

EDARADD gene

EDAR associated via death domain

Normal Function

The *EDARADD* gene provides instructions for making a protein called the EDAR-associated via death domain (EDARADD) protein. This protein is part of a signaling pathway that plays an important role in development before birth. Specifically, it is critical for interactions between two embryonic cell layers called the ectoderm and the mesoderm. In the early embryo, these cell layers form the basis for many of the body's organs and tissues. Ectoderm-mesoderm interactions are essential for the formation of several structures that arise from the ectoderm, including the skin, hair, nails, teeth, and sweat glands.

The EDARADD protein interacts with another protein, called the ectodysplasin A receptor, which is produced from the *EDAR* gene. This interaction occurs at a region called the death domain that is present in both proteins. The EDARADD protein acts as an adapter, which means it assists the ectodysplasin A receptor in triggering chemical signals within cells. These signals affect cell activities such as division, growth, and maturation. Starting before birth, this signaling pathway controls the formation of ectodermal structures such as hair follicles, sweat glands, and teeth.

Health Conditions Related to Genetic Changes

Hypohidrotic ectodermal dysplasia

Fewer than 10 mutations in the *EDARADD* gene have been found to cause hypohidrotic ectodermal dysplasia, the most common form of ectodermal dysplasia. Starting before birth, ectodermal dysplasias result in the abnormal development of the skin, hair, nails, teeth, and sweat glands. Hypohidrotic ectodermal dysplasia is characterized by a reduced ability to sweat (hypohidrosis), sparse scalp and body hair (hypotrichosis), and several missing teeth (hypodontia) or teeth that are malformed. *EDARADD* gene mutations are an infrequent cause of hypohidrotic ectodermal dysplasia, accounting for only about 1 percent of all cases.

Most of the *EDARADD* gene mutations associated with hypohidrotic ectodermal dysplasia change single protein building blocks (amino acids) in the receptor protein. These changes occur in or near the death domain, preventing the EDARADD protein from interacting effectively with the ectodysplasin A receptor. As a result, the receptor

cannot trigger the signals needed for ectoderm-mesoderm interactions in early development. Without these signals, hair follicles, teeth, sweat glands, and other ectodermal structures do not form properly, which leads to the characteristic features of hypohidrotic ectodermal dysplasia.

Other Names for This Gene

- ectodysplasia A receptor associated death domain
- ectodysplasin A receptor associated adapter protein
- EDAD_HUMAN
- EDAR-associated death domain

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of EDARADD ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=128178\[genedj\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=128178[genedj]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28EDARADD%5BTIAB%5D%29+OR+%28EDAR-associated+death+domain%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D>)

Catalog of Genes and Diseases from OMIM

- EDAR-ASSOCIATED DEATH DOMAIN; EDARADD (<https://omim.org/entry/606603>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/128178>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=EDARADD\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=EDARADD[gene]))

References

- Chassaing N, Cluzeau C, Bal E, Guigue P, Vincent MC, Viot G, Ginisty D, Munnich A, Smahi A, Calvas P. Mutations in EDARADD account for a small proportion of hypohidrotic ectodermal dysplasia cases. *Br J Dermatol*. 2010 May;162(5):1044-8. doi: 10.1111/j.1365-2133.2010.09670.x. Epub 2010 Mar 5. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/20222921>)

- Chaudhary AK, Girisha KM, Bashyam MD. A novel EDARADD 5' splice site mutation resulting in activation of two alternate cryptic 5' splice sites causes autosomal recessive Hypohidrotic Ectodermal Dysplasia. Am J Med Genet A. 2016 Jun;170(6):1639-41. doi: 10.1002/ajmg.a.37607. Epub 2016 Mar 15. No abstract available. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/26991760>)
- Cluzeau C, Hadj-Rabia S, Jambou M, Mansour S, Guigue P, Masmoudi S, Bal E, Chassaing N, Vincent MC, Viot G, Clauss F, Maniere MC, Toupenay S, Le Merrer M, Lyonnet S, Cormier-Daire V, Amiel J, Faivre L, de Prost Y, Munnich A, Bonnefont JP, Bodemer C, Smahi A. Only four genes (EDA1, EDAR, EDARADD, and WNT10A) account for 90% of hypohidrotic/anhidrotic ectodermal dysplasia cases. Hum Mutat. 2011 Jan;32(1):70-2. doi: 10.1002/humu.21384. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/20979233>)
- Headon DJ, Emmal SA, Ferguson BM, Tucker AS, Justice MJ, Sharpe PT, Zonana J, Overbeek PA. Gene defect in ectodermal dysplasia implicates a death domain adapter in development. Nature. 2001 Dec 20-27;414(6866):913-6. doi:10.1038/414913a. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/11780064>)
- Wohlfart S, Hammersen J, Schneider H. Mutational spectrum in 101 patients with hypohidrotic ectodermal dysplasia and breakpoint mapping in independent cases of rare genomic rearrangements. J Hum Genet. 2016 Oct;61(10):891-897. doi: 10.1038/jhg.2016.75. Epub 2016 Jun 16. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/27305980>)
- Wohlfart S, Soder S, Smahi A, Schneider H. A novel missense mutation in the gene EDARADD associated with an unusual phenotype of hypohidrotic ectodermal dysplasia. Am J Med Genet A. 2016 Jan;170A(1):249-53. doi: 10.1002/ajmg.a.37412. Epub 2015 Oct 5. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/26440664>)
- Wright JT, Grange DK, Fete M. Hypohidrotic Ectodermal Dysplasia. 2003 Apr 28 [updated 2022 Oct 27]. In: Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE, Bean LJH, Gripp KW, Amemiya A, editors. GeneReviews(R) [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. Available from <http://www.ncbi.nlm.nih.gov/books/NBK1112/> Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/20301291>)

Genomic Location

The *EDARADD* gene is found on chromosome 1 (<https://medlineplus.gov/genetics/chromosome/1/>).

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