

What is CHD2?

The CHD2 gene is located on chromosome 15 and provides instructions for making a protein called chromodomain-DNA-helicase-binding protein 2. This protein is found in cells throughout the body and regulates gene activity (expression) through a process known as chromatin remodeling. Chromatin is the complex of DNA and proteins that package DNA into chromosomes. The structure of chromatin may be changed (remodeled) to alter how tightly DNA is packaged. When DNA is tightly packed, gene expression is less likely than when DNA is loosely packed. The CHD2 protein appears to play an important role in the brain, although its function is not well understood. Research suggests that it may help control development or functioning of brain cells (neurons). The clinical features of CHD2-related neurodevelopmental disorder include, among other things, [drug-resistant epilepsy](#). The majority of known pathogenic (disease-causing) variants in the gene that cause CHD2-related neurodevelopmental disorders lead to non-functional protein (truncation of the protein), suggesting that epilepsy and other features develop as a result of not enough CHD2 protein in the brain.

What types of seizures (and epilepsies) are associated with CHD2?

Seizure types associated with CHD2-related neurodevelopmental disorders may include the following:

- [Myoclonic seizures](#) - body jerks or involuntary muscle twitches
- [Eyelid flutters/myoclonia](#)
- [Tonic-clonic seizures](#), which involve loss of consciousness, muscle rigidity and convulsions.
- [Atonic seizures](#) or drop attacks.
- Atonic-myoclonic-absence seizures
- [Photosensitive epilepsy](#) caused by flashing lights.
- A rapid onset of multiple seizure types associated with generalized spike-waves on an EEG.

CHD2-related neurodevelopmental disorders may be characterized by early-onset [developmental and epileptic encephalopathy \(DEE\)](#). DEEs are a group of epilepsies characterized by seizures that do not respond well to anti-seizure medications and are often associated with learning and developmental impairment and regression. The onset of seizures and other non-seizure type symptoms of CHD2-related neurodevelopmental disorders typically first present within the first five (5) years of life. The frequency of seizures may vary significantly from person to person, from daily to infrequently, and not all individuals diagnosed with CHD2 variants will have seizures at the time of diagnosis.

Epilepsies commonly associated with the CHD2 gene include the following because the seizure types in these syndromes are seen in individuals with CHD2 variants:

- [Doose syndrome](#)
- [Jeavons syndrome](#)
- [Lennox-Gastaut syndrome](#)
- [West syndrome](#)

What non-seizure symptoms are seen in CHD2?

Common non-seizure symptoms of CHD2-related neurodevelopmental disorders include the following:

- Intellectual disability (ID) ranging from mild to severe.
- Autism spectrum disorders (ASD)
- Developmental delay
- Neuropsychiatric conditions, including bipolar disorder, psychosis, attention deficit hyperactivity disorder (ADHD)
- Other challenging behaviors such as aggression
- Low muscle tone
- Strabismus

Not all individuals with CHD2 variants have the same clinical features, and the full spectrum of features is yet to be defined.

How is CHD2 diagnosed?

A pathogenic variant in the CHD2 gene is identified by molecular [genetic testing](#). If a CHD2-related disorder is suspected, single gene testing involving only the CHD2 gene would be reasonable to pursue. More commonly, a multi-gene panel or exome sequencing will be used to evaluate a patient with the above epilepsy types and other symptoms and will identify a CHD2 variant.

Genetic counseling prior to genetic testing is an important step in making sure that the best testing strategy is selected, and that patients and families understand the risks, benefits, limitations, and possible outcomes of testing.

How are CHD2-related disorders treated?

There are no current treatments or therapies specific to CHD2-related disorders, so treatment is directed at specific symptoms in each individual.

While CHD2-related disorders are commonly associated with drug-resistant epilepsy, individuals with CHD2-related disorders are typically prescribed [anti-seizure medications](#) that target generalized seizures (e.g., valproic acid, lamotrigine, clobazam, levetiracetam, zonisamide, topiramate, Epidiolex,



felbamate, clonazepam) and in some cases the ketogenic diet. Fintepla (fenfluramine) has been approved for Dravet syndrome, and since the myoclonic seizures seen in patients with that syndrome resemble those with CHD2-related epilepsy, this drug may be useful as well.

Many individuals diagnosed with a CHD2 disorder have features of autism spectrum disorder, developmental (e.g., speech) delay, and intellectual disability. Thus, appropriate therapies include, but are not limited to, speech therapy, occupational therapy, physical therapy, behavioral therapy, and psychological therapy.

Specialists commonly seen include neurologists, orthopedists, dieticians, special needs dentists, cardiologists, gastroenterologists, and geneticists.

How common are CHD2-related disorders?

To date, there have been at least 205 patients diagnosed with a pathogenic variant in the CHD2 gene, but we know there are likely thousands more who have yet been diagnosed. Individuals with pathogenic CHD2 variants reside all over the world, and this condition is equally present in males and females.

What is the outlook for CHD2-related disorders?

Some individuals with the CHD2-related disorders experience normal development prior to the onset of seizures, but once seizures occur, developmental delays may become more prevalent and, in some cases, regression may occur. While some may outgrow their seizures, many will likely live with their seizures (although controlled to some degree for some) throughout their lifetime.

A number of researchers and pharmaceutical companies are either currently working on, or are considering working on or investing in, the development of drugs or precision therapies that may improve the lives of those living with CHD2, or that may even lead to a cure for this disorder.



For more information

- [Coalition to Cure CHD2, Inc.](#)

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