Test Definition: HEXAZ

HEXA Gene, Full Gene Analysis

Overview

Useful For

Second-tier test for confirming a biochemical diagnosis of Tay-Sachs disease (TSD)

Carrier testing of individuals with a family history of TSD but an affected individual is not available for testing or disease-causing mutations have not been identified

Testing individuals with enzyme activity consistent with carrier status but negative molecular testing by a panel of common mutations

Testing Algorithm

The following algorithms are available in Special Instructions:Â Â Â

-Tay-Sachs Disease Carrier Testing Protocol

-Tay-Sachs and Related Disorders Diagnostic Testing Algorithm

Special Instructions

- Molecular Genetics: Biochemical Disorders Patient Information
- Informed Consent for Genetic Testing
- Tay-Sachs Disease Carrier Testing Protocol
- Tay-Sachs and Related Disorders Diagnostic Testing Algorithm

Method Name

Polymerase Chain Reaction (PCR) Amplification/DNA Sequencing

NY State Available

Yes

Specimen

Specimen Type

Varies

Shipping Instructions

Specimen preferred to arrive within 96 hours of draw.

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 specimen in original tube.

Forms

1. **New York Clients-Informed consent is required.** Please document on the request form or electronic order that a copy is on file. An Informed Consent for Genetic Testing (T576) is available in Special Instructions.

2. Molecular Genetics: Biochemical Disorders Patient Information (T527) in Special Instructions

3. If not ordering electronically, complete, print, and send an Inborn Errors of Metabolism Test Request (T798) with the specimen.

Specimen Minimum Volume

0.5 mL

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 and Interpretive

Clinical Information

Tay-Sachs disease (TSD) is an inherited lysosomal storage disease caused by a deficiency of the enzyme beta-hexosaminidase A. It is characterized by accumulation of GM2 gangliosides in cells of the brain and central nervous system. The *HEXA* gene encodes the alpha subunit of beta-hexosaminidase A and mutations in this gene cause TSD. TSD occurs in approximately 1 in 200,000 live births with a carrier frequency of 1 in 250 to 1 in 300 in the general population. The carrier frequency for this disease in individuals of Ashkenazi Jewish ancestry is 1 in 31.

The classic form of TSD becomes apparent in infancy when mild motor weakness is noted along with impaired visual acuity and the presence of a "startle response." Other manifestations include progressive neurodegeneration, seizures, and blindness, leading to total incapacitation and death. The subacute and adult-onset types of TSD are characterized by later ages of onset and a broad spectrum of disease symptoms and severity.

TSD is inherited in an autosomal recessive manner. Several common mutations in the *HEXA* gene account for 92% of disease-causing mutations in the Ashkenazi Jewish population. Testing for these mutations is available as a panel, TSDP / Tay-Sachs Disease, Mutation Analysis, *HEXA*. In non-Ashkenazi Jewish individuals, the detection rate for the common mutations is significantly decreased. Sequencing of the entire *HEXA* gene detects less common

disease-causing mutations.

The recommended first-tier test for TSD carrier screening and diagnosis in all patients is a biochemical test that measures hexosaminidase A activity in white blood cells, NAGW / Hexosaminidase A and Total Hexosaminidase, Leukocytes.

Reference Values

An interpretive report will be provided.

Interpretation

All detected alterations are evaluated according to American College of Medical Genetics recommendations.(1) Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

Cautions

A small percentage of individuals who are carriers or have a diagnosis of Tay-Sachs disease (TSD) may have a mutation that is not identified by this method (eg, large genomic deletions, promoter mutations). The absence of a mutation(s), therefore, does not eliminate the possibility of positive carrier status or the diagnosis of TSD. For carrier testing, it is important to first document the presence of a *HEXA* gene mutation in an affected family member.

In some cases, DNA alterations of undetermined significance may be identified.

Rare polymorphisms exist that could lead to false-negative or false-positive results. If results obtained do not match the clinical findings, additional testing should be considered.

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

Clinical Reference

1. Richards S, Aziz N, Bale S, et al: Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med 2015 May;17(5):405-424

2. Gravel RA, Kaback MM, Proia RL, et al: The GM2 gangliosidosis. In The Metabolic and Molecular Bases of Inherited Disease. Eigth edition. Edited by CR Scriver, AL Beaudet, WS Sly, et al. New York, McGraw-Hill Book Company, 2001, pp 3827-3876

3. ACOG Committee on Genetics: ACOG Committee Opinion #318; Screening for Tay-Sachs disease. Obstet Gynecol 2005;106(4):893-894

Performance

Method Description

Bidirectional sequence analysis is performed to test for the presence of a mutation in all coding regions and intron/exon boundaries of the beta-hexosaminidase A gene (*HEXA*).(Unpublished Mayo method)

PDF Report

No

Day(s) and Time(s) Test Performed

Performed weekly, varies

Analytic Time

14 days

Maximum Laboratory Time

20 days

Specimen Retention Time

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

Performing Laboratory Location

Rochester

Fees and 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 Regional Manager. 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 U.S. Food and Drug Administration.

CPT Code Information

81406

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
HEXAZ	HEXA Gene, Full Gene Analysis	76033-0

Result ID	Test Result Name	Result LOINC Value
53943	Result Summary	50397-9
53944	Result	82939-0
53945	Interpretation	69047-9
53946	Additional Information	48767-8
53947	Specimen	31208-2
53948	Source	31208-2
53949	Released By	18771-6