CREBBP gene

CREB binding protein

Normal Function

The *CREBBP* gene provides instructions for making CREB binding protein, which regulates the activity of many genes in tissues throughout the body. This protein plays an essential role in controlling cell growth and division and prompting cells to mature and assume specialized functions (differentiate). CREB binding protein appears to be critical for normal development before and after birth. Studies show that this protein is involved in development of the brain and may also be involved in the formation of long-term memories.

CREB binding protein carries out its functions by turning on (activating) transcription, which is the first step in the production of proteins from the instructions stored in DNA. The CREB binding protein ensures the DNA is ready for transcription by attaching a small molecule called an acetyl group to proteins called histones (a process called acetylation). Histones are structural proteins that bind DNA and give chromosomes their shape. Acetylation of the histone changes the shape of the chromosome, making genes available for transcription. On the basis of this function, CREB binding protein is called a histone acetyltransferase.

In addition, CREB binding protein connects other proteins that start the transcription process (known as transcription factors) with the group of proteins that carries out transcription. On the basis of this function, CREB binding protein is called a transcriptional coactivator.

Health Conditions Related to Genetic Changes

Rubinstein-Taybi syndrome

Mutations in the *CREBBP* gene have been found to cause Rubinstein-Taybi syndrome, a condition characterized by short stature, moderate to severe intellectual disability, distinctive facial features, and broad thumbs and first toes. More than 300 mutations have been identified, including the loss (deletion) or addition (insertion) of genetic material in the gene and changes in single DNA building blocks (nucleotides).

Because one copy of the *CREBBP* gene is altered in people with Rubinstein-Taybi syndrome, their cells make only half of the normal amount of functional CREB binding

protein. Although researchers are uncertain how a reduction in the amount of this protein leads to the features of Rubinstein-Taybi syndrome, it is clear that variations in the *CREBBP* gene disrupt normal development before and after birth. Problems with development of the brain are thought to underlie intellectual disability in people with Rubinstein-Taybi syndrome. Other features of the condition likely result from abnormal development of other systems.

Deletion of genetic material from the short (p) arm of chromosome 16 can cause severe Rubinstein-Taybi syndrome, which features an inability to grow or gain weight in infancy, serious infections, and abnormalities of certain organs, such as the heart or spleen, in addition to the classic symptoms of the condition. Multiple genes, including the *CREBBP* gene, are missing as a result of the deletion. Researchers believe that the loss of multiple genes in this region probably accounts for the serious complications associated with severe Rubinstein-Taybi syndrome. Some researchers suggest that these cases are a separate condition called chromosome 16p13.3 deletion syndrome. However, a few studies indicate that large deletions in the p arm of chromosome 16 do not always cause severe signs and symptoms, so it is unclear if the disorders are separate.

Bladder cancer

MedlinePlus Genetics provides information about Bladder cancer

Other disorders

Mutations in the *CREBBP* gene can cause a condition called Menke-Hennekam syndrome. While this condition shares some features with Rubinstein-Taybi syndrome (described above), such as intellectual disability and growth delays, individuals with Menke-Hennekam syndrome do not have the facial features and thumb and toe abnormalities characteristic of Rubinstein-Taybi syndrome. Other features of Menke-Hennekam syndrome are variable and can include vision or hearing impairment, recurrent seizures (epilepsy), frequent airway infections, and autistic behaviors that affect communication.

The *CREBBP* gene mutations that cause Menke-Hennekam syndrome occur in regions of the gene known as exon 30 or exon 31. They result in changes to single protein building blocks (amino acids) in CREB binding protein. Researchers suggest that these changes give the altered protein a new function, which alters development and causes the signs and symptoms of Menke-Hennekam syndrome.

In some people, a region of DNA on chromosome 16 that includes the *CREBBP* gene is copied (duplicated). This genetic change causes a condition called chromosome 16p13. 3 duplication syndrome, which is characterized by intellectual disability, distinctive facial features (different from those of Rubinstein-Taybi syndrome, described above), abnormal thumbs, and rigid joints (arthrogryposis). Some affected individuals also have abnormalities of the heart, genitals, roof of the mouth, or the eyes.

While other genes can be included in the duplicated region, depending on its size, research shows that the *CREBBP* gene is most likely responsible for the characteristic

signs and symptoms of chromosome 16p13.3 duplication syndrome. Researchers suspect that an extra copy of the *CREBBP* gene leads to the production of excess CREB binding protein and an increase in protein function. The resulting changes in gene transcription and protein production likely alter development of various systems, causing the signs and symptoms of chromosome 16p13.3 duplication syndrome.

Cancers

Genetic changes involving the *CREBBP* gene have been associated with certain types of cancer. These mutations are somatic, which means they are acquired during a person's lifetime and are present only in certain cells. In some cases, chromosomal rearrangements (translocations) disrupt the region of chromosome 16 that contains the *CREBBP* gene. For example, researchers have found a translocation between chromosome 8 and chromosome 16 in some people with a cancer of blood-forming cells called acute myeloid leukemia (AML). Another translocation, involving chromosomes 11 and 16, has been found in some people who have undergone cancer treatment. This chromosomal change is associated with the later development of AML and two other cancers of blood-forming tissues (chronic myelogenous leukemia and myelodysplastic syndrome). These are sometimes described as treatment-related cancers because the translocation between chromosomes 11 and 16 occurs following chemotherapy for other forms of cancer.

Somatic mutations in the *CREBBP* gene have also been found in people with another blood cell cancer called B-cell non-Hodgkin lymphoma. Many of these mutations reduce the amount of functional CREB binding protein. Other mutations impair the protein's histone acetyltransferase activity. Reduction of CREB binding protein activity in certain immune cells called B cells prevents the normal control of cell growth and division, contributing to the development of B-cell non-Hodgkin lymphoma.

Other Names for This Gene

- CBP
- CBP_HUMAN
- CREB binding protein (Rubinstein-Taybi syndrome)

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of CREBBP (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=1387[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28CREBBP%5BTI%5D%29+OR+%28CREB+binding+protein%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+1800+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- CREB-BINDING PROTEIN; CREBBP (https://omim.org/entry/600140)
- LEUKEMIA, ACUTE MYELOID; AML (https://omim.org/entry/601626)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/1387)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=CREBBP[gene])

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Genomic Location

The *CREBBP* gene is found on chromosome 16 (https://medlineplus.gov/genetics/chromosome/16/).

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