BRCA2 gene

BRCA2, DNA repair associated

Normal Function

The *BRCA2* gene provides instructions for making a protein that acts as a tumor suppressor. Tumor suppressor proteins help prevent cells from growing and dividing too rapidly or in an uncontrolled way.

The BRCA2 protein is involved in repairing damaged DNA. In the nucleus of many types of normal cells, the BRCA2 protein interacts with several other proteins to mend breaks in DNA. These breaks can be caused by natural and medical radiation or other environmental exposures, and they also occur when chromosomes exchange genetic material in preparation for cell division. By helping to repair DNA, the BRCA2 protein plays a critical role in maintaining the stability of a cell's genetic information.

Researchers suspect that the BRCA2 protein has additional functions within cells. For example, the protein may help regulate cytokinesis, which is the step in cell division when the fluid surrounding the nucleus (the cytoplasm) divides to form two separate cells. Researchers are investigating the protein's other potential activities.

Health Conditions Related to Genetic Changes

Breast cancer

Researchers have identified more than 1,800 mutations in the *BRCA2* gene. Many of these mutations are associated with an increased risk of breast cancer in both men and women, as well as several other types of cancer. These mutations are present in every cell in the body and can be passed from one generation to the next. As a result, they are associated with cancers that cluster in families. However, not everyone who inherits a mutation in the *BRCA2* gene will develop cancer. Other genetic, environmental, and lifestyle factors also contribute to a person's cancer risk.

Most *BRCA2* gene mutations lead to the production of an abnormally small, nonfunctional version of the BRCA2 protein from one copy of the gene in each cell. As a result, less of this protein is available to help repair damaged DNA or fix mutations that occur in other genes. As these defects accumulate, they can trigger cells to grow and divide uncontrollably to form a tumor.

Ovarian cancer

Many of the same *BRCA2* gene mutations that increase the risk of breast cancer (described above) also increase the risk of ovarian cancer. Families with these mutations are often said to be affected by hereditary breast and ovarian cancer syndrome. Women with *BRCA2* gene mutations have an approximately 12 to 25

percent chance of developing ovarian cancer in their lifetimes, as compared with 1.6 percent in the general population.

Prostate cancer

More than 30 inherited *BRCA2* gene mutations have been found to increase the risk of prostate cancer. Men with these mutations are also more likely to develop prostate cancer at an earlier age and may be at increased risk of having an aggressive form of the disease. They may also be at increased risk for other cancers.

BRCA2 gene mutations likely reduce the BRCA2 protein's ability to repair DNA, allowing potentially damaging mutations to persist in various other genes. The accumulation of damaging mutations can lead to the out-of-control cell growth and division that can result in development of a tumor.

Fanconi anemia

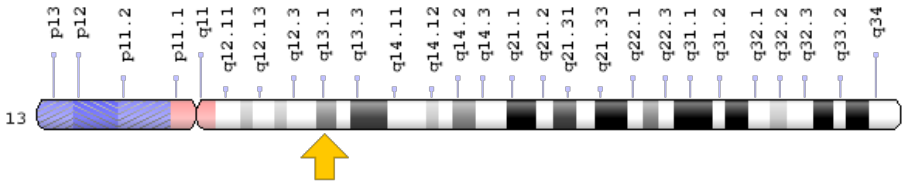
Other cancers

Inherited mutations in the *BRCA2* gene also increase the risk of several other types of cancer, including pancreatic cancer and an aggressive form of skin cancer called melanoma. These mutations impair the ability of the BRCA2 protein to help repair damaged DNA. As defects accumulate in DNA, they can trigger cells to grow and divide without order to form a tumor. It is not clear why different individuals with *BRCA2* mutations develop cancers in different organs. Environmental factors that affect specific organs may contribute to the development of cancers at particular sites.

Chromosomal Location

Cytogenetic Location: 13q13.1, which is the long (q) arm of chromosome 13 at position 13.1

Molecular Location: base pairs 32,315,480 to 32,399,672 on chromosome 13 (Homo sapiens Updated Annotation Release 109.20190905, GRCh38.p13) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- brca 2 gene
- BRCA2_HUMAN
- BRCC2
- breast cancer 2
- breast cancer 2 gene
- breast cancer 2, early onset
- breast cancer 2, early onset gene
- breast cancer type 2 susceptibility gene
- breast cancer type 2 susceptibility protein
- FACD
- FAD
- FAD1
- FANCB
- FANCD1

Additional Information & Resources

Educational Resources

- Cancer Medicine (sixth edition, 2003): BRCA1 and BRCA2: Gene Structure and Function
  https://www.ncbi.nlm.nih.gov/books/NBK12959/#A4564
- Madame Curie Bioscience Database: Origin, Recognition, Signaling and Repair of DNA Double-Strand Breaks in Mammalian Cells
  https://www.ncbi.nlm.nih.gov/books/NBK6555/
- 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

- BRCA1- and BRCA2-Associated Hereditary Breast and Ovarian Cancer
  https://www.ncbi.nlm.nih.gov/books/NBK1247
- Fanconi Anemia
  https://www.ncbi.nlm.nih.gov/books/NBK1401

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28BRCA2%5BMAJR%5D%29+AND+%28BRCA2%5BTI%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

- BRCA2 GENE
  http://omim.org/entry/600185
- FANCONI ANEMIA, COMPLEMENTATION GROUP D1
  http://omim.org/entry/605724

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/BRCA2ID164ch13q13.html
- Cancer Genetics Web: BRCA2
  http://www.cancerindex.org/geneweb/BRCA2.htm
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=BRCA2%5Bgene%5D
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:1101
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:675
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/675
- UniProt
  https://www.uniprot.org/uniprot/P51587

Sources for This Summary

- Chen S, Parmigiani G. Meta-analysis of BRCA1 and BRCA2 penetrance. J Clin Oncol. 2007 Apr 10; 25(11):1329-33.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17416853
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2267287/
- Foulkes WD, Shuen AY. In brief: BRCA1 and BRCA2. J Pathol. 2013 Aug;230(4):347-9. doi: 10.1002/path.4205. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23620175
- Foulkes WD. BRCA1 and BRCA2 - update and implications on the genetics of breast cancer: a clinical perspective. Clin Genet. 2014 Jan;85(1):1-4. doi: 10.1111/cge.12291. Epub 2013 Oct 25. Review. Erratum in: Clin Genet. 2014 Mar;85(3):302.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/24116874

- Friebel TM, Domchek SM, Rebbeck TR. Modifiers of cancer risk in BRCA1 and BRCA2 mutation carriers: systematic review and meta-analysis. J Natl Cancer Inst. 2014 Jun;106(6):dju091. doi: 10.1093/jnci/dju091. Review. Erratum in: J Natl Cancer Inst. 2014 Aug;106(8):dju235 doi:10.1093/jnci/dju235.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/24824314
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4081625/
- Kobayashi H, Ohno S, Sasaki Y, Matsuura M. Hereditary breast and ovarian cancer susceptibility genes (review). Oncol Rep. 2013 Sep;30(3):1019-29. doi: 10.3892/or.2013.2541. Epub 2013 Jun 19. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23779253
- National Cancer Institute: Genetics of Breast and Gynecologic Cancers (PDQ) https://www.cancer.gov/types/breast/hp/breast-ovarian-genetics-pdq
- Nelson HD, Fu R, Goddard K, Mitchell JP, Okinaka-Hu L, Pappas M, Zakher B. Risk Assessment, Genetic Counseling, and Genetic Testing for BRCA-Related Cancer: Systematic Review to Update the U.S. Preventive Services Task Force Recommendation [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2013 Dec. Available from http://www.ncbi.nlm.nih.gov/books/NBK179201/
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/24432435
- Pennington KP, Swisher EM. Hereditary ovarian cancer: beyond the usual suspects. Gynecol Oncol. 2012 Feb;124(2):347-53. doi: 10.1016/j.ygyno.2011.12.415. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22264603
- Petrucelli N, Daly MB, Pal T. BRCA1- and BRCA2-Associated Hereditary Breast and Ovarian Cancer. 1998 Sep 4 [updated 2016 Dec 15]. In: Pagon RA, Adam MP, Ardinger HH, Wallace SE, Amemiya A, Bean LJH, Bird TD, Ledbetter N, Mefford HC, Smith RJH, Stephens K, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017. Available from http://www.ncbi.nlm.nih.gov/books/NBK1247/
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20301425
- Shahid T, Soroka J, Kong EH, Malivert L, McIlwraith MJ, Pape T, West SC, Zhang X. Structure and mechanism of action of the BRCA2 breast cancer tumor suppressor. Nat Struct Mol Biol. 2014 Nov; 21(11):962-8. doi: 10.1038/nsmb.2899. Epub 2014 Oct 5.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/25282148
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4222816/
- Shulman LP. Hereditary breast and ovarian cancer (HBOC): clinical features and counseling for BRCA1 and BRCA2, Lynch syndrome, Cowden syndrome, and Li-Fraumeni syndrome. Obstet Gynecol Clin North Am. 2010 Mar;37(1):109-33, Table of Contents. doi: 10.1016/j.ogc.2010.03.003. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20494261
- Toss A, Tomasello C, Razzaboni E, Contu G, Grandi G, Cagnacci A, Schilder RJ, Cortesi L. Hereditary ovarian cancer: not only BRCA 1 and 2 genes. Biomed Res Int. 2015;2015:341723. doi: 10.1155/2015/341723. Epub 2015 May 17. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/26075229
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4449870/
- Wagner JE, Tolar J, Levran O, Scholl T, Deffenbaugh A, Satagopan J, Ben-Porat L, Mah K, Batish SD, Kutler DI, MacMillan ML, Hanenberg H, Auerbach AD. Germline mutations in BRCA2: shared genetic susceptibility to breast cancer, early onset leukemia, and Fanconi anemia. Blood. 2004 Apr 15;103(8):3226-9. Epub 2004 Jan 8.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15070707

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/gene/BRCA2

Reviewed: October 2015
Published: November 12, 2019

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services