



GLRA1 gene

glycine receptor alpha 1

Normal Function

The *GLRA1* gene provides instructions for making one part, the alpha (α)1 subunit, of the glycine receptor protein. The glycine receptor is embedded in the membrane of nerve cells (neurons) in the spinal cord and the part of the brain that is connected to the spinal cord (the brainstem). The glycine receptor is made up of five subunits: two α 1 subunits and three beta (β) subunits. The β subunit is produced from a different gene.

Receptor proteins have specific sites into which certain other molecules, called ligands, fit like keys into locks. Together, ligands and their receptors trigger signals that affect cell development and function. The ligand for the glycine receptor is the protein building block (amino acid) glycine. This molecule also acts as a neurotransmitter, which is a chemical messenger that transmits signals in the nervous system.

When glycine attaches (binds) to the glycine receptor, the receptor opens to allow negatively charged chlorine atoms (chloride ions) to enter the neuron. This influx of chloride ions reduces the neurons's ability to transmit signals to other neurons. Because they stop (inhibit) signaling, glycine receptors are known as inhibitory receptors.

Health Conditions Related to Genetic Changes

Hereditary hyperekplexia

More than 60 mutations in the *GLRA1* gene have been found to cause hereditary hyperekplexia. This condition is most often seen in infants who experience increased muscle tone (hypertonia) and an exaggerated startle reaction to unexpected stimuli, especially loud noises. The startle reaction can trigger a brief period of rigidity and immobility, and in some cases, infants stop breathing. Most *GLRA1* gene mutations change single amino acids in the α 1 subunit of the glycine receptor protein. The most common mutation replaces the amino acid arginine with the amino acid leucine at protein position 271 (written as Arg271Leu or R271L).

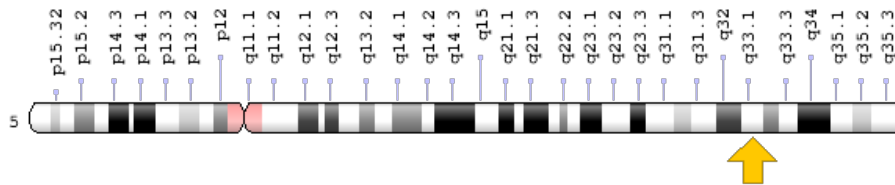
GLRA1 gene mutations that cause hereditary hyperekplexia impair the ability of the glycine receptor protein to respond to the ligand glycine. Some *GLRA1* gene mutations alter the structure of the glycine receptor, which can prevent the receptor from opening or cause it to open without the presence of glycine. Other mutations prevent the receptor from reaching the cell membrane. When the glycine receptor is dysfunctional or missing, chloride ions enter the cell when they are not needed or cannot enter the cell at all. The resulting increase in cell signaling in the spinal cord

and brainstem likely causes the abnormal muscle movements, exaggerated startle reaction, and other signs and symptoms of hereditary hyperekplexia.

Chromosomal Location

Cytogenetic Location: 5q33.1, which is the long (q) arm of chromosome 5 at position 33.1

Molecular Location: base pairs 151,822,513 to 151,924,851 on chromosome 5 (Homo sapiens Updated Annotation Release 109.20190607, GRCh38.p13) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- GLRA1_HUMAN
- glycine receptor, alpha 1
- glycine receptor, alpha 1 isoform 1 precursor
- glycine receptor, alpha 1 isoform 2 precursor
- STHE

Additional Information & Resources

Educational Resources

- Basic Neurochemistry (sixth edition, 1999): Glycine Receptors
<https://www.ncbi.nlm.nih.gov/books/NBK28003/>
- Molecular Biology of the Cell (fourth edition, 2002): Chemical Synapses Can Be Excitatory or Inhibitory
<https://www.ncbi.nlm.nih.gov/books/NBK26910/#A2054>
- Molecular Cell Biology (fourth edition, 2000): GABA- and Glycine-Gated Cl- Channels Are Found at Many Inhibitory Synapses
<https://www.ncbi.nlm.nih.gov/books/NBK21586/#A6238>
- Washington University, St. Louis: Neuromuscular Disease Center
<https://neuromuscular.wustl.edu/mother/activity.html#hyperekplexia>

Clinical Information from GeneReviews

- Hyperekplexia
<https://www.ncbi.nlm.nih.gov/books/NBK1260>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28GLRA1%5BTIAB%5D%29+OR+%28glycine+receptor+alpha+1%5BTIAB%5D%29%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

- GLYCINE RECEPTOR, ALPHA-1 SUBUNIT
<http://omim.org/entry/138491>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
http://atlasgeneticsoncology.org/Genes/GC_GLRA1.html
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=GLRA1%5Bgene%5D>
- HGNC Gene Symbol Report
https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:4326
- Monarch Initiative
<https://monarchinitiative.org/gene/NCBIGene:2741>
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/2741>
- UniProt
<https://www.uniprot.org/uniprot/P23415>

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