Test Definition: NPABZ
Niemann-Pick A-B Full Gene Analysis

Overview

Useful For
Confirmation of a diagnosis of Niemann-Pick disease type A or B

Carrier screening in cases where there is a family history of Niemann-Pick disease type A or B, but disease-causing variants have not been identified in an affected individual

Genetics Test Information
Testing includes full gene sequencing of the SMPD1 gene.

Reflex Tests

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Reporting Name</th>
<th>Available Separately</th>
<th>Always Performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>FIBR</td>
<td>Fibroblast Culture</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>CRYOB</td>
<td>Cryopreserve for Biochem Studies</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

Testing Algorithm
If a skin biopsy is received, fibroblast culture and cryopreservation for biochemical studies will be performed at an additional charge.

See Newborn Screen Follow-up for Niemann Pick Type A and B in Special Instructions.

For more information, see Newborn Screening Act Sheet Niemann-Pick A/B Disease: Decreased Acid Sphingomyelinase in Special Instructions.

Special Instructions
- Molecular Genetics: Biochemical Disorders Patient Information
- Informed Consent for Genetic Testing
- Blood Spot Collection Card-Spanish Instructions
- Newborn Screening Act Sheet Niemann-Pick A/B Disease: Decreased Acid Sphingomyelinase
- Newborn Screen Follow-up for Niemann Pick Type A and B
- Blood Spot Collection Card-Chinese Instructions
- Informed Consent for Genetic Testing (Spanish)
- Blood Spot Collection Instructions

Method Name
Polymerase Chain Reaction (PCR) followed by DNA Sequencing

NY State Available
Yes

Specimen
**Specimen Type**

Varies

**Advisory Information**

Both ASMW / Acid Sphingomyelinase, Leukocytes and OXNP / Oxysterols, Plasma should be performed prior to targeted variant or full gene analyses.

**Shipping Instructions**

Specimen preferred to arrive within 96 hours of collection.

**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.

Submit only 1 of the following specimens:

**Preferred**

**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.

**Specimen Stability Information:** Ambient (preferred)/Refrigerated/Frozen

**Specimen Type:** Cultured fibroblasts

**Container/Tube:** T-75 or T-25 flask

**Specimen Volume:** 1 Full T-75 or 2 full T-25 flasks

**Specimen Stability Information:** Ambient (preferred)/Refrigerated <24 hours

**Specimen Type:** Skin biopsy
**Test Definition: NPABZ**
Niemann-Pick A-B Full Gene Analysis

**Supplies:** Fibroblast Biopsy Transport Media (T115)

**Container/Tube:** Sterile container with any standard cell culture media (eg, minimal essential media, RPMI 1640). The solution should be supplemented with 1% penicillin and streptomycin.

**Specimen Volume:** 4-mm punch

**Specimen Stability Information:** Refrigerated (preferred)/Ambient

**Specimen Type:** Blood spot

**Supplies:** Card-Blood Spot Collection (Filter Paper) (T493)

**Container/Tube:**

**Preferred:** Collection card (Whatman Protein Saver 903 Paper)

**Acceptable:** Ahlstrom 226 filter paper, or Blood Spot Collection Card

**Specimen Volume:** 2 to 5 Blood Spots on collection card

**Collection Instructions:**

1. An alternative blood collection option for a patient older than 1 year of age is finger stick.

2. Let blood dry on the filter paper at ambient temperature in a horizontal position for 3 hours.

3. Do not expose specimen to heat or direct sunlight.

4. Do not stack wet specimens.

5. Keep specimen dry

**Specimen Stability Information:** Ambient (preferred)/Refrigerated

**Additional Information:**

1. For collection instructions, see Blood Spot Collection Instructions in Special Instructions.

2. For collection instructions in Spanish, see Blood Spot Collection Card-Spanish Instructions (T777) in Special Instructions.

3. For collection instructions in Chinese, see Blood Spot Collection Card-Chinese Instructions (T800) in Special Instructions.

**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 in Special Instructions:

   - Informed Consent for Genetic Testing (T576)
Test Definition: NPABZ
Niemann-Pick A-B Full Gene Analysis

-Informed Consent for Genetic Testing-Spanish (T826)

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
Blood: 1 mL
Blood Spots: 5 punches-3 mm diameter

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

Specimen Stability Information

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varies</td>
<td>Varies</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Clinical and Interpretive

Clinical Information
Niemann-Pick disease (types A and B) is an autosomal recessive lysosomal storage disease caused by a deficiency of the enzyme acid sphingomyelinase. The clinical presentation of type A disease is characterized by jaundice, progressive loss of motor skills, feeding difficulties, learning disabilities, and hepatosplenomegaly. Death usually occurs by age 3. Type B disease is generally milder, though variable in its clinical presentation. Most type B patients do not have neurologic involvement and survive to adulthood.

Variants in the SMPD1 gene are responsible for the clinical manifestations of Niemann-Pick disease types A and B. Although this disease is panethnic, it has a significantly higher frequency in individuals of Ashkenazi Jewish and Northern African descent. The carrier rate for type A in the Ashkenazi Jewish population is 1 in 90 individuals. There are 3 common variants in the Ashkenazi Jewish population: L302P, R496L, and fsP330, which account for approximately 97% of variant alleles in this population. The deltaR608 alteration accounts for approximately 90% of the type B variant alleles in individuals from the Maghreb region of North Africa and 100% of the variant alleles in Gran Canaria Island.

For diagnostic testing, analysis of the acid sphingomyelinase enzyme (ASMW / Acid Sphingomyelinase, Leukocytes) and OXNP / Oxysterols, Plasma should be performed prior to targeted mutation analysis or full gene analysis.

Reference Values
An interpretive report will be provided.

Interpretation
All detected alterations are evaluated according to American College of Medical Genetics and Genomics (ACMG) 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 Niemann-Pick disease type A or B may have a variant that is not identified by this method (eg, large genomic deletions, promoter alterations). The absence of a variant, therefore, does not eliminate the possibility of positive carrier status or the diagnosis of Niemann-Pick disease type A or B.

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

Performance

Method Description
Bidirectional sequence analysis is performed to test for the presence of variants in all coding regions and intron/exon boundaries of the SMPD1 gene.(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
Test Definition: NPABZ
Niemann-Pick A-B Full Gene Analysis

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
81479-Unlisted molecular pathology procedure
88233-Tissue culture, skin or solid tissue biopsy (if appropriate)
88240-Cryopreservation (if appropriate)

LOINC® Information

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Test Order Name</th>
<th>Order LOINC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NPABZ</td>
<td>Niemann-Pick A-B Full Gene Analysis</td>
<td>34518-1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Result ID</th>
<th>Test Result Name</th>
<th>Result LOINC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>53093</td>
<td>Result Summary</td>
<td>50397-9</td>
</tr>
<tr>
<td>53094</td>
<td>Result</td>
<td>82939-0</td>
</tr>
<tr>
<td>53095</td>
<td>Interpretation</td>
<td>69047-9</td>
</tr>
<tr>
<td>53096</td>
<td>Additional Information</td>
<td>48767-8</td>
</tr>
<tr>
<td>53097</td>
<td>Specimen</td>
<td>31208-2</td>
</tr>
<tr>
<td>53098</td>
<td>Source</td>
<td>31208-2</td>
</tr>
<tr>
<td>53099</td>
<td>Released By</td>
<td>18771-6</td>
</tr>
</tbody>
</table>