

# CEBPA Gene

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## 1. 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.

## 2. Health Conditions Related to Genetic Changes

### 2.1. 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.

### 2.2. 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.

### 3. 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

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