas NK, Michelucci R, Siebert R, Nobile C, Perez-Tur J, Lopez de Munain A. Mutations in the LGI1/Epitempin gene on 10q24 cause autosomal dominant lateral temporal epilepsy. *Hum Mol Genet*. 2002 May1;

11(9):1119-28. doi: 10.1093/hmg/11.9.1119. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/11978770>)

- Ottman R, Winawer MR, Kalachikov S, Barker-Cummings C, Gilliam TC, Pedley TA, Hauser WA. LGI1 mutations in autosomal dominant partial epilepsy with auditory features. *Neurology*. 2004 Apr 13;62(7):1120-6. doi:10.1212/01.wnl.0000120098.39231.6e. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15079011>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1361770/>)
- Piepoli T, Jakupoglu C, Gu W, Lualdi E, Suarez-Merino B, Poliani PL, Cattaneo MG, Ortino B, Goplen D, Wang J, Mola R, Inverardi F, Frassoni C, Bjerkvig R, Steinlein O, Vicentini LM, Brustle O, Finocchiaro G. Expression studies in gliomas and glial cells do not support a tumor suppressor role for LGI1. *NeuroOncol*. 2006 Apr;8(2):96-108. doi: 10.1215/15228517-2005-006. Epub 2006 Mar 2. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16533756>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1871933/>)
- Schulte U, Thumfart JO, Klocker N, Sailer CA, Bildl W, Biniossek M, Dehn D, Deller T, Eble S, Abbass K, Wangler T, Knaus HG, Fakler B. The epilepsy-linked Lgi1 protein assembles into presynaptic Kv1 channels and inhibits inactivation by Kvbeta1. *Neuron*. 2006 Mar 2;49(5):697-706. doi: 10.1016/j.neuron.2006.01.033. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16504945>)
- Senechal KR, Thaller C, Noebels JL. ADPEAF mutations reduce levels of secreted LGI1, a putative tumor suppressor protein linked to epilepsy. *Hum Mol Genet*. 2005 Jun 15;14(12):1613-20. doi: 10.1093/hmg/ddi169. Epub 2005 Apr 27. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15857855>)
- Sirerol-Piquer MS, Ayerdi-Izquierdo A, Morante-Redolat JM, Herranz-Perez V, Favell K, Barker PA, Perez-Tur J. The epilepsy gene LGI1 encodes a secreted glycoprotein that binds to the cell surface. *Hum Mol Genet*. 2006 Dec 1;15(23):3436-45. doi: 10.1093/hmg/ddl421. Epub 2006 Oct 26. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/17067999>)

Genomic Location

The *LGI1* gene is found on chromosome 10 (<https://medlineplus.gov/genetics/chromosome/10/>).

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