CDKL5 Gene

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Contributor: Vicky Zhou

cyclin dependent kinase like 5

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1. Normal Function

The *CDKL5* gene provides instructions for making a protein that is found in cells and tissues throughout the body. However, it is most active in the brain and is essential for normal brain development and function. There are five versions (isoforms) of the CDKL5 protein. These isoforms vary in length and in the tissues in which they are most abundant.

Studies suggest that the CDKL5 protein is involved in the formation, growth, and movement (migration) of nerve cells (neurons), as well as cell division. It also plays a role in the transmission of chemical signals at the connections (synapses) between neurons.

The CDKL5 protein acts as a kinase, which is an enzyme that changes the activity of other proteins by adding a cluster of oxygen and phosphorus atoms (a phosphate group) at specific positions. It is possible that one of the proteins targeted by the CDKL5 protein is MeCP2, which is produced from the *MECP2* gene. The MeCP2 protein plays important roles in the function of neurons and other brain cells and in the maintenance of neuronal synapses. Researchers have not determined which other proteins are targeted by the CDKL5 protein.

2. Health Conditions Related to Genetic Changes

CDKL5 Deficiency Disorder

At least 150 mutations in the *CDKL5* gene have been found to cause CDKL5 deficiency disorder. This rare condition is characterized by seizures that begin in infancy, followed by significant delays in many aspects of development. Affected individuals have severe intellectual disability and most do not walk independently. About 90 percent of people diagnosed with CDKL5 deficiency disorder are female.

CDKL5 deficiency disorder was previously classified as an atypical form of Rett syndrome. However, CDKL5 deficiency disorder is now considered a separate condition. Rett syndrome, which affects development in girls and women, results from mutations in the *MECP2* gene. Because the CDKL5 and MeCP2 proteins may interact in the brain, the two disorders might be caused by a similar mechanism.

Mutations in the *CDKL5* gene reduce the amount of functional CDKL5 protein or alter its activity in neurons. A shortage (deficiency) of CDKL5 or impairment of its function disrupts brain development, but it is unclear how these changes cause the specific features of CDKL5 deficiency disorder.

Most *CDKL5* gene mutations change single protein building blocks (amino acids) in the CDKL5 protein. This type of mutation occurs most often in a region of the protein called the kinase domain, which is essential for the protein's kinase function. Mutations in the kinase domain disrupt the ability of CDKL5 to add phosphate groups to other proteins. Compared with other types of mutation, these mutations are associated with more severe signs and symptoms of CDKL5 deficiency disorder.

Other *CDKL5* gene mutations alter different regions of the CDKL5 protein or lead to the production of an abnormally short version of the protein. Research has shown that mutations affecting parts of the protein other than the kinase domain tend to cause less severe signs and symptoms of CDKL5 deficiency disorder than other types of mutations.

3. Other Names for This Gene

- CDKL5_HUMAN
- CFAP247
- cyclin-dependent kinase-like 5
- serine/threonine kinase 9
- STK9

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