

## Overview

### Useful For

[Molecular confirmation of clinically suspected \*CSTB\*-related progressive myoclonic epilepsy](#)

Identifying full penetrance dodecamer repeat expansions within *CSTB* known to cause *CSTB*-related progressive myoclonic epilepsy, allowing for predictive testing of at-risk family members

Impacting patient treatment and management through the identification of a specific underlying etiology for epilepsy (eg, directing appropriate use of anti-epileptic drugs and other treatment modalities)

### Genetics Test Information

This test assesses for CCC-CGC-CCC-GCG dodecamer repeat expansions in the promoter region of *CSTB* to confirm a molecular diagnosis of *CSTB*-related progressive myoclonic epilepsy, also known as progressive myoclonic epilepsy type 1 (EPM1).

### Testing Algorithm

For more information see [Epilepsy: Unexplained Refractory and/or Familial Testing Algorithm](#)

### Special Instructions

- [Informed Consent for Genetic Testing](#)
- [Molecular Genetics: Neurology Patient Information](#)
- [Epilepsy: Unexplained Refractory and/or Familial Testing Algorithm](#)
- [Informed Consent for Genetic Testing \(Spanish\)](#)

### Method Name

Polymerase Chain Reaction (PCR)

### NY State Available

Yes

## Specimen

### Specimen Type

Varies

### Ordering Guidance

This test only detects dodecamer repeat expansions. If testing for both dodecamer repeat expansions and other *CSTB* variants is requested, order a custom gene panel for the *CSTB* gene. For more information see CGPH / Custom Gene Panel, Hereditary, Next-Generation Sequencing, Varies.

### Shipping Instructions

Specimen preferred to arrive within 96 hours of collection.

**Specimen Required**

**Patient Preparation:** A previous bone marrow transplant from an allogenic donor will interfere with testing. Call 800-533-1710 for instructions for testing patients who have received a bone marrow transplant.

**Specimen Type:** Whole blood

**Container/Tube:**

**Preferred:** Lavender top (EDTA) or yellow top (ACD)

**Acceptable:** Any anticoagulant

**Specimen Volume:** 3 mL

**Collection Instructions:**

1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot.**

**Specimen Stability Information:** Ambient (preferred)/Refrigerated

**Forms**

1. **New York Clients-Informed consent is required.** Please document on the request form or electronic order that a copy is on file. The following documents are available:

[-Informed Consent for Genetic Testing \(T576\)](#)

[-Informed Consent for Genetic Testing \(Spanish\) \(T826\)](#)

2. [Molecular Genetics: Neurology Patient Information](#)

3. If not ordering electronically, complete, print, and send a [Neurology Specialty Testing Client Test Request \(T732\)](#) with the specimen.

**Reject Due To**

All specimens will be evaluated by Mayo Clinic Laboratories for test suitability.

**Specimen Stability Information**

Specimen Type	Temperature	Time	Special Container
Varies	Ambient (preferred)		
	Frozen		
	Refrigerated		

**Clinical & Interpretive****Clinical Information**

*CSTB*-related progressive myoclonic epilepsy (PME), also known as progressive myoclonic epilepsy type 1 (EPM1) or Unverricht-Lundborg disease, is the most common and least severe of the collective progressive myoclonic epilepsies. *CSTB*-related PME is inherited in an autosomal recessive pattern and is associated with inter- and intrafamilial variability. Individuals with *CSTB*-related PME have normal early development with onset of symptoms typically in the first or second decade of life. *CSTB*-related PME is characterized by involuntary myoclonus that is action- or stimulus-precipitated. Individuals with the condition are at increased risk for seizures, including tonic-clonic, absence, psychomotor and focal motor. The condition is progressive, leading to wheelchair dependence in some individuals. Later symptoms may also include ataxia, incoordination, intention tremor, dysarthria, mood disorders, and mild cognitive

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decline.

*CSTB*-related PME is caused by disease-causing variants in the *CSTB* gene. An expansion of a dodecamer repeat sequence in the promoter region of the *CSTB* gene accounts for approximately 90% of disease-causing variants (99% in Finnish individuals). Full penetrance *CSTB* expansions are greater than or equal to 30 repeats, while normal alleles are typically 2 or 3 repeats. Allele sizes between 5 and 29 repeats are of unclear significance. The remainder of disease-causing variants are sequence variants including missense, nonsense, splice site variants, and small deletions and duplications.

Genotype/phenotype correlation suggests that individuals who are homozygous for nonexpansion variants or compound heterozygous for one expansion allele and one nonexpansion allele have earlier onset and more severe symptoms than those individuals with biallelic expansion alleles. Instability of the repeat expansion has been reported with vertical transmission, including both minimal expansion and contraction of repeat sizes. Alleles in the uncertain range are not associated with symptoms of *CSTB*-related PME but may demonstrate instability with transmission. Since repeat alleles in this size range have rarely been reported, the risk of repeat expansion into the full penetrance allele range (>29 repeats) is not fully understood. Additionally, correlation of repeat size with onset of symptoms is unclear.

### Reference Values

Normal: <5 dodecamer repeats

Repeat Size of Uncertain Significance: 5-29 dodecamer repeats

Full Penetrance Expansion: >29 dodecamer repeats

An interpretive report will be provided.

### Interpretation

An interpretive report will be provided.

### Cautions

For predictive testing, it is important to first document the molecular etiology of disease in an affected family member to confirm that a *CSTB* repeat expansion is the underlying mechanism of disease in the family. Specifically, this assay will not detect nonrepeat expansion variants and progressive myoclonic epilepsy may be caused by variants in other genes.

It is recommended that patients undergoing predictive testing receive genetic counseling both prior to testing and after results are available.

Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Errors in test interpretation may occur if the provided information is inaccurate or incomplete.

Rare variants (ie, polymorphisms) exist which could lead to false-negative results.

Bone marrow transplants from allogenic donors will interfere with testing. Call Mayo Clinic Laboratories for instructions for testing patients who have received a bone marrow transplant.

### Clinical Reference

1. Lehesjoki AE, Koskimiemi M: Progressive myoclonus epilepsy of Unverricht-Lundborg type. *Epilepsia*. 1999;40 Suppl 3:23-28
2. Hypponen J, Aikia M, Joensuu T, et al: Refining the phenotype of Unverricht-Lundborg disease (EPM1): a population-wide Finnish study. *Neurology*. 2015 Apr 14;84(15):1529-1536

3. Canafoglia L, Gennaro E, Capovilla G, et al: Electroclinical presentation and genotype-phenotype relationships in patients with Unverricht-Lundborg disease carrying compound heterozygous CSTB point and indel mutations. *Epilepsia*. 2012 Dec;53(12):2120-2127

## Performance

### Method Description

A combined amplicon-length and repeat-primed polymerase chain reaction-based assay is utilized to detect expansions of a dodecamer repeat region in the *CSTB* gene.(Unpublished Mayo method)

### PDF Report

No

### Day(s) Performed

Varies

### Report Available

28 to 42 days

### Specimen Retention Time

Whole blood: 2 weeks (if available); Extracted DNA: 3 months

### Performing Laboratory Location

Rochester

## Fees & Codes

### Fees

- Authorized users can sign in to [Test Prices](#) for detailed fee information.
- Clients without access to Test Prices can contact [Customer Service](#) 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact [Customer Service](#).

### Test Classification

This test was developed, and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

### CPT Code Information

81188

### LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
CSTB	CSTB, Repeat Expansion Analysis	41110-8

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Result ID	Test Result Name	Result LOINC® Value
616516	Result Summary	50397-9
616517	Result	82939-0
616518	Interpretation	69047-9
616519	Reason for Referral	42349-1
616520	Specimen	31208-2
616521	Method	85069-3
616522	Source	31208-2
616523	Released By	18771-6