

CEBPA gene

CCAAT enhancer binding protein alpha

Normal Function

The *CEBPA* gene provides instructions for making a protein called CCAAT enhancer-binding protein alpha. This protein is a transcription factor, which means that it attaches (binds) to specific regions of DNA and helps control the activity (expression) of certain genes. CCAAT enhancer-binding protein alpha is involved in the maturation (differentiation) of certain blood cells. It is also believed to act as a tumor suppressor, which means that it is involved in cellular mechanisms that help prevent the cells from growing and dividing too rapidly or in an uncontrolled way.

Health Conditions Related to Genetic Changes

Familial acute myeloid leukemia with mutated CEBPA

At least six mutations in the *CEBPA* gene have been identified in families with familial acute myeloid leukemia with mutated *CEBPA*, which is a form of a blood cancer known as acute myeloid leukemia. These inherited mutations are present throughout a person's life in virtually every cell in the body. The mutations result in a shorter version of CCAAT enhancer-binding protein alpha. This shortened protein is produced from one copy of the *CEBPA* gene in each cell, and it is believed to interfere with the tumor suppressor function of the normal protein produced from the second copy of the gene. Absence of the tumor suppressor function of CCAAT enhancer-binding protein alpha is believed to disrupt the regulation of blood cell production, leading to the uncontrolled production of abnormal cells that occurs in acute myeloid leukemia.

In addition to the inherited mutation in one copy of the *CEBPA* gene in each cell, most individuals with familial acute myeloid leukemia with mutated *CEBPA* also acquire a mutation in the second copy of the *CEBPA* gene. The additional mutation, which is called a somatic mutation, is found only in the cancerous leukemia cells and is not inherited. The somatic *CEBPA* gene mutations that have been identified in leukemia cells generally decrease the DNA-binding ability of CCAAT enhancer-binding protein alpha. Researchers suggest that this second mutation may affect the normal differentiation of blood cells, although exactly how the mutation is involved in the development of acute myeloid leukemia is unclear.

Cytogenetically normal acute myeloid leukemia

Mutations in the *CEBPA* gene have been identified in some people with a form of acute myeloid leukemia known as cytogenetically normal acute myeloid leukemia (CN-AML). While large chromosomal abnormalities can be involved in the development of acute myeloid leukemia, about half of cases do not have these abnormalities; these are classified as CN-AML. Mutations in this gene are found in approximately 18 percent of individuals with CN-AML. When associated with *CEBPA* gene mutations, this condition can be inherited, in which case it is called familial acute myeloid leukemia with mutated *CEBPA* (described above), or not inherited (sporadic acute myeloid leukemia with mutated *CEBPA*).

Two types of *CEBPA* gene mutations can occur in both the inherited and non-inherited forms of CN-AML. One type leads to production of an abnormally short protein that interferes with the tumor suppressor function of normal versions of CCAAT enhancer-binding protein alpha. The other type of mutation blocks the DNA-binding ability of CCAAT enhancer-binding protein alpha. Impaired DNA binding interferes with the protein's ability to regulate gene expression and impairs its tumor suppressor function. Impairment of the tumor suppressor function of CCAAT enhancer-binding protein alpha leads to the uncontrolled production of abnormal white blood cells that occurs in acute myeloid leukemia.

Between 50 and 75 percent of all individuals who have acute myeloid leukemia with mutations in the *CEBPA* gene, both sporadic and familial, have two mutated *CEBPA* genes in each leukemia cell. The rest have only one *CEBPA* gene mutation. In the sporadic cases the mutation appears only in the leukemia cells, and in the familial cases it is present throughout the body. Somatic mutations in other genes can also contribute to the development of CN-AML.

Other Names for This Gene

- c/EBP alpha
- C/EBP-alpha
- CCAAT/enhancer binding protein (C/EBP), alpha
- CCAAT/enhancer binding protein alpha
- CCAAT/enhancer-binding protein alpha
- CEBP
- CEBPA_HUMAN

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of CEBPA ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=1050\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=1050[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28CEBPA%5BTIAB%5D%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

- CCAAT/ENHANCER-BINDING PROTEIN, ALPHA; CEBPA (<https://omim.org/entry/116897>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/1050>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=CEBPA\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=CEBPA[gene]))

References

- Carmichael CL, Wilkins EJ, Bengtsson H, Horwitz MS, Speed TP, Vincent PC, Young G, Hahn CN, Escher R, Scott HS. Poor prognosis in familial acute myeloidleukaemia with combined biallelic CEBPA mutations and downstream events affectingthe ATM, FLT3 and CDX2 genes. *Br J Haematol*. 2010 Aug;150(3):382-5. doi:10.1111/j.1365-2141.2010.08204.x. Epub 2010 Apr 29. No abstract available. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/20456351>)
- Nanri T, Uike N, Kawakita T, Iwanaga E, Mitsuya H, Asou N. A family harboringa germ-line N-terminal C/EBPalphamutation and development of acute myeloidleukemia with an additional somatic C-terminal C/EBPalphamutation. *GenesChromosomes Cancer*. 2010 Mar;49(3):237-41. doi: 10.1002/gcc.20734. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/19953636>)
- Owen C, Barnett M, Fitzgibbon J. Familial myelodysplasia and acute myeloidleukaemia--a review. *Br J Haematol*. 2008 Jan;140(2):123-32. doi:10.1111/j.1365-2141.2007.06909.x. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/18173751>)
- Pabst T, Eyholzer M, Haefliger S, Schardt J, Mueller BU. Somatic CEBPAmutations are a frequent second event in families with germline CEBPA mutationsand familial acute myeloid leukemia. *J Clin Oncol*. 2008 Nov 1;26(31):5088-93.doi: 10.1200/JCO.2008.16.5563. Epub 2008 Sep 2. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/18768433>)
- Pabst T, Mueller BU, Zhang P, Radomska HS, Narravula S, Schnittger S, Behre G, Hiddemann W, Tenen DG. Dominant-negative mutations of CEBPA, encodingCCAAT/enhancer binding protein-alpha (C/EBPalphamutation), in acute myeloid leukemia. *NatGenet*. 2001 Mar;27(3):263-70. doi: 10.1038/85820. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/11242107>)
- Pabst T, Mueller BU. Complexity of CEBPA dysregulation in human acute

myeloidleukemia. Clin Cancer Res. 2009 Sep 1;15(17):5303-7. doi:10.1158/1078-0432.CCR-08-2941. Epub 2009 Aug 25. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/19706798>)

- Quintana-Bustamante O, Lan-Lan Smith S, Griessinger E, Reyat Y, Vargaftig J, Lister TA, Fitzgibbon J, Bonnet D. Overexpression of wild-type or mutants forms of CEBPA alter normal human hematopoiesis. Leukemia. 2012 Jul;26(7):1537-46. doi: 10.1038/leu.2012.38. Epub 2012 Feb 10. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/22371011>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3378638/>)
- Renneville A, Mialou V, Philippe N, Kagialis-Girard S, Biggio V, Zabet MT, Thomas X, Bertrand Y, Preudhomme C. Another pedigree with familial acute myeloid leukemia and germline CEBPA mutation. Leukemia. 2009 Apr;23(4):804-6. doi:10.1038/leu.2008.294. Epub 2008 Oct 23. No abstract available. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/18946494>)
- Smith ML, Cavenagh JD, Lister TA, Fitzgibbon J. Mutation of CEBPA in familial acute myeloid leukemia. N Engl J Med. 2004 Dec 2;351(23):2403-7. doi:10.1056/NEJMoa041331. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15575056>)

Genomic Location

The *CEBPA* gene is found on chromosome 19 (<https://medlineplus.gov/genetics/chromosome/19/>).

Last updated January 1, 2014