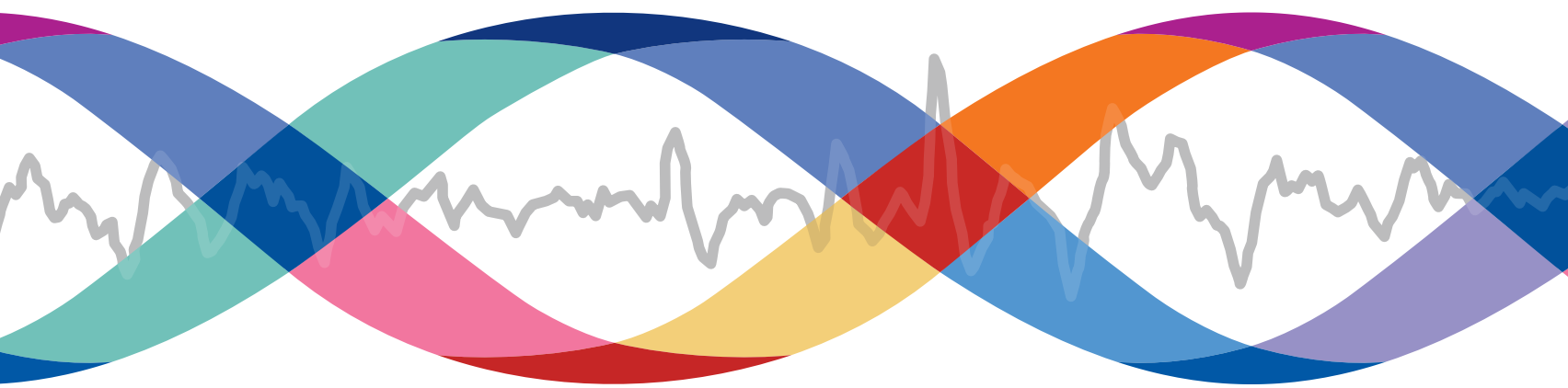
Test early to expedite care

NO-CHARGE* EPILEPSY GENE PANEL FOR CHILDREN UNDER THE AGE OF 8



*This is a sponsored testing program. While third parties and commercial organizations may provide financial support for this program, tests and services are performed by Invitae. Healthcare professionals must confirm that patients meet certain criteria to use the program. Third parties and commercial organizations may receive de-identified patient data from this program, but at no time would they receive patient-identifiable information. Third parties and commercial organizations may receive contact information for healthcare professionals who use this program. Genetic testing and counseling is available in the US and Canada. Healthcare professionals and patients who participate in this program have no obligation to recommend, purchase, order, prescribe, promote, administer, use, or support any other products or services from Invitae or from third parties or commercial organizations.

BEHIND the SEIZURE®

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START WITH

Early genetic testing to impact patient care

More than 50% of epilepsies have some genetic basis[1]

Genetic research is rapidly advancing our understanding of the underlying causes of pediatric epilepsy and potential treatments. When a patient presents with seizures, genetic testing can help identify 100+ underlying genetic causes. Early genetic testing may be the most direct, cost-effective, and accurate diagnostic tool for some epilepsies.[1]

Not all seizures are benign

Genetic testing can help rule out or confirm a suspected diagnosis. Additionally, it can help uncover rare or fatal diseases, such as neurodegenerative disorders.

Many genes are actionable

Early diagnosis is critical—results from genetic testing can increase the likelihood of diagnosis and inform treatment decisions. Ordering an epilepsy gene panel early offers patients and their families many other benefits, including:

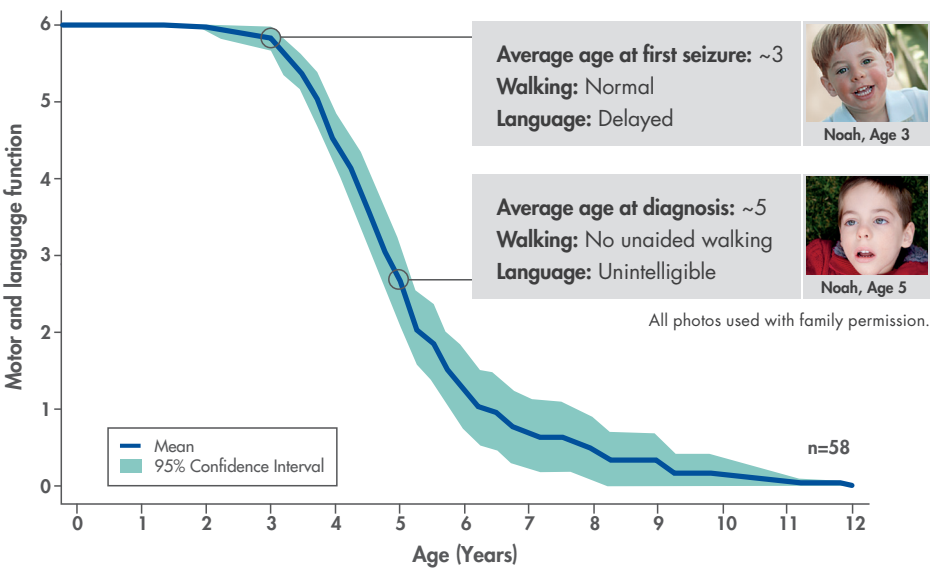
- Tailoring care to a patient's specific needs
- Identifying potential clinical trials to enroll patients
- Shortening the time to diagnosis
- Connecting families to patient advocacy organizations and other resources
- Predicting or identifying risk of disease for family members

Early diagnosis: Critical for neurodegenerative disorders, such as CLN2 disease

CLN2 disease is a rare and rapidly progressing pediatric neurodegenerative disorder caused by mutations in the *TPP1* gene (also known as the *CLN2* gene)[2,3]—one of the 300+ genes tested by the Behind the Seizure® gene panel. This autosomal recessive lysosomal storage disorder (LSD) classically presents with a late-infantile onset and is associated with deficiency of the tripeptidyl peptidase 1 (TPP1) enzyme.[2,4]

Because CLN2 disease is rare and has nonspecific early symptoms, patients endure an average delay of 2 years between onset of seizure and diagnosis.[5] During this time, symptoms worsen and function is lost. Children commonly experience a complete loss of cognitive abilities, motor function, vision failure, and premature death.[4]

CLN2 disease follows a devastatingly rapid course[2,5]



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Longitudinal data from 58 subjects with CLN2 disease in the DEM-CHILD registry, a multinational neuronal ceroid lipofuscinosis (NCL) patient database.

The CLN2 Clinical Rating Scale quantitatively measures disease progression based on motor and language function.[5]

Early signs or symptoms of CLN2 disease[6]:

- Language development delay
- Motor disturbances or ataxia
- Abnormal EEG: PPR with low-frequency (1-2 Hz) IPS[6,7]
- Abnormal MRI: cerebellar atrophy or periventricular white matter hyperintensities

Visit CLN2Connection.com to learn more about CLN2 disease.

EEG, electroencephalogram; IPS, intermittent photic stimulation; MRI, magnetic resonance imaging; PPR, photoparoxysmal response.

Danny and Bekah Bowmans' sons, Titus (left) and Ely (right), were both diagnosed with CLN2 disease.

Case study: The Bowman family

Titus

Age at diagnosis
4.5 years

Before diagnosis:

- Displayed language development delay
- Showed decreased motor function (clumsiness)
- Experienced multiple seizures (unresponsive; tonic/clonic)
- Was placed on multiple AEDs, but still experienced refractory seizures

CLN2 disease diagnosis:

- Confirmed after a 14-month diagnostic journey and multiple tests
- Diagnosed via an epilepsy gene panel

Ineligible to enroll in a clinical study.

Ely

Age at diagnosis
2 years

CLN2 disease diagnosis:

- Confirmed a few months after Titus
- Tested with gene panel after learning of his brother's diagnosis

Eligible to enroll in a therapeutic clinical study.

Test early. Uncover whether there's a genetic cause ***behind the seizure***.

BEHIND the SEIZURE®

DISCOVER

What's Behind the Seizure®

The diagnostic journey can be time-consuming, costly, and emotionally draining. The epilepsy gene panel can bring you closer to identifying what's *behind the seizure*, helping your patients and their caregivers benefit from knowledge and timely care.

Who it's for

Children under the age of 8 who have had an unprovoked seizure.

What it costs

Testing is provided to eligible patients at no charge.

Genes that this panel tests

The Invitae Epilepsy Panel is a broad, comprehensive panel that tests 300+ genes associated with both syndromic and nonsyndromic causes of epilepsy including neurodegenerative conditions.

How to order

Placing an order is simple. Instructions for requesting a collection kit, submitting a sample, and placing your order can be found at BehindTheSeizure.com. Or contact Invitae Client Services at clientservices@invitae.com or 800.436.3037.

Receiving results

Once Invitae receives the sample, you will receive results within 10 to 21 calendar days (14 days on average). If you have created an online account, you can log in to view the status of your order at any time. You will receive a notification email from Invitae once the test results are ready.

Order a test for your eligible patients today at **BehindTheSeizure.com**.

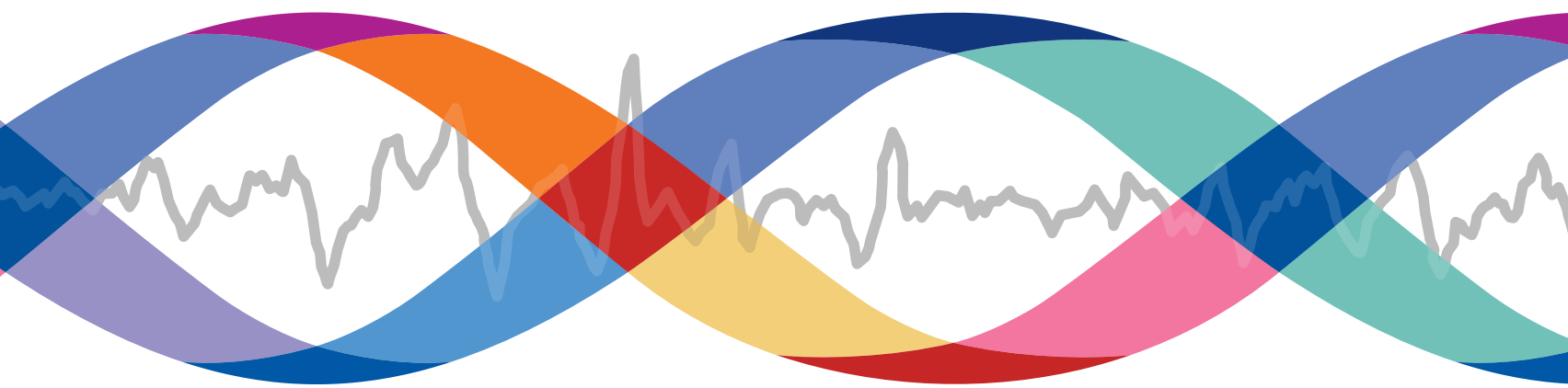
For more information or to speak with a genetic counselor, email **clientservices@invitae.com** or call **800.436.3037**.

BEHIND the SEIZURE®

BEHIND THE SEIZURE®

Test today. Diagnose sooner. Customize care faster.

- **The Behind the Seizure® no-charge epilepsy gene panel** is for children under the age of 8 who have had an unprovoked seizure
- **By incorporating the Behind the Seizure® panel into your initial workup, you can help:**
  - **Impact patient care**
  - **Provide patients with actionable benefits**, such as clinical trial enrollment, genetic counseling, disease-specific management, and more
  - **Diagnose earlier**, which can be critical when caring for patients with neurodegenerative disorders, such as CLN2 disease
  - **Make a difference** in the lives of your patients and their families



Order a kit **Place an order** **Get more information**

At **BehindTheSeizure.com** or contact Invitae Client Services at **clientservices@invitae.com** or **800.436.3037**.

References: 1. Pal DK, Pong AW, Chung WK. Genetic evaluation and counseling for epilepsy. *Nat Rev Neurol.* 2010;6:445-453. **2.** Schulz A, Kohlschütter A, Mink J, Simonati A, Williams R. NCL diseases—clinical perspectives. *Biochim Biophys Acta.* 2013;1832:1801-1806. **3.** Claussen M, Heim P, Knispel J, Goebel HH, Kohlschütter A. Incidence of neuronal ceroid-lipofuscinoses in West Germany: variation of a method for studying autosomal recessive disorders. *Am J Med Genet.* 1992;42:536-538. **4.** Mole SE, Williams RE. Neuronal ceroid-lipofuscinoses. In: Pagon RA, Adam MP, Ardinger HH, et al, eds. *GeneReviews®*. Seattle: University of Washington; 2001 (updated August 1, 2013). **5.** Nickel M, Jacoby D, Lezius S, et al. Natural history of CLN2 disease: quantitative assessment of disease characteristics and rate of progression. Poster session presented at: The 12th Annual WORLD Symposium; February-March 2016; San Diego, CA. **6.** Fietz M, AlSayed M, Burke D, et al. Diagnosis of neuronal ceroid lipofuscinosis type 2 (CLN2 disease): Expert recommendations for early detection and laboratory diagnosis. *Mol Genet Metab.* 2016;119:160-167. **7.** Specchio N, Bellusci M, Pietrafusa N, Trivisano M, de Palma L, Vigevano F. Photosensitivity is an early marker of neuronal ceroid lipofuscinosis type 2 disease. *Epilepsia.* 2017;58(8):1380-1388.

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Expedite Diagnosis. Impact Care.

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