EZH2 gene

enhancer of zeste 2 polycomb repressive complex 2 subunit

Normal Function

The *EZH2* gene provides instructions for making a type of enzyme called a histone methyltransferase. Histone methyltransferases modify proteins called histones, which are structural proteins that attach (bind) to DNA and give chromosomes their shape. By adding a molecule called a methyl group to histones (methylation), histone methyltransferases can turn off (suppress) the activity of certain genes, an essential process in normal development. Specifically, the EZH2 enzyme forms part of a protein group called the polycomb repressive complex-2. By turning off particular genes, this complex is involved in the process that determines the type of cell an immature cell will ultimately become (cell fate determination).

Health Conditions Related to Genetic Changes

Weaver syndrome

More than 30 *EZH2* gene mutations have been identified in people with Weaver syndrome, which involves tall stature, a variable degree of intellectual disability (usually mild), and characteristic facial features. These features can include a broad forehead; widely spaced eyes (hypertelorism); large, low-set ears; a dimpled chin; and a small lower jaw (micrognathia). Some affected individuals have a large head size (macrocephaly). Most of the *EZH2* gene mutations associated with Weaver syndrome change single protein building blocks (amino acids) in the EZH2 enzyme; others insert or delete small amounts of genetic material from the *EZH2* gene, leading to production of an altered EZH2 enzyme. It is unclear how these *EZH2* gene mutations result in the abnormalities characteristic of Weaver syndrome.

Prostate cancer

MedlinePlus Genetics provides information about Prostate cancer

Cancers

Changes in the *EZH2* gene have been associated with various types of cancers. Mutations of this gene have been identified in cancers of blood-forming tissues (lymphomas and leukemias). These mutations are described as "gain-of-function"

because they appear to enhance the activity of the EZH2 enzyme or give the enzyme a new, atypical function. In addition, excessive activity (overexpression) of the *EZH2* gene has been identified in cancerous tumors of the prostate, breast, and other parts of the body. Changes involving the *EZH2* gene likely impair normal control of cell division (proliferation), allowing cells to grow and divide too fast or in an uncontrolled way and leading to the development of cancer.

Other Names for This Gene

- enhancer of zeste homolog 2 (Drosophila)
- ENX-1
- EZH2_HUMAN
- histone-lysine N-methyltransferase EZH2
- KMT6
- KMT6A
- lysine N-methyltransferase 6

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of EZH2 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=2146[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28EZH2%5BTI%5D%29+OR+%28enhancer+of+zeste+homolog+2%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

- ENHANCER OF ZESTE 2 POLYCOMB REPRESSIVE COMPLEX 2 SUBUNIT; EZH2 (https://omim.org/entry/601573)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/2146)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=EZH2[gene])

References

- Gibson WT, Hood RL, Zhan SH, Bulman DE, Fejes AP, Moore R, Mungall AJ, EydouxP, Babul-Hirji R, An J, Marra MA; FORGE Canada Consortium; Chitayat D, BoycottKM, Weaver DD, Jones SJ. Mutations in EZH2 cause Weaver syndrome. Am J Hum Genet.2012 Jan 13;90(1):110-8. doi: 10.1016/j.ajhg.2011.11.018. Epub 2011 Dec 15. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/22177091) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3257956/)

- Majer CR, Jin L, Scott MP, Knutson SK, Kuntz KW, Keilhack H, Smith JJ, MoyerMP, Richon VM, Copeland RA, Wigle TJ. A687V EZH2 is a gain-of-function mutationfound in lymphoma patients. FEBS Lett. 2012 Sep 21;586(19):3448-51. doi: 10.1016/j.febslet.2012.07.066. Epub 2012 Jul 28. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/22850114)
- Melling N, Thomsen E, Tsourlakis MC, Kluth M, Hube-Magg C, Minner S, Koop C, Graefen M, Heinzer H, Wittmer C, Sauter G, Wilczak W, Huland H, Simon R, SchlommT, Steurer S, Krech T. Overexpression of enhancer of zeste homolog 2 (EZH2)characterizes an aggressive subset of prostate cancers and predicts patientprognosis independently from pre- and postoperatively assessedclinicopathological parameters. Carcinogenesis. 2015 Nov;36(11):1333-40. doi:10.1093/carcin/bgv137. Epub 2015 Sep 21. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/26392259)
- Tatton-Brown K, Hanks S, Ruark E, Zachariou A, Duarte Sdel V, Ramsay E, SnapeK, Murray A, Perdeaux ER, Seal S, Loveday C, Banka S, Clericuzio C, Flinter F,Magee A, McConnell V, Patton M, Raith W, Rankin J, Splitt M, Strenger V, TaylorC, Wheeler P, Temple KI, Cole T; Childhood Overgrowth Collaboration; Douglas J,Rahman N. Germline mutations in the oncogene EZH2 cause Weaver syndrome andincreased human height. Oncotarget. 2011 Dec;2(12):1127-33. doi:10.18632/oncotarget.385. Erratum In: Oncotarget. 2018 Nov 30;9(94):36719. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/22190405) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3282071/)
- Tatton-Brown K, Rahman N. The NSD1 and EZH2 overgrowth genes, similarities anddifferences. Am J Med Genet C Semin Med Genet. 2013 May;163C(2):86-91. doi:10.1002/ajmg.c.31359. Epub 2013 Apr 16. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/23592277) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4845886/)
- Yap DB, Chu J, Berg T, Schapira M, Cheng SW, Moradian A, Morin RD, Mungall AJ, Meissner B, Boyle M, Marquez VE, Marra MA, Gascoyne RD, Humphries RK, ArrowsmithCH, Morin GB, Aparicio SA. Somatic mutations at EZH2 Y641 act dominantly througha mechanism of selectively altered PRC2 catalytic activity, to increase H3K27trimethylation. Blood. 2011 Feb 24;117(8):2451-9. doi:10.1182/blood-2010-11-321208. Epub 2010 Dec 29. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21190999) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3062411/)

Genomic Location

The *EZH2* gene is found on chromosome 7 (https://medlineplus.gov/genetics/chromosome/7/).

Last updated March 1, 2016