EVC Gene

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EvC ciliary complex subunit 1

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1. Normal Function

The *EVC* gene provides instructions for making a protein whose function is unclear. However, it appears to be important for normal growth and development, particularly the development of bones and teeth. The EVC 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 EVC 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.

EVC and another gene, *EVC2*, 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.

2. Health Conditions Related to Genetic Changes

2.1 Ellis-Van Creveld Syndrome

More than 25 mutations in the *EVC* gene have been reported 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 *EVC* gene in each cell. These genetic changes disrupt the normal function of the EVC protein or lead to the production of an abnormally small, nonfunctional version of the 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.

2.2 Weyers Acrofacial Dysostosis

At least one mutation in the *EVC* gene has been found to cause the characteristic features of Weyers acrofacial dysostosis, affecting the development of the teeth, nails, and bones. The signs and symptoms of Weyers acrofacial dysostosis are similar to, but typically milder than, those of Ellis-van Creveld syndrome.

The *EVC* gene mutation that causes Weyers acrofacial dysostosis occurs in one copy of the gene in each cell. It changes a single protein building block (amino acid) in the EVC protein, replacing the amino acid serine with the amino acid proline at position 307 (written as Ser307Pro). It is unclear how this genetic change leads to the specific features of Weyers acrofacial dysostosis. Studies suggest that the abnormal protein interferes with Sonic Hedgehog signaling in the developing embryo, disrupting the normal formation and growth of the teeth, nails, and bones.

3. Other Names for This Gene

- DWF-1
- Ellis van Creveld protein
- Ellis van Creveld syndrome
- Ellis van Creveld syndrome protein

- EVC1
- EVC_HUMAN
- EVCL

References

1. Blair HJ, Tompson S, Liu YN, Campbell J, MacArthur K, Ponting CP, Ruiz-PerezVL, Goodship JA. Evc2 is a positive modulator of Hedgehog signalling thatinteracts with Evc at the cilia membrane and is also found in the nucleus. BMCBiol. 2011 Feb 28;9:14. doi: 10.1186/1741-7007-9-14.
2. Howard TD, Guttmacher AE, McKinnon W, Sharma M, McKusick VA, Jabs EW.Autosomal dominant postaxial polydactyly, nail dystrophy, and dentalabnormalities map to chromosome 4p16, in the region containing the Ellis-vanCreveld syndrome locus. Am J Hum Genet. 1997 Dec;61(6):1405-12.
3. Morrell CH, Brant LJ. Modelling hearing thresholds in the elderly. Stat Med.1991 Sep;10(9):1453-64.
4. Ruiz-Perez VL, Blair HJ, Rodriguez-Andres ME, Blanco MJ, Wilson A, Liu YN,Miles C, Peters H, Goodship JA. Evc is a positive mediator of Ihh-regulated bone growth that localises at the base of chondrocyte cilia. Development. 2007Aug;134(16):2903-12.
5. Ruiz-Perez VL, Goodship JA. Ellis-van Creveld syndrome and Weyers acrodentaldysostosis 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. Review.
6. Ruiz-Perez VL, Ide SE, Strom TM, Lorenz B, Wilson D, Woods K, King L,Francomano C, Freisinger P, Spranger S, Marino B, Dallapiccola B, Wright M,Meitinger T, Polymeropoulos MH, Goodship J. Mutations in a new gene in Ellis-van Creveld syndrome and Weyers acrodental dysostosis. Nat Genet. 2000Mar;24(3):283-6. Erratum in: Nat Genet 2000 May;25(1):125.
7. Ruiz-Perez VL, Tompson SW, Blair HJ, Espinoza-Valdez C, Lapunzina P, Silva EO,Hamel B, Gibbs JL, Young ID, Wright MJ, Goodship JA. Mutations in twononhomologous genes in a head-to-head configuration cause Ellis-van Creveldsyndrome. Am J Hum Genet. 2003 Mar;72(3):728-32.
8. Sund KL, Roelker S, Ramachandran V, Durbin L, Benson DW. Analysis of Ellis vanCreveld syndrome gene products: implications for cardiovascular development anddisease. Hum Mol Genet. 2009 May 15;18(10):1813-24. doi: 10.1093/hmg/ddp098.
9. Tompson SW, Ruiz-Perez VL, Blair HJ, Barton S, Navarro V, Robson JL, WrightMJ, Goodship JA. Sequencing EVC and EVC2 identifies mutations in two-thirds ofEllis-van Creveld syndrome patients. Hum Genet. 2007 Jan;120(5):663-70.
10. Valencia M, Lapunzina P, Lim D, Zannolli R, Bartholdi D, Wollnik B, Al-AjlouniO, 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 andEVC2: ectopic expression of Weyer variants in NIH 3T3 fibroblasts disruptsHedgehog signaling. Hum Mutat. 2009 Dec;30(12):1667-75. doi: 10.1002/humu.21117.