EYA1 gene

EYA transcriptional coactivator and phosphatase 1

Normal Function

The *EYA1* gene provides instructions for making a protein that plays a role in regulating the activity of other genes. Based on this role, the EYA1 protein is called a transcription factor or transcription coactivator.

The EYA1 protein interacts with several other proteins, including a group known as SIX proteins, to turn on (activate) and turn off (inactivate) genes that are important for normal development. Before birth, these protein interactions appear to be essential for the normal formation of many tissues. These include the second branchial arch, which gives rise to tissues in the front and side of the neck, and the eyes, ears, and kidneys. After birth, these interactions are important for normal organ function.

Health Conditions Related to Genetic Changes

Branchiootorenal/branchiootic syndrome

At least 160 mutations in the *EYA1* gene have been identified in people with branchiootorenal (BOR) syndrome, a condition that disrupts the development of tissues in the neck and causes malformations of the ears and kidneys. *EYA1* gene mutations have also been found to cause branchiootic (BO) syndrome, which includes many of the same features as BOR syndrome except for kidney (renal) malformations. The two conditions are otherwise so similar that researchers often consider them together (BOR/BO syndrome or branchiootorenal spectrum disorders).

Many of the mutations that cause BOR/BO syndrome change the 3-dimensional structure of the EYA1 protein, which prevents it from interacting effectively with other proteins. Because these protein interactions are necessary for the activation of certain genes during embryonic development, the altered EYA1 protein impairs the normal development of many tissues before birth. The major signs and symptoms of BOR/BO syndrome result from abnormal development of the second branchial arch, the ears, and (in BOR syndrome) the kidneys.

In some cases, the same *EYA1* gene mutation causes BOR syndrome in some members of a family and BO syndrome in others. This variability might result from changes in other, unidentified genes that affect how the EYA1 protein functions in the kidneys.

Congenital anomalies of kidney and urinary tract

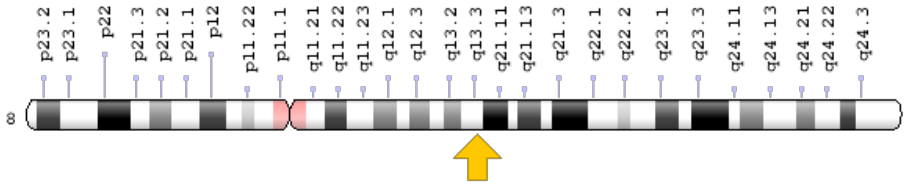
Other disorders

Several mutations in the *EYA1* gene have been associated with eye abnormalities including clouding of the lens (cataracts) and clouding of the clear front surface of the eye (the cornea). These abnormalities occur without the characteristic features of BOR/BO syndrome. Researchers believe that the *EYA1* gene mutations responsible for eye abnormalities have less severe effects on protein function than the mutations that underlie BOR/BO syndrome.

Chromosomal Location

Cytogenetic Location: 8q13.3, which is the long (q) arm of chromosome 8 at position 13.3

Molecular Location: base pairs 71,197,433 to 71,548,130 on chromosome 8 (Homo sapiens Annotation Release 109, GRCh38.p12) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- BOP
- BOR
- EYA1_HUMAN
- eyes absent 1
- eyes absent homolog 1 (Drosophila)
- eyes absent, Drosophila, homolog of, 1

Additional Information & Resources

Educational Resources

- Developmental Biology (sixth edition, 2000): Transcription Factors https://www.ncbi.nlm.nih.gov/books/NBK10023/#A763

Clinical Information from GeneReviews

- Branchiootorenal Spectrum Disorder https://www.ncbi.nlm.nih.gov/books/NBK1380

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28EYA1%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

- EYES ABSENT 1
  http://omim.org/entry/601653

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_EYA1.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=EYA1%5Bgene%5D
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:3519
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:2138
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/2138
- UniProt
  https://www.uniprot.org/uniprot/Q99502

Sources for This Summary

- Abdelhak S, Kalatzis V, Heilig R, Compain S, Samson D, Vincent C, Weil D, Cruaud C, Sahly I, Leibovici M, Bitner-Glindzicz M, Francis M, Lacombe D, Vigneron J, Charachon R, Boven K, Bedbeder P, Van Regemorter N, Weissenbach J, Petit C. A human homologue of the Drosophila eyes absent gene underlies branchio-oto-renal (BOR) syndrome and identifies a novel gene family. Nat Genet. 1997 Feb;15(2):157-64.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/9020840
- Azuma N, Hirakiyama A, Inoue T, Asaka A, Yamada M. Mutations of a human homologue of the Drosophila eyes absent gene (EYA1) detected in patients with congenital cataracts and ocular anterior segment anomalies. Hum Mol Genet. 2000 Feb 12;9(3):363-6.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10655545
- Chang EH, Menezes M, Meyer NC, Cucci RA, Vervoort VS, Schwartz CE, Smith RJ. Branchio-oto-renal syndrome: the mutation spectrum in EYA1 and its phenotypic consequences. Hum Mutat. 2004 Jun;23(6):582-9.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15146463

- Krug P, Morinière V, Marlin S, Koubi V, Gabriel HD, Colin E, Bonneau D, Salomon R, Antignac C, Heidet L. Mutation screening of the EYA1, SIX1, and SIX5 genes in a large cohort of patients harboring branchio-oto-renal syndrome calls into question the pathogenic role of SIX5 mutations. Hum Mutat. 2011 Feb;32(2):183-90. doi: 10.1002/humu.21402.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21280147
- Orten DJ, Fischer SM, Sorensen JL, Radhakrishna U, Cremers CW, Marres HA, Van Camp G, Welch KO, Smith RJ, Kimberling WJ. Branchio-oto-renal syndrome (BOR): novel mutations in the EYA1 gene, and a review of the mutational genetics of BOR. Hum Mutat. 2008 Apr;29(4):537-44. doi: 10.1002/humu.20691.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18220287
- Rayapureddi JP, Hegde RS. Branchio-oto-renal syndrome associated mutations in Eyes Absent 1 result in loss of phosphatase activity. FEBS Lett. 2006 Jul 10;580(16):3853-9. Epub 2006 Jun 15.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16797546
- Reis LM, Tyler RC, Muheisen S, Raggio V, Salviati L, Han DP, Costakos D, Yonath H, Hall S, Power P, Semina EV. Whole exome sequencing in dominant cataract identifies a new causative factor, CRYBA2, and a variety of novel alleles in known genes. Hum Genet. 2013 Jul;132(7): 761-70. doi: 10.1007/s00439-013-1289-0. Epub 2013 Mar 19.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23508780
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3683360/
- Smith RJH. Branchiootorenal Spectrum Disorders. 1999 Mar 19 [updated 2015 Oct 22]. In: Pagon RA, Adam MP, Ardinger HH, Wallace SE, Amemiya A, Bean LJH, Bird TD, Ledbetter N, Mefford HC, Smith RJH, Stephens K, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017. Available from http://www.ncbi.nlm.nih.gov/books/NBK1380/
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20301554

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