EPCAM gene

epithelial cell adhesion molecule

Normal Function

The *EPCAM* gene provides instructions for making a protein known as epithelial cellular adhesion molecule (EpCAM). This protein is found in epithelial cells, which are the cells that line the surfaces and cavities of the body. The EpCAM protein is found spanning the membrane that surrounds epithelial cells, where it helps cells stick to one another (cell adhesion). In addition, the protein in the cell membrane can be cut at a specific location, releasing a piece called the intracellular domain (EpICD), which helps relay signals from outside the cell to the nucleus of the cell. EpICD travels to the nucleus and associates with other proteins, forming a group (complex) that regulates the activity of several genes that are involved in cell growth and division (proliferation), maturation (differentiation), and movement (migration), all of which are important processes for the proper development of cells and tissues.

Health Conditions Related to Genetic Changes

Lynch syndrome

Certain mutations in the *EPCAM* gene are associated with Lynch syndrome, a condition that increases the risk of developing many types of cancer, particularly cancers of the large intestine (colon) and the rectum (collectively called colorectal cancer). These mutations account for up to 6 percent of Lynch syndrome cases. On chromosome 2, the *EPCAM* gene lies next to another gene called *MSH2*. Each gene provides instructions for making an individual messenger RNA (mRNA), which serves as the genetic blueprint for making the protein. The *EPCAM* gene mutations involved in Lynch syndrome remove a region that signals the end of the gene, which leads to formation of a long mRNA that includes both *EPCAM* and *MSH2*.

For unknown reasons, these *EPCAM* gene mutations cause the *MSH2* gene to be turned off (inactivated) by a mechanism known as promoter hypermethylation. The promoter is a region of DNA near the beginning of the gene that controls gene activity (expression). Hypermethylation occurs when too many small molecules called methyl groups are attached to the promoter region. The extra methyl groups attached to the *MSH2* promoter reduce the expression of the *MSH2* gene, which means that less protein is produced in epithelial cells.

The MSH2 protein plays an essential role in repairing errors in DNA; loss of this protein prevents proper DNA repair, and errors accumulate as the cells continue to divide. These errors can lead to uncontrolled cell growth and increase the risk of cancer.

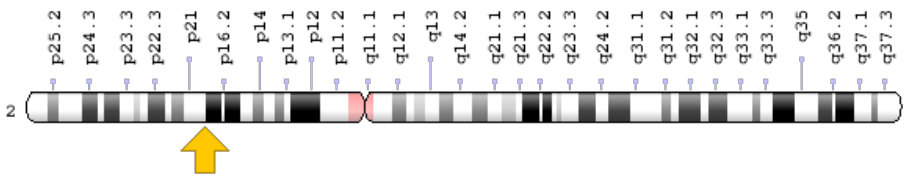
Other disorders

Mutations in the *EPCAM* gene can also cause congenital tufting enteropathy. This condition is characterized by abnormal development of epithelial cells in the intestines. In this condition, the villi, which are small finger-like projections that line the small intestine, are abnormal. In particular, they have "tufts" of extra epithelial cells on their tips. Normally, these projections provide a greatly increased surface area to absorb nutrients. The altered villi are less able to absorb nutrients and fluids than normal tissue, which causes life-threatening diarrhea and poor growth. Congenital tufting enteropathy develops in newborns within days of birth and lasts throughout life. *EPCAM* gene mutations involved in this condition lead to the loss of functional EpCAM protein. The resulting loss of EpICD signaling leads to abnormal development of intestinal epithelial cells, causing congenital tufting enteropathy.

Chromosomal Location

Cytogenetic Location: 2p21, which is the short (p) arm of chromosome 2 at position 21

Molecular Location: base pairs 47,369,148 to 47,387,028 on chromosome 2 (Homo sapiens Annotation Release 109, GRCh38.p12) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- 17-1A
- 323/A3
- CD326
- CO-17A
- EGP-2
- EGP34
- EGP40
- Ep-CAM
- epithelial cell adhesion molecule precursor
- epithelial glycoprotein 314

- ESA
- GA733-2
- HEA125
- human epithelial glycoprotein-2
- KS1/4
- KSA
- Ly74
- M4S1
- MH99
- MIC18
- MK-1
- MOC31
- TACST-1
- TACSTD1
- TROP1
- tumor-associated calcium signal transducer 1

Additional Information & Resources

Educational Resources

- Holland-Frei Cancer Medicine (sixth edition, 2003): DNA Mismatch Repair Gene Defects and HNPCC
  https://www.ncbi.nlm.nih.gov/books/NBK12469/#A1595
- Molecular Biology of the Cell (fourth edition, 2002): Defects in DNA Mismatch Repair Provide an Alternative Route to Colorectal Cancer
  https://www.ncbi.nlm.nih.gov/books/NBK26902/#A4345

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28EPCAM%5BTIAB%5D%29+OR+%28epithelial+cell+adhesion+molecule%5BTIAB%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

- DIARRHEA 5, WITH TUFTING ENTEROPATHY, CONGENITAL
  http://omim.org/entry/613217
- EPITHELIAL CELLULAR ADHESION MOLECULE
  http://omim.org/entry/185535
- MutS, E. COLI, HOMOLOG OF, 2
  http://omim.org/entry/609309

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/TACSTD1ID42459ch2p21.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=EPCAM%5Bgene%5D
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:11529
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:4072
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/4072
- UniProt
  https://www.uniprot.org/uniprot/P16422

Sources for This Summary

- OMIM: EPITHELIAL CELLULAR ADHESION MOLECULE
  http://omim.org/entry/185535
- Kuiper RP, Vissers LE, Venkatachalam R, Bodmer D, Hoenselaar E, Goossens M, Haufe A, Kamping E, Niessen RC, Hogervorst FB, Gille JJ, Redeker B, Tops CM, van Gijn ME, van den Ouweland AM, Rahner N, Steinke V, Kahl P, Holinski-Feder E, Morak M, Kloor M, Stemmler S, Betz B, Hutter P, Bunyan DJ, Syngal S, Culver JO, Graham T, Chan TL, Nagtegaal ID, van Krieken JH, Schackert HK, Hoogerbrugge N, van Kessel AG, Ligtenberg MJ. Recurrence and variability of germline EPCAM deletions in Lynch syndrome. Hum Mutat. 2011 Apr;32(4):407-14. doi: 10.1002/humu.21446. Epub 2011 Mar 1.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21309036
- Ligtenberg MJ, Kuiper RP, Chan TL, Goossens M, Hebeda KM, Voorendt M, Lee TY, Bodmer D, Hoenselaar E, Hendriks-Cornelissen SJ, Tsui WY, Kong CK, Brunner HG, van Kessel AG, Yuen ST, van Krieken JH, Leung SY, Hoogerbrugge N. Heritable somatic methylation and inactivation of MSH2 in families with Lynch syndrome due to deletion of the 3' exons of TACSTD1. Nat Genet. 2009 Jan;41(1):112-7. doi: 10.1038/ng.283. Epub 2008 Dec 21.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19098912

- Maetzel D, Denzel S, Mack B, Canis M, Went P, Benk M, Kieu C, Papior P, Baeuerle PA, Munz M, Gires O. Nuclear signalling by tumour-associated antigen EpCAM. Nat Cell Biol. 2009 Feb;11(2): 162-71. doi: 10.1038/ncb1824. Epub 2009 Jan 11.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19136966
- Niessen RC, Hofstra RM, Westers H, Ligtenberg MJ, Kooi K, Jager PO, de Groote ML, Dijkhuizen T, Olderode-Berends MJ, Hollema H, Kleibeuker JH, Sijmons RH. Germline hypermethylation of MLH1 and EPCAM deletions are a frequent cause of Lynch syndrome. Genes Chromosomes Cancer. 2009 Aug;48(8):737-44. doi: 10.1002/gcc.20678.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19455606
- Schnell U, Kuipers J, Mueller JL, Veenstra-Algra A, Sivagnanam M, Giepmans BN. Absence of cell-surface EpCAM in congenital tufting enteropathy. Hum Mol Genet. 2013 Jul 1;22(13):2566-71. doi: 10.1093/hmg/ddt105. Epub 2013 Mar 5.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23462293
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3674798/
- Sivagnanam M, Mueller JL, Lee H, Chen Z, Nelson SF, Turner D, Zlotkin SH, Pencharz PB, Ngan BY, Libiger O, Schork NJ, Lavine JE, Taylor S, Newbury RO, Kolodner RD, Hoffman HM. Identification of EpCAM as the gene for congenital tufting enteropathy. Gastroenterology. 2008 Aug; 135(2):429-37. doi: 10.1053/j.gastro.2008.05.036. Epub 2008 May 15.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18572020
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2574708/

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