# BEST1 gene

bestrophin 1

## Normal Function

The *BEST1* gene provides instructions for making a protein called bestrophin-1, which appears to play a critical role in normal vision. Bestrophin-1 is found in a thin layer of cells at the back of the eye called the retinal pigment epithelium. This cell layer supports and nourishes the retina, which is the light-sensitive tissue that lines the back of the eye. The retinal pigment epithelium is involved in the growth and development of the eye, maintenance of the retina, and the normal function of specialized cells called photoreceptors that detect light and color.

Bestrophin-1 functions as a channel across cell membranes in the retinal pigment epithelium. Charged chlorine atoms (chloride ions) are transported through these channels in response to cellular signals. Some studies suggest that bestrophin-1 may also help regulate the entry of charged calcium atoms (calcium ions) into cells of the retinal pigment epithelium. Other potential functions of bestrophin-1 are under study.

## Health Conditions Related to Genetic Changes

Vitelliform macular dystrophy

More than 100 mutations in the *BEST1* gene have been identified in people with vitelliform macular dystrophy. These mutations can cause either the early-onset form of the disorder (known as Best disease) or the adult-onset form. Both types of vitelliform macular dystrophy are characterized by the buildup of a fatty yellow pigment (lipofuscin) in cells of the retinal pigment epithelium. Over time, the abnormal accumulation of this substance can damage the photoreceptors that are critical for sharp central vision.

Most *BEST1* mutations involved in vitelliform macular dystrophy change single protein building blocks (amino acids) in bestrophin-1. The altered protein probably forms an abnormally shaped channel that cannot properly regulate the flow of chloride ions into or out of cells in the retinal pigment epithelium. It remains unclear how this defect is related to the buildup of lipofuscin and a progressive loss of central vision in people with vitelliform macular dystrophy.

Age-related macular degeneration

MedlinePlus Genetics provides information about Age-related macular degeneration

Autosomal dominant vitreoretinochoroidopathy

*BEST1* gene mutations can cause a rare eye disorder called autosomal dominant vitreoretinochoroidopathy (ADVIRC); at least four mutations in this gene have been found in affected individuals. ADVIRC is characterized by abnormalities of the clear gel that fills the eye (the vitreous), the retina, and the network of blood vessels within the retina (the choroid). These abnormalities can lead to vision impairment.

*BEST1* gene mutations involved in ADVIRC change single DNA building blocks ( nucleotides) in the gene. These changes alter how the gene's instructions are used to make bestrophin-1, which leads to production of versions of the protein that are missing certain segments or have extra segments. It is not clear how these versions of bestrophin-1 affect chloride ion transport or lead to the eye abnormalities characteristic of ADVIRC. Researchers suspect that the abnormalities are related to defects in the retinal pigment epithelium or the photoreceptors.

Retinitis pigmentosa

MedlinePlus Genetics provides information about Retinitis pigmentosa

Other disorders

*BEST1* gene mutations cause several additional eye disorders. For example, mutations in this gene have been found in individuals who have eye abnormalities such as increased pressure in the eyes (glaucoma); clouding of the lens (cataracts); and a condition called nanophthalmos, which is characterized by very small eyes and extreme farsightedness. These eye abnormalities may be related to defects in the retinal pigment epithelium.

A recently described eye disorder called autosomal recessive bestrophinopathy (ARB) is also caused by mutations in the *BEST1* gene. This condition is characterized by progressive vision loss and an autosomal recessive inheritance pattern. Autosomal recessive inheritance means affected individuals have mutations in both copies of the *BEST1* gene in each cell. The mutations that cause ARB alter the structure of bestrophin-1 or prevent production of the protein. Abnormalities or loss of bestrophin-1 impairs the flow of chloride ions into or out of cells of the retinal pigment epithelium. It is unclear how changes in bestrophin-1 lead to vision loss in people with this disorder.

*BEST1* gene mutations have also been found in a small number of individuals with eye abnormalities similar to those in retinitis pigmentosa, although some doctors think these individuals have a form of ADVIRC or ARB (described above). Retinitis pigmentosa is a group of related eye disorders that occurs when photoreceptors in the retina gradually deteriorate, leading to vision loss. The *BEST1* gene mutations involved in retinitis pigmentosa appear to impair the flow of chloride ions, but it is unclear how these changes lead to the vision problems of this disorder.

Additionally, researchers have studied *BEST1* gene mutations related to age-related

macular degeneration. This eye disease is a leading cause of vision loss among older people worldwide. Mutations in the *BEST1* gene have been found in a small number of people with age-related macular degeneration, although it is not clear if the mutations are involved in the development of the condition. Changes in the *BEST1* gene are probably not a major risk factor for this common eye disorder. A combination of genetic and environmental factors likely determine the risk of developing age-related macular degeneration.

## Other Names for This Gene

- BEST
- BEST1_HUMAN
- BMD
- RP50
- TU15B
- vitelliform macular dystrophy 2 (Best disease, bestrophin)
- VMD2

## Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of BEST1 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=7439[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28VMD2%5BTIAB%5D%29+OR+%28bestrophin%5BTIAB%5D%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

- BESTROPHIN 1; BEST1 (https://omim.org/entry/607854)
- BESTROPHINOPATHY, AUTOSOMAL RECESSIVE; ARB (https://omim.org/entry/611809)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/7439)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=BEST1[gene])

## References


- Burgess R, MacLaren RE, Davidson AE, Urquhart JE, Holder GE, Robson AG, MooreAT, Keefe RO, Black GC, Manson FD. ADVIRC is caused by distinct mutations inBEST1 that alter pre-mRNA splicing. J Med Genet. 2009 Sep;46(9):620-5. doi:10.1136/jmg.2008.059881. Epub 2008 Jul 8. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18611979)
- Burgess R, Millar ID, Leroy BP, Urquhart JE, Fearon IM, De Baere E, Brown PD, Robson AG, Wright GA, Kestelyn P, Holder GE, Webster AR, Manson FD, Black GC. Biallelic mutation of BEST1 causes a distinct retinopathy in humans. Am J HumGenet. 2008 Jan;82(1):19-31. doi: 10.1016/j.ajhg.2007.08.004. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18179881) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2253971/)
- Davidson AE, Millar ID, Urquhart JE, Burgess-Mullan R, Shweikh Y, Parry N,O'Sullivan J, Maher GJ, McKibbin M, Downes SM, Lotery AJ, Jacobson SG, Brown PD,Black GC, Manson FD. Missense mutations in a retinal pigment epithelium protein,bestrophin-1, cause retinitis pigmentosa. Am J Hum Genet. 2009 Nov;85(5):581-92.doi: 10.1016/j.ajhg.2009.09.015. Epub 2009 Oct 22. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/19853238) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2775838/)
- Hartzell C, Qu Z, Putzier I, Artinian L, Chien LT, Cui Y. Looking chloridechannels straight in the eye: bestrophins, lipofuscinosis, and retinaldegeneration. Physiology ( Bethesda). 2005 Oct;20:292-302. doi:10.1152/physiol.00021.2005. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16174869)
- Hartzell HC, Qu Z, Yu K, Xiao Q, Chien LT. Molecular physiology ofbestrophins: multifunctional membrane proteins linked to best disease and otherretinopathies. Physiol Rev. 2008 Apr;88(2):639-72. doi:10.1152/physrev.00022.2007. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18391176)
- Johnson AA, Lee YS, Chadburn AJ, Tammaro P, Manson FD, Marmorstein LY, Marmorstein AD. Disease-causing mutations associated with four bestrophinopathiesexhibit disparate effects on the localization, but not the oligomerization, ofBestrophin-1. Exp Eye Res. 2014 Apr;121:74-85. doi: 10.1016/j.exer.2014.02.006.Epub 2014 Feb 19. Erratum In: Exp Eye Res. 2014 Oct;127:300. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/24560797) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4123461/)
- Kramer F, White K, Pauleikhoff D, Gehrig A, Passmore L, Rivera A, Rudolph G, Kellner U, Andrassi M, Lorenz B, Rohrschneider K, Blankenagel A, Jurklies B, Schilling H, Schutt F, Holz FG, Weber BH. Mutations in the VMD2 gene areassociated with juvenile-onset vitelliform macular dystrophy (Best disease) andadult vitelliform macular dystrophy but not age-related macular degeneration. EurJ Hum Genet. 2000 Apr;8(4):286-92. doi: 10.1038/sj.ejhg.5200447. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/10854112)
- Marmorstein AD, Kinnick TR. Focus on molecules: bestrophin (best-1). Exp EyeRes. 2007 Oct;85(4):423-4. doi: 10.1016/j.exer.2006.03.021. Epub 2006 May 23. Noabstract available. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16720022) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PM

C2832840/)

- Petrukhin K, Koisti MJ, Bakall B, Li W, Xie G, Marknell T, Sandgren O, ForsmanK, Holmgren G, Andreasson S, Vujic M, Bergen AA, McGarty-Dugan V, Figueroa D, Austin CP, Metzker ML, Caskey CT, Wadelius C. Identification of the generesponsible for Best macular dystrophy. Nat Genet. 1998 Jul;19(3):241-7. doi: 10.1038/915. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/9662395)
- Renner AB, Tillack H, Kraus H, Kohl S, Wissinger B, Mohr N, Weber BH, KellnerU, Foerster MH. Morphology and functional characteristics in adult vitelliformmacular dystrophy. Retina. 2004 Dec;24(6):929-39. doi:10.1097/00006982-200412000-00014. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/15579992)
- Renner AB, Tillack H, Kraus H, Kramer F, Mohr N, Weber BH, Foerster MH,Kellner U. Late onset is common in best macular dystrophy associated with VMD2gene mutations. Ophthalmology. 2005 Apr;112(4):586-92. doi:10.1016/j.ophtha.2004.10.041. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/15808248)
- Seddon JM, Afshari MA, Sharma S, Bernstein PS, Chong S, Hutchinson A, Petrukhin K, Allikmets R. Assessment of mutations in the Best macular dystrophy( VMD2) gene in patients with adult-onset foveomacular vitelliform dystrophy,age-related maculopathy, and bull's-eye maculopathy. Ophthalmology. 2001Nov; 108(11):2060-7. doi: 10.1016/s0161-6420(01)00777-1. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/11713080)
- Sun H, Tsunenari T, Yau KW, Nathans J. The vitelliform macular dystrophyprotein defines a new family of chloride channels. Proc Natl Acad Sci U S A. 2002Mar 19;99(6):4008-13. doi: 10.1073/pnas.052692999. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/11904445) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC122639/)
- White K, Marquardt A, Weber BH. VMD2 mutations in vitelliform maculardystrophy ( Best disease) and other maculopathies. Hum Mutat. 2000;15(4):301-8.doi: 10.1002/(SICI)1098-1004(200004)15:43.0.CO;2-N. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/10737974)
- Yardley J, Leroy BP, Hart-Holden N, Lafaut BA, Loeys B, Messiaen LM, PerveenR, Reddy MA, Bhattacharya SS, Traboulsi E, Baralle D, De Laey JJ, Puech B,Kestelyn P, Moore AT, Manson FD, Black GC. Mutations of VMD2 splicing regulatorscause nanophthalmos and autosomal dominant vitreoretinochoroidopathy (ADVIRC).Invest Ophthalmol Vis Sci. 2004 Oct;45(10):3683-9. doi: 10.1167/iovs.04-0550. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/15452077)
- Yu K, Qu Z, Cui Y, Hartzell HC. Chloride channel activity of bestrophinmutants associated with mild or late-onset macular degeneration. InvestOphthalmol Vis Sci. 2007 Oct;48(10):4694-705. doi: 10.1167/iovs.07-0301. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17898294)

## Genomic Location

The *BEST1* gene is found on chromosome 11 (https://medlineplus.gov/genetics/chromosome/11/).

**Last updated November 1, 2014**