

## **EVC2 gene**

EvC ciliary complex subunit 2

### **Normal Function**

The *EVC2* gene provides instructions for making a protein whose function is unknown. However, it appears to be important for normal growth and development, particularly the development of bones and teeth. The EVC2 protein is found in primary cilia, which are microscopic, finger-like projections that stick out from the surface of cells and are involved in signaling pathways that transmit information between cells. In particular, the EVC2 protein is thought to help regulate a signaling pathway known as Sonic Hedgehog, which plays roles in cell growth, cell specialization, and the normal shaping (patterning) of many parts of the body.

*EVC2* and another gene, *EVC*, are located very close together on chromosome 4. Researchers believe that the two genes may have related functions and that their activity may be coordinated.

### **Health Conditions Related to Genetic Changes**

#### Ellis-van Creveld syndrome

More than 30 mutations in the *EVC2* gene have been found to cause Ellis-van Creveld syndrome, an inherited disorder characterized by dwarfism, abnormal nails and teeth, and heart defects. The mutations that cause this condition occur in both copies of the *EVC2* gene in each cell. Most of the genetic changes lead to the production of an abnormally small, nonfunctional version of the EVC2 protein. Although it is unclear how the loss of this protein's function underlies the signs and symptoms of Ellis-van Creveld syndrome, researchers believe that it may prevent normal Sonic Hedgehog signaling in the developing embryo. Problems with this signaling pathway may ultimately lead to the abnormal bone growth and heart defects seen with this condition.

#### Weyers acrofacial dysostosis

At least three mutations in the *EVC2* gene have been found to cause Weyers acrofacial dysostosis, a condition that affects the development of the teeth, nails, and bones. Its signs and symptoms are similar to, but typically milder than, those of Ellis-van Creveld syndrome.

The mutations that cause Weyers acrofacial dysostosis occur in one copy of the *EVC2* gene in each cell. Each mutation changes a single protein building block (amino acid) near the end of the EVC2 protein. These mutations probably result in the production of an abnormally short, malfunctioning version of the protein. It is unclear how the defective protein leads to the specific features of Weyers acrofacial dysostosis. Studies suggest that it interferes with Sonic Hedgehog signaling in the developing embryo, disrupting the normal formation and growth of the teeth, nails, and bones.

### Other Names for This Gene

- Ellis van Creveld syndrome 2
- Ellis van Creveld syndrome 2 (limbin)
- LBN
- LBN\_HUMAN
- limbin

### Additional Information & Resources

#### Tests Listed in the Genetic Testing Registry

- Tests of EVC2 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=132884\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=132884[geneid]))

#### Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28EVC2%5BTIAB%5D%29+OR+%28%28limbin%5BTIAB%5D%29+OR+%28LBN%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D%5D>)

#### Catalog of Genes and Diseases from OMIM

- EVC CILIARY COMPLEX SUBUNIT 2; EVC2 (<https://omim.org/entry/607261>)

#### Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/132884>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=EVC2\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=EVC2[gene]))

### References

- Blair HJ, Thompson S, Liu YN, Campbell J, MacArthur K, Ponting CP, Ruiz-Perez VL, Goodship JA. Evc2 is a positive modulator of Hedgehog signalling that interacts with

Evc at the cilia membrane and is also found in the nucleus. BMC Biol. 2011 Feb 28;9:14. doi: 10.1186/1741-7007-9-14. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/21356043>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3052239/>)

- Dorn KV, Hughes CE, Rohatgi R. A Smoothed-Evc2 complex transduces the Hedgehog signal at primary cilia. Dev Cell. 2012 Oct 16;23(4):823-35. doi:10.1016/j.devcel.2012.07.004. Epub 2012 Sep 13. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/22981989>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3586260/>)
- Galdzicka M, Patnala S, Hirshman MG, Cai JF, Nitowsky H, Egeland JA, Ginns EI. A new gene, EVC2, is mutated in Ellis-van Creveld syndrome. Mol Genet Metab. 2002 Dec;77(4):291-5. doi: 10.1016/s1096-7192(02)00178-6. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12468274>)
- Morrell CH, Brant LJ. Modelling hearing thresholds in the elderly. Stat Med. 1991 Sep;10(9):1453-64. doi: 10.1002/sim.4780100912. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/1925173>)
- Ruiz-Perez VL, Goodship JA. Ellis-van Creveld syndrome and Weyers acrorenal dysostosis are caused by cilia-mediated diminished response to hedgehog ligands. Am J Med Genet C Semin Med Genet. 2009 Nov 15;151C(4):341-51. doi:10.1002/ajmg.c.30226. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/19876929>)
- Ruiz-Perez VL, Thompson SW, Blair HJ, Espinoza-Valdez C, Lapunzina P, Silva EO, Hamel B, Gibbs JL, Young ID, Wright MJ, Goodship JA. Mutations in two nonhomologous genes in a head-to-head configuration cause Ellis-van Creveld syndrome. Am J Hum Genet. 2003 Mar;72(3):728-32. doi: 10.1086/368063. Epub 2003 Feb 4. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12571802>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1180248/>)
- Sund KL, Roelker S, Ramachandran V, Durbin L, Benson DW. Analysis of Ellis van Creveld syndrome gene products: implications for cardiovascular development and disease. Hum Mol Genet. 2009 May 15;18(10):1813-24. doi: 10.1093/hmg/ddp098. Epub 2009 Feb 27. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/19251731>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2671989/>)
- Thompson SW, Ruiz-Perez VL, Blair HJ, Barton S, Navarro V, Robson JL, Wright MJ, Goodship JA. Sequencing EVC and EVC2 identifies mutations in two-thirds of Ellis-van Creveld syndrome patients. Hum Genet. 2007 Jan;120(5):663-70. doi:10.1007/s00439-006-0237-7. Epub 2006 Sep 21. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/17024374>)
- Valencia M, Lapunzina P, Lim D, Zannolli R, Bartholdi D, Wollnik B, Al-Ajlouni O, Eid SS, Cox H, Buoni S, Hayek J, Martinez-Frias ML, Antonio PA, Temtamy S, Aglan M, Goodship JA, Ruiz-Perez VL. Widening the mutation spectrum of EVC and EVC2: ectopic expression of Weyer variants in NIH 3T3 fibroblasts disrupts Hedgehog signaling. Hum Mutat. 2009 Dec;30(12):1667-75. doi: 10.1002/humu.21117. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/19810119>)

- Ye X, Song G, Fan M, Shi L, Jabs EW, Huang S, Guo R, Bian Z. A novel heterozygous deletion in the EVC2 gene causes Weyers acrofacial dysostosis. Hum Genet. 2006 Mar;119(1-2):199-205. doi: 10.1007/s00439-005-0129-2. Epub 2006 Jan 11. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16404586>)

## **Genomic Location**

The *EVC2* gene is found on chromosome 4 (<https://medlineplus.gov/genetics/chromosome/4/>).

**Last updated December 1, 2012**