

## CLRN1 gene

clarin 1

### Normal Function

The *CLRN1* gene provides information for making a protein called clarin 1. This protein is probably involved in normal hearing and vision. Clarin 1 has been found in several areas of the body, including sensory cells in the inner ear called hair cells. These cells help transmit sound and motion signals to the brain. This protein is also active in the retina, which is the light-sensing tissue that lines the back of the eye. Although the function of clarin 1 has not been determined, studies suggest that it plays a role in communication between nerve cells (neurons) in the inner ear and in the retina. Clarin 1 may be important for the development and function of synapses, which are junctions between neurons where cell-to-cell communication occurs.

### Health Conditions Related to Genetic Changes

#### Usher syndrome

At least 15 mutations in the *CLRN1* gene have been identified in people with Usher syndrome type III, which is characterized by a combination of hearing loss and vision loss. Some affected individuals also have problems with balance and coordination. *CLRN1* gene mutations cause a form of the condition known as Usher syndrome type IIIA (USH3A). This form of Usher syndrome is rare in most countries, although it represents about 40 percent of all Usher syndrome cases in the Finnish population.

Several *CLRN1* gene mutations change single protein building blocks (amino acids) in the clarin 1 protein. In some cases, these mutations lead to the production of an abnormally short version of the protein or prevent the production of any functional clarin 1. Other mutations insert or delete small amounts of DNA in the *CLRN1* gene, which probably impairs the normal function of the protein. It is unclear how a missing or altered clarin 1 protein leads to the signs and symptoms of Usher syndrome type IIIA.

Two particular *CLRN1* gene mutations are most common in families of Finnish ancestry. One mutation, sometimes called Finmajor and written as Tyr176Ter or Y176X, leads to the production of an abnormally short, nonfunctional version of clarin 1. The other mutation, written as Met120Lys or M120K and also known as Finminor, substitutes the amino acid lysine for the amino acid methionine at protein position 120. This mutation appears to disrupt the protein's normal function.

## Retinitis pigmentosa

MedlinePlus Genetics provides information about Retinitis pigmentosa

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

- USH3
- USH3A
- USH3A\_HUMAN
- Usher syndrome 3A
- Usher syndrome type 3 protein

### **Additional Information & Resources**

#### Tests Listed in the Genetic Testing Registry

- Tests of CLRN1 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=7401\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=7401[geneid]))

#### Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28USH3A%5BTIAB%5D%29+OR+%28CLRN1%5BTIAB%5D%29%29+OR+%28%28USH3%5BTIAB%5D%29+OR+%28clarin+1%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D%29%29%29>)

#### Catalog of Genes and Diseases from OMIM

- CLARIN 1; CLRN1 (<https://omim.org/entry/606397>)

#### Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/7401>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=CLRN1\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=CLRN1[gene]))

### **References**

- Adato A, Vreugde S, Joensuu T, Avidan N, Hamalainen R, Belenkiy O, Olender T, Bonne-Tamir B, Ben-Asher E, Espinos C, Millan JM, Lehesjoki AE, Flannery JG, Avraham KB, Pietrovski S, Sankila EM, Beckmann JS, Lancet D. USH3A transcripts encode clarin-1, a four-transmembrane-domain protein with a possible role in sensory synapses. *Eur J Hum Genet.* 2002 Jun;10(6):339-50. doi:10.1038/sj.ejhg.5200831. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12080385>)

- Aller E, Jaijo T, Oltra S, Alio J, Galan F, Najera C, Beneyto M, Millan JM. Mutation screening of USH3 gene (clarin-1) in Spanish patients with Usher syndrome: low prevalence and phenotypic variability. *Clin Genet*. 2004 Dec;66(6):525-9. doi: 10.1111/j.1399-0004.2004.00352.x. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15521980>)
- Fields RR, Zhou G, Huang D, Davis JR, Moller C, Jacobson SG, Kimberling WJ, Sumegi J. Usher syndrome type III: revised genomic structure of the USH3 gene and identification of novel mutations. *Am J Hum Genet*. 2002 Sep;71(3):607-17. doi: 10.1086/342098. Epub 2002 Jul 16. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12145752>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC449697/>)
- Geng R, Geller SF, Hayashi T, Ray CA, Reh TA, Bermingham-McDonogh O, Jones SM, Wright CG, Melki S, Imanishi Y, Palczewski K, Alagramam KN, Flannery JG. Usher syndrome IIIA gene clarin-1 is essential for hair cell function and associated neural activation. *Hum Mol Genet*. 2009 Aug 1;18(15):2748-60. doi:10.1093/hmg/ddp210. Epub 2009 May 3. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/19414487>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2706682/>)
- Geng R, Melki S, Chen DH, Tian G, Furness DN, Oshima-Takago T, Neef J, Moser T, Askew C, Horwitz G, Holt JR, Imanishi Y, Alagramam KN. The mechanosensory structure of the hair cell requires clarin-1, a protein encoded by Usher syndrome III causative gene. *J Neurosci*. 2012 Jul 11;32(28):9485-98. doi:10.1523/JNEUROSCI.0311-12.2012. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/22787034>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3422646/>)
- Isosomppi J, Vastinsalo H, Geller SF, Heon E, Flannery JG, Sankila EM. Disease-causing mutations in the CLRN1 gene alter normal CLRN1 protein trafficking to the plasma membrane. *Mol Vis*. 2009 Sep 8;15:1806-18. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/19753315>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2742642/>)
- Joensuu T, Hamalainen R, Yuan B, Johnson C, Tegelberg S, Gasparini P, Zelante L, Pirvola U, Pakarinen L, Lehesjoki AE, de la Chapelle A, Sankila EM. Mutations in a novel gene with transmembrane domains underlie Usher syndrome type 3. *Am J Hum Genet*. 2001 Oct;69(4):673-84. doi: 10.1086/323610. Epub 2001 Aug 27. Erratum in: *Am J Hum Genet* 2001 Nov;69(5):1160. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/11524702>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1226054/>)
- Khan MI, Kersten FF, Azam M, Collin RW, Hussain A, Shah ST, Keunen JE, Kremer H, Cremers FP, Qamar R, den Hollander AI. CLRN1 mutations cause nonsyndromic retinitis pigmentosa. *Ophthalmology*. 2011 Jul;118(7):1444-8. doi:10.1016/j.ophtha.2010.10.047. Epub 2011 Feb 18. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/21310491>)

## Genomic Location

The *CLRN1* gene is found on chromosome 3 (<https://medlineplus.gov/genetics/chromosome/3/>).

**Last updated June 1, 2016**