CSTB gene

cystatin B

Normal Function

The *CSTB* gene provides instructions for making a protein called cystatin B. This protein reduces the activity of (inhibits) enzymes called cathepsins. Cathepsins help break down certain proteins in the lysosomes, which are compartments in the cell that digest and recycle different types of molecules. Cystatin B may help protect the cells' proteins from cathepsins that leak out of the lysosomes.

Cystatin B is also believed to play a role in the development, movement, and communication of nerve cells. In addition, cystatin B helps control the nervous system's immune response (inflammation) and protects cells from harm caused by unstable molecules in the body (oxidative stress).

Health Conditions Related to Genetic Changes

Progressive myoclonic epilepsy type 1

Most variants (also called mutations) in the *CSTB* gene cause progressive myoclonic epilepsy type 1, a rare inherited form of epilepsy. One region of DNA that controls the activity of the *CSTB* gene has a particular repeating sequence of 12 DNA building blocks (nucleotides). This sequence is known as the dodecamer repeat. Normally, this sequence is repeated two or three times. However, in most people with progressive myoclonic epilepsy type 1, this sequence is repeated more than 30 times (called a repeat expansion). Most people with progressive myoclonic epilepsy type 1 have two copies of this variant.

A small number of people with progressive myoclonic epilepsy type 1 have one copy of the dodecamer repeat expansion and one copy of the *CSTB* gene with another type of variant. Some of these variants substitute one protein building block (amino acid) for another amino acid in the cystatin B protein. Other variants cause the protein to be pieced together incorrectly or lead to the production of a shortened protein that may not function properly. Researchers have suggested that people who carry one copy of the expanded repeat plus another type of variant may have more severe signs and symptoms than those with two copies of the expanded dodecamer repeat.

The expanded dodecamer repeat in the *CSTB* gene seems to interfere with the production of cystatin B protein. Levels of cystatin B in affected individuals are only 5 to 10 percent of normal. This change is believed to cause the signs and symptoms of progressive myoclonic epilepsy type 1, but the specific mechanism is unknown.

Other Disorders

Rarely, some individuals have two variants in the *CSTB* gene that result in no cystatin B production. These individuals have more severe signs and symptoms, which may include a small head size (microcephaly), severe developmental delays, abnormal movements (dyskinesia), seizures, and encephalopathy (abnormal brain function). These symptoms resemble those seen in a group of severe epilepsies known as developmental and epileptic encephalopathies.

Other Names for This Gene

- CPI-B
- CST6
- cystatin B (stefin B)
- EPM1
- EPM1A
- PME
- stefin B
- STFB
- ULD

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of CSTB (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=1476[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28CSTB%5BTIAB%5D%29+OR+%28cystatin+B%5BTIAB%5D%29%29+OR+%28%28EPM1%5BTIAB%5D%29+OR+%28STFB%5BTIAB%5D%29+OR+%28cystatin+B%5BTIAB%5D%29+OR+%28CPI-B%5BTIAB%5D%29+OR+%28stefin+B%5BTIAB%5D%29+OR+%28liver+thiol+proteinase+inhibitor%5BTIAB%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+1440+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- CYSTATIN B; CSTB (https://omim.org/entry/601145)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/1476)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=CSTB[gene])

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Genomic Location

The *CSTB* gene is found on chromosome 21 (https://medlineplus.gov/genetics/chromosome/21/).

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