MAYO CLINIC LABORATORIES

Test Definition: CSTB

CSTB Gene, Repeat Expansion Analysis, Varies

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)

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
CULFB	Fibroblast Culture for Genetic Test	Yes	No
CULAF	Amniotic Fluid Culture/Genetic Test	Yes	No
_STR1	Comp Analysis using STR (Bill only)	No, (Bill only)	No
_STR2	Add'l comp analysis w/STR (Bill Only)	No, (Bill only)	No
MATCC	Maternal Cell Contamination, B	Yes	No

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 cord blood specimens that have an accompanying maternal blood specimen, maternal cell contamination studies will be performed at an additional charge.

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.

Specimen Required

Patient Preparation: A previous hematopoietic stem cell transplant from an allogenic donor will interfere with testing. For information about testing patients who have received a hematopoietic stem cell transplant, call 800-533-1710.

Submit only 1 of the following specimens:

Specimen Type: Whole blood
Container/Tube:
Preferred: Lavender top (EDTA) or yellow top (ACD)
Acceptable: Green top (sodium heparin)
Specimen Volume: 3 mL
Collection Instructions:
1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot**.
3. Whole blood collected postnatal from an umbilical cord is also acceptable. See Additional Information.
Specimen Stability Information: Ambient 4 days (preferred)/Refrigerated 4 days/Frozen 4 days
Additional Information:
1. Specimens are preferred to be received within 4 days of collection. Extraction will be attempted for specimens received after 4 days, and DNA yield will be evaluated to determine if testing may proceed.
2. To ensure minimum volume and concentration of DNA are met, the requested volume must be submitted. Testing may be canceled if DNA requirements are inadequate.
3. For postnatal umbilical cord whole blood specimens, maternal cell contamination studies are recommended to ensure test results reflect that of the patient tested. A maternal blood specimen is required to complete maternal cell contamination studies. Order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on both the cord blood and maternal blood specimens under separate order numbers.

Specimen Type: Extracted DNA
Container/Tube:

Preferred: Screw Cap Micro Tube, 2 mL with skirted conical base
Acceptable: Matrix tube, 1 mL
Collection Instructions:
1. The preferred volume is at least 100 mcL at a concentration of 75 ng/mcL.
2. Include concentration and volume on tube.
Specimen Stability Information: Frozen (preferred) 1 year/Ambient/Refrigerated
Additional Information: DNA must be extracted in a CLIA-certified laboratory or equivalent and must be extracted from a specimen type listed as acceptable for this test (including applicable anticoagulants). Our laboratory has experience with Chemagic, Puregene, Autopure, MagnaPure, and EZ1 extraction platforms and cannot guarantee that all extraction methods are compatible with this test. If testing fails, one repeat will be attempted, and if unsuccessful, the test will be reported as failed and a charge will be applied. If applicable, specific gene regions that were unable to be interrogated due to DNA quality will be noted in the report.

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	Varies		

Clinical & Interpretive

Clinical Information

CSTB-related progressive myoclonus epilepsy (PME), also known as progressive myoclonus epilepsy type 1 (EPM1) or Unverricht-Lundborg disease, is the most common and least severe of the collective progressive myoclonus epilepsies. *CSTB*-related PME is inherited in an autosomal recessive pattern and is associated with inter- and intrafamilial variability.(1) 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 decline.(1-4)

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.(1)

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.(4) Instability of the repeat expansion has been reported with vertical transmission, including both minimal expansion and contraction of repeat sizes.(2) Alleles in the uncertain range are not associated with symptoms of CSTB-related PME but may demonstrate instability with transmission.(1) 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

The interpretive report includes an overview of the findings as well as the associated clinical significance.

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, Kalviainen R. Progressive Myoclonic Epilepsy Type 1. In: Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE, Amemiya A, et al. GeneReviews [Internet]. University of Washington, Seattle; 1993-2025. Updated July 2, 2020. Accessed June 24, 2004
2. Lehesjoki AE, Koskimiemi M. Progressive myoclonus epilepsy of Unverricht-Lundborg type. Epilepsia. 1999;40 Suppl 3:23-28
3. Hypponen J, Aikia M, Joensuu T, et al. Refining the phenotype of Unverricht-Lundborg disease (EPM1): a population-wide Finnish study. Neurology. 2015;84(15):1529-1536
4. 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;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
14 to 28 days

Specimen Retention Time
Whole blood: 28 days (if available); Extracted DNA: 3 months

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

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. It 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