MAYO CLINIC LABORATORIES

Test Definition: HAD

Huntington Disease, Molecular Analysis, Varies

Overview

Useful For

Molecular confirmation of clinically suspected cases of Huntington disease (HD)

Presymptomatic testing for individuals with a family history of HD and a documented expansion in the *HTT* gene

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

Necessary Information

Molecular Genetics: Neurology Patient Information or a recent clinical note is required. Testing cannot proceed without this information.

Specimen Required

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.
Specimen Type: Whole blood
Container/Tube: Lavender top (EDTA) or yellow top (ACD)
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. **Molecular Genetics: Neurology Patient Information is required.**

2. 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)
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 by Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

Huntington disease (HD) is an autosomal dominant progressive neurodegenerative disorder associated with progressive involuntary and voluntary motor disturbances (chorea, dystonia, dysarthria, gait disturbance, postural instability, oculomotor dysfunction), cognitive decline leading to dementia, and a wide range of neuropsychiatric problems including apathy, depression, anxiety, and other behavioral disturbances. Onset occurs typically in the late 30's to early 40's, but rare individuals may present with juvenile onset.

Huntington disease is caused by a CAG (cystine, adenine, guanine) repeat expansion in the *HTT* gene and is associated with genetic anticipation, whereby repeat sizes may expand with transmission to subsequent generations. Correlation exists between the size of the CAG repeat and disease onset and severity, with larger alleles associated with earlier onset and more severe disease presentation. Full penetrance *HTT* expansions are greater than 39 repeats, while normal alleles are less than 27 repeats. Allele sizes between 36 and 39 repeats are associated with reduced penetrance of clinical HD symptoms. Intermediate alleles (27-35 repeats) are not typically associated with clinical symptoms; however, both reduced penetrance and intermediate alleles may expand into the full penetrance range with transmission to offspring.

Identification of a disease-associated repeat expansion has important implications for family members. Testing of at-risk individuals is possible, but it is recommended that predictive testing be performed in conjunction with appropriate pre- and post-test counseling. Additionally, presymptomatic testing of minors is strongly discouraged.

Reference Values
Normal alleles: <27 CAG repeats
Intermediate alleles: 27-35 CAG repeats
Reduced penetrance: 36-39 CAG repeats
Full penetrance: >39 CAG repeats
An interpretive report will be provided.

Interpretation
The provided 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 a CAG-repeat amplification in the *HTT* 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 the interpretation of results may occur if the information given is inaccurate or incomplete.

Clinical Reference
1. Bean L, Bayrak-Toydemir P. American College of Medical Genetics and Genomics Standards and Guidelines for Clinical Genetics Laboratories, 2014 edition: technical standards and guidelines for Huntington disease. Genet Med. 2014;16(12):e2. doi:10.1038/gim.2014.146
2. Testa C, Jankovic J. Huntington disease: A quarter century of progress since the gene discovery. J Neurol Sci. 2019:396:52-68. doi:10.1016/j.jns.2018.09.022

Performance

Method Description
A polymerase chain reaction-based assay is utilized to detect expansions of a CAG trinucleotide tract in exon 1 of the *HTT* gene.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Wednesday

Report Available
7 to 11 days upon receipt of sufficient clinical information for testing

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

81271-HTT (huntingtin) (eg, Huntington disease) gene analysis; evaluation to detect abnormal (eg, expanded) alleles

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
HAD	Huntington Disease Analysis	21763-8

Result ID	Test Result Name	Result LOINC® Value
52885	Result Summary	50397-9
52886	Result	53782-9
52887	Interpretation	69047-9
52888	Reason for Referral	42349-1
52889	Specimen	31208-2
52890	Source	31208-2
52891	Released By	18771-6