Overview

Useful For

Diagnosis of Niemann-Pick disease type C

This test is **not useful** for Niemann-Pick disease type C carrier detection.

Genetics Test Information

This is a diagnostic test for Niemann-Pick type C.

Additional Tests

Test ID	Reporting Name	Available Separately	Always Performed
FIBR	Fibroblast Culture	Yes	Yes
CRYOB	Cryopreserve for Biochem Studies	No	Yes

Testing Algorithm

When this test is ordered, a fibroblast culture and cryopreservation for biochemical studies will always be performed at an additional charge. However, for multiple lysosomal enzyme assays on a patient utilizing fibroblast culture, only 1 culture is required regardless of the number of enzyme assays ordered. If viable cells are not obtained within 10 days, client will be notified.

Special Instructions

- Informed Consent for Genetic Testing
- Biochemical Genetics Patient Information
- Informed Consent for Genetic Testing (Spanish)

Method Name

NIEM: Radiolabeled Lipid Extraction Using Thin Layer Chromatography

CRYOB: Fibroblast Subculture Followed by Cryopreservation and Storage

NY State Available

Yes

Specimen

Specimen Type

Tissue

Ordering Guidance

This test is recommended only after appropriate analyte testing of oxysterols:Â see OXNP / Oxysterols, Plasma; OXYBS / Oxysterols, Blood Spot; or OXYWB / Oxysterols, Blood for more information.

Specimen Required

Submit only 1 of the following specimens:

Specimen Type: Cultured fibroblasts

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

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

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

Specimen Type: Skin biopsy

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. Tubes can be supplied upon request (Eagle's minimum essential medium with 1% penicillin and streptomycin).

Specimen Volume: 4-mm punch

Specimen Stability Information: Refrigerated (preferred)/Ambient

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)

-Informed Consent for Genetic Testing-Spanish (T826)

2. Biochemical Genetics Patient Information (T602) in Special Instructions

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

Reject Due To

Tissue	Specimen in formalin or fixative preservative

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Tissue	Varies		

Clinical and Interpretive

Clinical Information

Niemann-Pick disease type C (NPC) is an autosomal recessive lipid storage disorder resulting from mutations in

either the *NPC1* (95% of cases) or *NPC2* genes. Impaired cellular cholesterol trafficking results in progressive accumulation of unesterified cholesterol in late endosomes/lysosomes. NPC has a variable age of onset (range: perinatal period to adulthood) and a highly variable clinical presentation. Most individuals are diagnosed during childhood with symptoms that include ataxia, vertical supranuclear gaze palsy, dystonia, progressive speech deterioration, and seizures. Infants may present with or without hepatosplenomegaly and respiratory failure. Those without liver and pulmonary disease may present with hypotonia and developmental delay. Adult-onset NPC is associated with a slower progression and is characterized by psychiatric illness, ataxia, dystonia, and speech difficulties. The incidence of NPC is approximately 1 in 120,000 to 150,000 live births.

Measurement of oxysterols (products of cholesterol oxidation) are an effective, quick, and less invasive option for screening in an individual with suspected NPC (see OXNP / Oxysterols, Plasma; OXYBS / Oxysterols, Blood Spot; OXYWB / Oxysterols, Blood). Elevated levels of cholestane-3-beta, 5-alpha, 6-beta-triol (COT), lyso-sphingomyelin 509 (LSM 509), and 7-ketocholesterol (7-KC) may be seen; however, individuals with cholestasis may also present with this finding. Molecular testing of *NPC1* and *NPC2* (see NPCZ / Niemann-Pick Type C Disease, Full Gene Analysis) is helpful for disease confirmation, but may reveal variants of unknown significance, heterozygosity or absence of mutations in a patient with presumed NPC. Demonstration of impaired cholesterol esterification and positive filipin staining in cultured fibroblasts can be used to assess the functional significance of *NPC1* or *NPC2* variants and is helpful for disease confirmation in cases with a high clinical suspicion of NPC with ambiguous oxysterol results or cases where molecular testing is not informative.

Reference Values

If the results indicate that the patient's cultured fibroblasts esterify cholesterol at a level that is <10% of normal cultured fibroblasts and when filipin staining shows excessive storage of free cholesterol, it will be stated that the patient is positive for Niemann-Pick type C disease. All samples will be stained by filipin to see if a milder biochemical phenotype is the likely cause of the Niemann-Pick disease-like clinical picture.

Interpretation

Values expected in Niemann-Pick disease type C are below 10% of that found in normal cultured fibroblasts.

Values between 10% and 80% of normal will have to be judged on other diagnostic criteria.

All values will be followed up by filipin staining for cholesterol.

Cautions

No significant cautionary statements

Clinical Reference

1. Patterson MC, Vanier MT, Suzuki K, et al: Niemann-Pick Disease Type C: A Lipid Trafficking Disorder. In The Online Metabolic and Molecular Bases of Inherited Disease. Edited by D Valle, AL Beaudet, B Vogelstein, et al. New York, McGraw-Hill. Accessed March 19, 2019. Available at http://ommbid.mhmedical.com/content.aspx?bookid=971&sectionid=62643647

2. Patterson M: Niemann-Pick Disease Type C. Updated 29 Aug 2019 In GeneReviews Edited by MP Adam, HH Ardinger, RA Pagon, et al. University of Washington, Seattle. Accessed March 19, 2019. Available at https://www.ncbi.nlm.nih.gov/books/NBK1296/

3. Patterson MC, Clayton P, Gissen P, et al: Recommendations for the detection and diagnosis of Niemann-Pick disease type C: An update. Neurol Clin Pract 2017;7(6):499-511

4. Bauer P, Balding DJ, Klunemann HH, et al: Genetic screening for Niemann-Pick disease type C in adults with neurological and psychiatric symptoms: findings from the ZOOM study. Hum Mol Gen 2013;22(21):4349-4356

5. Patterson MC, Mengel E, Wijburg FA, et al: Disease and patient characteristics in NP-C patients: findings from an international disease registry. Orphanet J Rare Dis 2013;8:12

Performance

Method Description

The formation of (3)H-cholesterol oleate is measured against cells that are fed only (3)H-oleic acid without low-density lipoprotein. The formed (3)H-cholesterol oleate is separated from (3)H-oleic acid and its other esterified forms by thin-layer chromatography (TLC). The areas on the TLC plates corresponding to the cholesterol oleate markers are then scraped and counted on a liquid scintillation counter. Lowry proteins are done on the cell pellet to normalize the assay roughly to cell numbers. Filipin staining for cholesterol is performed on all specimens with low values.(Kruth HS, Comly ME, Butler JD, et al: Type C Niemann-Pick disease: abnormal metabolism of low density lipoprotein in homozygous and heterozygous fibroblasts. J Biol Chem 1986;261:16769-16774; Pentchev PG, Kruth HS, Comley ME, et al: Type C Niemann-Pick disease: a parallel loss of regulatory responses in both the uptake and esterification of low density lipoprotein-derived cholesterol in cultured fibroblasts. J Biol Chem 1986;261:16775-16780; Cowan T, Pasquali M: Laboratory Investigations of Inborn Errors of Metabolism. In Pediatric Endocrinology and Inborn Errors of Metabolism. Second Edition. Edited by K Sarafoglou, GF Hoffman, KS Roth. 2017 pp 1139-1158)

PDF Report

No

Day(s) Performed

Varies

Report Available

70 to 80 days

Specimen Retention Time

3 years - Check with the lab for availability

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

82658-Niemann-Pick type C detection

88233-Fibroblast culture

88240-Cryopreservation for biochemical studies

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
NIEM	Niemann-Pick Type C, Fibro	In Process

Result ID	Test Result Name	Result LOINC Value
30173	Cholesterol Esterification	In Process
29746	Interpretation (NIEM)	59462-2
29748	Reviewed By	18771-6