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 α1 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 α1 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.

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

Tests Listed in the Genetic Testing Registry

- Tests of GLRA1 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=2741[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?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%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- GLYCINE RECEPTOR, ALPHA-1 SUBUNIT; GLRA1 (https://omim.org/entry/138491)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/2741)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=GLRA1[gene])

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Genomic Location

The *GLRA1* gene is found on chromosome 5 (https://medlineplus.gov/genetics/chromosome/5/).

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