MAYO CLINIC LABORATORIES

Test Definition: HSAN1

Hereditary Sensory Neuropathy I, S

Overview

Useful For

Diagnosis of patients with clinical features suggestive of hereditary sensory and autonomic neuropathy, type I caused by variants in *SPTLC1* and *SPTLC2*

Monitoring of patients with hereditary sensory and autonomic neuropathy, type I caused by variants in *SPTLC1* and *SPTLC2*

Genetics Test Information

Deoxysphingolipids (dSL) are elevated in patients with hereditary sensory and autonomic neuropathy type I (HSAN1) due to variants in *SPTLC1* and *SPTLC2*, and measurement of dSL is useful to support a diagnosis of HSAN1.

Elevations in dSL may also be seen in patients with order disorders including type 2 diabetes mellitus, metabolic syndrome, mitochondrial disease, glycogen storage disease type I, and, possibly, disorders of serine biosynthesis.

Additional testing is required to determine the specific cause of elevated dSL.

Special Instructions

- Biochemical Genetics Patient Information

Method Name

Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS)

NY State Available

Yes

Specimen

Specimen Type

Serum

Necessary Information

The following information is required for interpretation of results:

1. Patient's age

2. Reason for testing

3. Diabetic diagnosis

Specimen Required

Patient Preparation: Fasting 8 hours

Collection Container/Tube:

Preferred: Serum gel

Acceptable: Red top

Submission Container/Tube: Plastic vial

Specimen Volume: 1 mL

Forms

1. Biochemical Genetics Patient Information (T602), see Special Instructions

2. If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

Reject Due To

Gross hemolysis	OK
Gross lipemia	Reject
Gross icterus	OK

Specimen Minimum Volume

0.5 mL

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Frozen (preferred)	90 days	
	Refrigerated		

Clinical & Interpretive

Clinical Information

Sphingolipids, a class of lipids derived from sphingosine, are essential components of plasma membranes and lipoproteins. They are synthesized from L-serine and palmitoyl-CoA by the enzyme serine palmitoyltransferase. Deoxysphingolipids (dSL) are atypical sphingolipids derived from the amino acids alanine or glycine instead of L-serine and cannot be degraded by normal catabolic pathways. Pathologically elevated dSL have been identified as potential biomarkers in a variety of conditions such as hereditary sensory and autonomic neuropathy type 1 (HSAN1), type 2 diabetes mellitus, metabolic syndrome, mitochondrial disease, glycogen storage disease type 1, and possibly disorders of serine biosynthesis.

Hereditary sensory and autonomic neuropathies are a group of clinically and genetically heterogeneous peripheral neuropathies. HSAN1 is inherited in an autosomal dominant fashion and is typically characterized by a later onset loss of pain and temperature sensation in the hands and feet, which can be accompanied by shooting pain attacks, lancinating pain, and skin ulcers predominantly affecting the lower limbs.

While variants in 5 different genes (*SPTLC1, SPTLC2, ATL1, RAB7A* and *DNMT1*) have been linked to HSAN1, the majority of variants are in *SPTLC1* and *SPTLC2,* which encode 2 of 3 subunits of the serine palmitoyltransferase (SPT) enzyme. Variants in these 2 genes lead to a shift in SPT substrate specificity from L-serine to L-alanine, which ultimately produces 2 neurotoxic deoxysphingolipids, 1-deoxymethylsphinganine and 1-deoxysphinganine. The accumulation of these metabolites in the cells and serum of affected patients is thought to cause the clinical features associated with HSAN1. A recent clinical trial found that L-serine supplementation safely reduced levels of 1-deoxysphingolipids in humans and suggested that supplementation may offer a clinical benefit.(1)

Reference Values

Sphinganine: < or =18.0 ng/mL

1-deoxysphinganine: < or =0.25 ng/mL

1-deoxymethylsphinganine: < or =0.04 ng/mL

Sphingosine: < or =80.0 ng/mL

1-deoxysphingosine: < or =0.05 ng/mL

1-deoxymethylsphingosine: < or =0.09 ng/mL

Interpretation

Elevation of deoxysphingolipids may indicate hereditary sensory and autonomic neuropathy, type I caused by variants in *SPTLC1* and *SPTLC2*.

Deoxysphingolipids may also be elevated in patients with other conditions such as type 2 diabetes mellitus, metabolic syndrome, mitochondrial disorders, glycogen storage disease type 1, and possibly disorders of serine biosynthesis.

Cautions

This assay is not intended to but may detect neuropathies other than hereditary sensory and autonomic neuropathy, type I.

Clinical Reference

1. Fridman V, Suriyanarayanan S, Novak P, et al: Randomized trial of l-serine in patients with hereditary sensory and autonomic neuropathy type 1. Neurology. 2019 Jan 22;92(4):e359-e370. doi: 10.1212/WNL.0000000000006811

2. Astudillo L, Sabourdy F, Therville N, et al: Human genetic disorders of sphingolipid biosynthesis. J Inherit Metab Dis. 2015 Jan;38(1):65-76

3. Gable K, Gupta SD, Han G, Niranjanakumari S, Harmon JM, Dunn TM: A disease-causing mutation in the active site of serine palmitoyltransferase causes catalytic promiscuity. J Biol Chem. 2010 Jul 23;285(30):22846-22852

4. Penno AK, Reilly MM, Houlden H, et al: Hereditary sensory neuropathy type I is caused by the accumulation of two neurotoxic sphingolipids. J Biol Chem. 2010 Apr 9;285(15):11178-11187

5. Lone MA, Santos T, Alecu I, Silva LC, Hornemann T: 1-Deoxysphingolipids. 2019 Apr;1864(4):512-521. doi: 10.1016/j.bbalip.2018.12.013

6. Ferreira CR, Goorden SMI, Soldatos A, et al: Deoxysphingolipid precursors indicate abnormal sphingolipid metabolism in individuals with primary and secondary disturbances of serine availability. Mol Genet Metab. 2018 Jul;124(3):204-209. doi: 10.1016/j.ymgme.2018.05.001

Performance

Method Description

Internal standard is added to the serum. Sphingolipids and deoxysphingolipids are extracted from the serum prior to injection onto a liquid chromatography-tandem mass spectrometry (LC-MS/MS) system. Following chromatographic isolation, the concentration is measured by MS/MS analysis in the selected reaction monitoring positive mode. The ratio of extracted peak area to internal standard is utilized to calculate the concentration of sphingolipid and deoxysphingolipid species in the sample.(Unpublished Mayo method)

PDF Report

No

Specimen Retention Time

1 month

Performing Laboratory Location

Rochester

Fees & Codes

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

82542

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
HSAN1	Hereditary Sensory Neuropathy I, S	In Process

Result ID	Reporting Name	LOINC®
BG718	Reason for Referral	42349-1
BG719	Diabetic diagnosis	In Process
605993	1-deoxysphinganine	In Process
605996	1-deoxysphingosine	In Process
605994	1-deoxymethylsphinganine	In Process
605997	1-deoxymethylsphingosine	In Process
605992	Sphinganine	In Process
605995	Sphingosine	In Process
605998	Interpretation (HSAN1)	59462-2
605991	Reviewed By	18771-6