



## CDH1 gene

cadherin 1

### Normal Function

The *CDH1* gene provides instructions for making a protein called epithelial cadherin or E-cadherin. This protein is found within the membrane that surrounds epithelial cells, which are the cells that line the surfaces and cavities of the body, such as the inside of the eyelids and mouth. E-cadherin belongs to a family of proteins called cadherins whose function is to help neighboring cells stick to one another (cell adhesion) to form organized tissues. Another protein called p120-catenin, produced from the *CTNND1* gene, helps keep E-cadherin in its proper place in the cell membrane, preventing it from being taken into the cell through a process called endocytosis and broken down prematurely.

E-cadherin is one of the best-understood cadherin proteins. In addition to its role in cell adhesion, E-cadherin is involved in transmitting chemical signals within cells, controlling cell maturation and movement, and regulating the activity of certain genes. Interactions between the E-cadherin and p120-catenin proteins, in particular, are thought to be important for normal development of the head and face (craniofacial development), including the eyelids and teeth. E-cadherin also acts as a tumor suppressor protein, which means it prevents cells from growing and dividing too rapidly or in an uncontrolled way.

### Health Conditions Related to Genetic Changes

#### Blepharocheilodontic syndrome

At least five inherited *CDH1* gene mutations have been identified in people with blepharocheilodontic (BCD) syndrome. This disorder is present at birth and causes abnormalities mainly affecting the eyelids and mouth, including openings on both sides of the upper lip (bilateral cleft lip) and an opening in the roof of the mouth (cleft palate). *CDH1* gene mutations that cause BCD syndrome are thought to result in an abnormal E-cadherin protein that is quickly broken down. A shortage of E-cadherin protein impairs the interaction between E-cadherin and p120-catenin and affects craniofacial development, leading to the features of BCD syndrome. Despite the association of *CDH1* gene mutations with increased cancer risk (see below), it is unclear whether people with BCD syndrome are at increased risk of developing cancer.

#### Breast cancer

Inherited mutations in the *CDH1* gene increase a woman's risk of developing a form of breast cancer that begins in the milk-producing glands (lobular breast cancer). In

many cases, this increased risk occurs as part of an inherited cancer disorder called hereditary diffuse gastric cancer (HDGC) (described below). Inherited mutations in the *CDH1* gene are thought to account for only a small fraction of all breast cancer cases.

*CDH1* gene mutations also occur commonly in lobular breast cancers in women without a family history of the disease. These genetic changes, known as somatic mutations, are not inherited. Somatic gene mutations are acquired during a person's lifetime and occur only in certain cells in the breast. Some of these genetic changes occur within the gene itself, while others turn off (inactivate) a region of nearby DNA that controls the gene's activity. Researchers believe that the resulting loss of E-cadherin protein may allow breast cells to grow and divide unchecked, leading to a cancerous tumor. A lack of this protein, which is critical for cell adhesion, may also make it easier for cancer cells to detach from a primary tumor and spread (metastasize) to other parts of the body.

#### Hereditary diffuse gastric cancer

More than 120 inherited mutations in the *CDH1* gene have been found to cause a familial cancer disorder called hereditary diffuse gastric cancer (HDGC). People with *CDH1* gene mutations associated with HDGC have a 56 to 70 percent chance of developing stomach (gastric) cancer in their lifetimes. Women with these mutations also have a 40 to 50 percent chance of developing lobular breast cancer (described above). People with HDGC caused by *CDH1* gene mutations are born with one mutated copy of the gene in each cell. An additional mutation that impairs the normal copy of the *CDH1* gene is needed for cancer to develop. This mutation is a somatic mutation and is present only in cells that give rise to cancer.

The mutations that cause HDGC often lead to the production of an abnormally short, nonfunctional version of the E-cadherin protein or lead to the production of a protein with an altered structure. The loss of normal E-cadherin prevents it from acting as a tumor suppressor, contributing to the uncontrollable growth and division of cells. A lack of E-cadherin impairs cell adhesion, increasing the likelihood that cancer cells will invade the stomach wall and small clusters of cancer cells will metastasize into nearby tissues. In combination, the inherited and somatic mutations lead to a lack of functional E-cadherin and result in HDGC.

#### Ovarian cancer

#### Prostate cancer

#### Other disorders

Individuals with inherited *CDH1* gene mutations may have cleft lip, cleft palate, or both (orofacial clefting) without the other signs and symptoms of BCD syndrome and with or without a family history of HDGC (both described above). The *CDH1* gene mutations in these individuals are thought to alter the E-cadherin protein and impair

normal craniofacial development, leading to orofacial clefting. It is unknown why some people with orofacial clefting caused by *CDH1* gene mutations have additional signs and symptoms while others do not.

### Other cancers

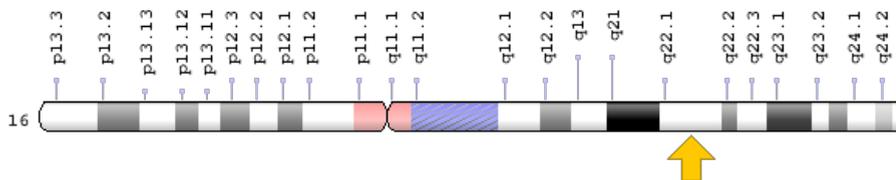
Somatic *CDH1* gene mutations are also associated with an increased risk of other cancers, including cancers of the lining of the uterus (endometrium) or the ovaries in women, and prostate cancer in men. These *CDH1* gene mutations are thought to result in a nonfunctional E-cadherin protein. A loss of functional E-cadherin in these cells prevents tumor suppression and cell adhesion, leading to rapid cell growth and metastasis.

In addition, a specific inherited variation in the *CDH1* gene is thought to increase the risk of prostate cancer. It is unclear why *CDH1* gene mutations increase the risk of cancer in certain tissues and not in others.

### **Chromosomal Location**

Cytogenetic Location: 16q22.1, which is the long (q) arm of chromosome 16 at position 22.1

Molecular Location: base pairs 68,737,290 to 68,835,542 on chromosome 16 (Homo sapiens Annotation Release 109, GRCh38.p12) (NCBI)



Credit: Genome Decoration Page/NCBI

### **Other Names for This Gene**

- Arc-1
- CADH1\_HUMAN
- cadherin 1, E-cadherin (epithelial)
- cadherin 1, type 1
- cadherin 1, type 1, E-cadherin (epithelial)
- calcium-dependent adhesion protein, epithelial
- CAM 120/80
- CD324

- CDHE
- cell-CAM 120/80
- E-cadherin
- ECAD
- LCAM
- liver cell adhesion molecule
- UVO
- uvomorulin

## **Additional Information & Resources**

### Educational Resources

- Developmental Biology (sixth edition, 2000): Cadherins and Cell Adhesion  
<https://www.ncbi.nlm.nih.gov/books/NBK10021/#A385>
- Molecular Biology of the Cell (fourth edition, 2002): Cadherins Have Crucial Roles in Development  
<https://www.ncbi.nlm.nih.gov/books/NBK26937/#A3516>
- National Cancer Institute: Genetics of Breast and Gynecologic Cancers (PDQ)  
<https://www.cancer.gov/types/breast/hp/breast-ovarian-genetics-pdq>

### Clinical Information from GeneReviews

- Hereditary Diffuse Gastric Cancer  
<https://www.ncbi.nlm.nih.gov/books/NBK1139>

### Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28CDH1%5BTI%5D%29+OR+%28E-cadherin%5BTI%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+360+days%22%5Bdp%5D>

### Catalog of Genes and Diseases from OMIM

- CADHERIN 1  
<http://omim.org/entry/192090>

### Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology  
<http://atlasgeneticsoncology.org/Genes/CDH1ID166ch16q22.html>
- Cancer Genetics Web  
<http://www.cancerindex.org/geneweb/CDH1.htm>

- HGNC Gene Symbol Report  
[https://www.genenames.org/data/gene-symbol-report#!/hgnc\\_id/HGNC:1748](https://www.genenames.org/data/gene-symbol-report#!/hgnc_id/HGNC:1748)
- Monarch Initiative  
<https://monarchinitiative.org/gene/NCBIGene:999>
- NCBI Gene  
<https://www.ncbi.nlm.nih.gov/gene/999>
- UniProt  
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