Test Definition: DRPL

Dentatorubral-Pallidoluysian Atrophy (DRPLA)
Gene Analysis, Varies

Overview

Useful For

Confirming the diagnosis of dentatorubral-pallidoluysian atrophy (DRPLA) for symptomatic patients

Predictive testing for individuals with a family history of DRPLA and a documented expansion in the *ATN1* gene in an affected family member

Special Instructions

- Informed Consent for Genetic Testing
- Molecular Genetics: Neurology Patient Information
- Informed Consent for Genetic Testing (Spanish)

Method Name

Polymerase Chain Reaction (PCR)

NY State Available

Yes

Specimen

Specimen Type

Varies

Specimen Required

Specimen Type: Whole blood
Patient Preparation: A previous bone marrow transplant from an allogenic donor will interfere with testing. For instructions for testing patients who have received a bone marrow transplant, call 800-533-1710.
Container/Tube:
Preferred: Lavender top (EDTA) or yellow top (ACD)
Acceptable: None
Specimen Volume: 3 mL
Collection Instructions:
1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot**.
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 is met, the preferred volume of blood must be submitted. Testing may be canceled if DNA requirements are inadequate.

Forms

1. **New York Clients-Informed consent is required.** 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.

Specimen Minimum Volume

See Specimen Required

Reject Due To

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

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

Dentatorubral-pallidoluysian atrophy (DRPLA) is a rare autosomal dominant neurodegenerative disorder characterized by ataxia, choreoathetosis, dementia, and psychiatric disturbance in adults and ataxia, myoclonus, seizures, and progressive intellectual deterioration in children. Characteristic neuropathologic observations include degeneration of the dentatorubral and pallidoluysian systems of the central nervous system.

The prevalence of DRPLA depends on the geographic and ethnic origin of the population being studied. DRPLA was first described in a European individual without a family history of the disorder; however, it is predominantly found as an inherited condition and is most prevalent in Japan (0.2-0.7 per 100,000). Although rare, DRPLA has been identified in other populations, including Europe and North America.

Dentatorubral-pallidoluysian atrophy is caused by an expansion of a CAG trinucleotide repeat in the *ATN1* gene. This trinucleotide repeat is polymorphic in the general population, with the number of repeats ranging from 6 to 35. Affected individuals, have 48 or greater CAG repeats. Repeat sizes between 35 and 47 are associated with incomplete penetrance and a milder clinical phenotype. As with other trinucleotide repeat disorders, anticipation is frequently observed, and larger CAG expansions are associated with earlier onset and a more severe and rapid clinical course. More marked expansion may occur with paternal transmission.

Reference Values

Normal alleles: 7-35 CAG repeats
Abnormal alleles: 49-93 CAG 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 presence of CAG-repeat amplification in the *ATN1* gene in an affected family member to confirm that molecular expansion is the underlying mechanism of disease in the family.

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

Predictive testing of an asymptomatic child is not recommended.

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.

The absence of an expansion in the *ATN1* gene does not eliminate the diagnosis of other inherited neurodegenerative disorders that have overlapping clinical features with dentatorubral-pallidoluysian atrophy, such as Huntington disease or spinocerebellar ataxias.

Supportive Data

Method validation involved comparative studies with other laboratories and testing 50 individuals from the general population (anonymous blood donors) and 48 patients with cerebellar ataxia. In each case, the distribution of observed repeat sizes closely correlated with previously reported values (ie, similar range and frequencies of specific repeat sizes). Sequencing of 2 specimens confirmed accuracy of CAG repeat numbers compared with estimations based on the size of polymerase chain reaction products.

Clinical Reference

1. Ikeuchi T, Onodera O, Oyake M, Koide R, Tanaka H, Tsuji S. Dentatorubral-pallidoluysian atrophy (DRPLA): close correlation of CAG repeat expansions with the wide spectrum of clinical presentations and prominent anticipation. Semin Cell Biol. 1995;6(1):37-44
2. Tsuji S. Dentatorubral-pallidoluysian atrophy: clinical aspects and molecular genetics. Ad Neurol. 2002;89:231-239
3. Carroll LS, Massey TH, Wardle M, Peall KJ. Dentatorubral-pallidoluysian atrophy: An update. Tremor Other Hyperkinet Mov (N Y). 2018;8:577
4. Prades S, Melo de Gusmao C, Grimaldi S, Shiloh-Malawsky Y, Felton T, Houlden H. DRPLA. In: Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE, Amemiya A, eds. GeneReviews [Internet]. University of Washington, Seattle; 1999. Updated September 21, 2023. Accessed November 14, 2024. Available at https://www.ncbi.nlm.nih.gov/books/NBK1491/

Performance

Method Description
A polymerase chain reaction-based assay is used to amplify across the region of the *ATN1* gene containing the CAG repeats. Assay products are separated by capillary electrophoresis and are sized by comparison with an internal size standard.(Dorschner MO, Barden D, Stephens K. Diagnosis of five spinocerebellar ataxia disorders by multiplex amplification and capillary electrophoresis. J Mol Diag. 2002;4(2):108-113)

PDF Report
No

Day(s) Performed
Tuesday

Report Available
14 to 21 days

Specimen Retention Time
Whole blood: 2 weeks (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
81177-ATN1 (ataxin 2) (eg, denatatorubral-pallidolyuysian atrophy) gene analysis, evaluation to detect abnormal (eg, expanded) alleles

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
DRPL	DRPLA Gene Analysis	49631-5

Test Definition: DRPL

Dentatorubral-Pallidoluysian Atrophy (DRPLA)

Gene Analysis, Varies

Result ID	Test Result Name	Result LOINC® Value
53234	Result Summary	50397-9
53235	Result	49631-5
53236	Interpretation	69047-9
53237	Specimen	31208-2
53238	Source	31208-2
53239	Released By	18771-6