GABRA1 gene

gamma-aminobutyric acid type A receptor alpha1 subunit

Normal Function

The *GABRA1* gene provides instructions for making one piece, the alpha-1 (α1) subunit, of the $GABA_A$ receptor protein. $GABA_A$ receptors are made up of different combinations of five protein subunits, each produced from a different gene. (Nineteen different genes provide instructions for $GABA_A$ receptor subunits.) These subunits form a hole (pore) in the cell membrane through which negatively charged chlorine atoms (chloride ions) can flow.

A chemical that transmits signals in the brain (a neurotransmitter) called gamma-amino butyric acid (GABA) attaches to $GABA_A$ receptors. Once GABA attaches, the pore formed by the subunits opens, and chloride ions flow across the cell membrane. After infancy, chloride ions flow into the cell through the open pore, which creates an environment in the cell that blocks (inhibits) signaling between neurons. The primary role of GABA in children and adults is to prevent the brain from being overloaded with too many signals. In contrast, in newborns and infants, chloride ions flow out of the cell when the pore is opened, creating an environment that allows signaling between neurons.

Health Conditions Related to Genetic Changes

Juvenile myoclonic epilepsy

A mutation in the *GABRA1* gene has been identified in at least one family with juvenile myoclonic epilepsy. This condition typically begins in childhood or adolescence and causes recurrent myoclonic seizures, which are characterized by rapid, uncontrolled muscle jerks. Affected individuals can also have other types of seizures called generalized tonic-clonic seizures (or grand mal seizures) and absence seizures. The mutation associated with this condition changes a single protein building block (amino acid) in the α1 subunit. The amino acid alanine at protein position 322 is replaced by the amino acid asparagine. This gene mutation is written as Ala322Asp or A322D.

This *GABRA1* gene mutation leads to the formation of an abnormal α1 subunit that reduces $GABA_A$ receptor function. $GABA_A$ receptors containing the abnormal subunit are broken down before they reach the cell membrane. Studies show that the altered receptors can also interfere with normal receptors inside the cell, leading to the additional loss of normal receptors. Because of the reduction of $GABA_A$ receptor function, signaling between neurons is not regulated, which can lead to

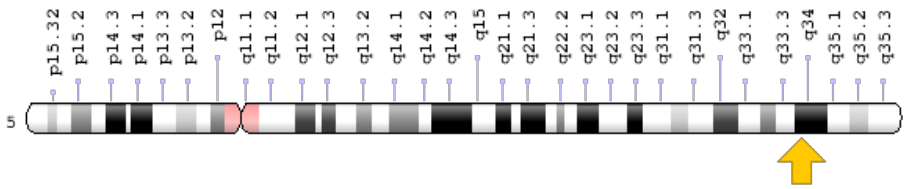
overstimulation of neurons. Researchers believe that the overstimulation of certain neurons in the brain triggers the abnormal brain activity associated with seizures.

Childhood absence epilepsy

Chromosomal Location

Cytogenetic Location: 5q34, which is the long (q) arm of chromosome 5 at position 34

Molecular Location: base pairs 161,847,191 to 161,899,971 on chromosome 5 (Homo sapiens Updated Annotation Release 109.20190905, GRCh38.p13) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- ECA4
- EJM
- EJM5
- GABA(A) receptor subunit alpha-1
- GABA(A) receptor, alpha 1
- gamma-aminobutyric acid (GABA) A receptor, alpha 1
- gamma-aminobutyric acid receptor subunit alpha-1
- gamma-aminobutyric acid receptor subunit alpha-1 precursor
- GBRA1_HUMAN

Additional Information & Resources

Educational Resources

- Neuroscience (second edition, 2001): GABA and Glycine https://www.ncbi.nlm.nih.gov/books/NBK11084/
- Neuroscience (second edition, 2001): GABA and Glycine Receptors https://www.ncbi.nlm.nih.gov/books/NBK10977/

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28GABRA1%5BTIAB%5D%29+OR+%28%28EJM%5BTIAB%5D%29+OR+%28ECA4%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+2160+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- GAMMA-AMINOBUTYRIC ACID RECEPTOR, ALPHA-1
  http://omim.org/entry/137160

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_GABRA1.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=GABRA1%5Bgene%5D
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:4075
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:2554
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/2554
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