CDKL5 gene

cyclin dependent kinase like 5

Normal Function

The *CDKL5* gene provides instructions for making a protein that is essential for normal brain development and function. 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. 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 nerve cells (neurons) and other brain cells and in the maintenance of connections (synapses) between neurons. Researchers have not determined which other proteins are targeted by the CDKL5 protein.

Health Conditions Related to Genetic Changes

X-linked infantile spasm syndrome

Mutations in the *CDKL5* gene can cause a disorder known as X-linked infantile spasm syndrome, which is characterized by recurrent seizures called infantile spasms that begin in the first year of life. Children with this condition also have intellectual disability. X-linked infantile spasm syndrome caused by *CDKL5* gene mutations occurs more often in females, but it has been identified in a small number of males.

Some cases of X-linked infantile spasm syndrome are caused by a deletion involving part or all of the *CDKL5* gene; others result from mutations that alter the function of the CDKL5 protein or prevent the production of any functional protein. It is unclear how defects in this protein cause seizures and intellectual disability.

other disorders

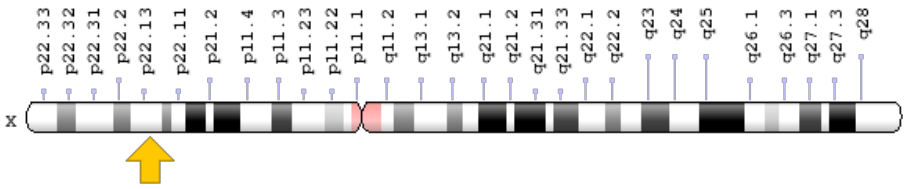
More than 10 mutations in the *CDKL5* gene have been identified in females with a condition similar to Rett syndrome, which is a disorder whose characteristic features include developmental problems, loss of language skills, and repeated hand wringing or hand washing movements. Girls with *CDKL5* gene mutations have many of the features of classic Rett syndrome. However, unlike girls with classic Rett syndrome, they also develop recurrent seizures beginning in infancy. Although this condition was previously described as an atypical form of Rett syndrome (often called the early-onset seizure variant), it is now usually considered to be a separate condition.

Some of the *CDKL5* gene mutations that cause this condition change a single protein building block (amino acid) in a region of the CDKL5 protein that is critical for its kinase function. Other mutations lead to the production of an abnormally short, nonfunctional version of the protein. Researchers are working to determine how these changes impair brain development, resulting in seizures and features similar to Rett syndrome.

Chromosomal Location

Cytogenetic Location: Xp22.13, which is the short (p) arm of the X chromosome at position 22.13

Molecular Location: base pairs 18,425,605 to 18,653,629 on the X chromosome (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

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

Additional Information & Resources

<u>Educational Resources</u>

- International Foundation for CDKL5 Research
  http://www.cdkl5.com/
- Jasper's Basic Mechanisms of the Epilepsies (fourth edition, 2012): The Monogenic Forms of Early Infantile Epileptic Encephalopathies
  https://www.ncbi.nlm.nih.gov/books/NBK98182/#depienne.s1

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28CDKL5%5BTIAB%5D%29+OR+%28cyclin-dependent+kinase-like+5%5BTIAB%5D%29%29+OR+%28%28STK9%5BTIAB%5D%29+OR+%28serine/threonine+kinase+9%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+1080+days%22%5Bdp%5D

OMIM

- CYCLIN-DEPENDENT KINASE-LIKE 5
  http://omim.org/entry/300203

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_CDKL5.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=CDKL5%5Bgene%5D
- HGNC Gene Family: Cyclin dependent kinases
  http://www.genenames.org/cgi-bin/genefamilies/set/496
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=11411
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/6792
- UniProt
  http://www.uniprot.org/uniprot/O76039

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