Test Definition: LSDS

Lysosomal Disorders Screen, Random, Urine

Overview

Useful For

Screening patients suspected of having a lysosomal disorder

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
CTS02	Ceramide Trihex and Sulfatide, U	Yes, (Order CTSU)	Yes
MPS02	Mucopolysaccharides Quant, U	Yes, (Order MPSQU)	Yes
OLI02	Oligosaccharide Screen, U	Yes, (Order OLIGU)	Yes
SAU02	Sialic Acid, Free and Total, U	Yes, (Order SAU)	Yes
BG721	Lysosomal Disorders Interpretation	No	Yes

Genetics Test Information

This is a general urine screening test for a broad array of lysosomal and related disorders (LD). Not all LD are detectable by this method.

Testing Algorithm

For information see:

-Lysosomal Disorders Diagnostic Algorithm, Part 1

-Lysosomal Disorders Diagnostic Algorithm, Part 2

-Lysosomal Disorders Screen Interpretive Algorithm

-Epilepsy: Unexplained Refractory and/or Familial Testing Algorithm

Special Instructions

- Fabry Disease Diagnostic Testing Algorithm
- Biochemical Genetics Patient Information
- Epilepsy: Unexplained Refractory and/or Familial Testing Algorithm
- Lysosomal Disorders Diagnostic Algorithm, Part 2
- Lysosomal Disorders Diagnostic Algorithm, Part 1
- Lysosomal Disorders Screen Interpretive Algorithm

Highlights

The first step in a diagnostic workup of an individual suspected of having a lysosomal disorder (LD) includes urine analyses for metabolites associated with mucopolysaccharidoses, oligosaccharidases, disorders of sulfatide degradation, and LDs with characteristic urine profiles.

This test contains a combined analysis of ceramide trihexosides, mucopolysaccharides, oligosaccharides, sulfatides, and

total and free sialic acid. The combined analysis of these disease-specific markers allows for the identification of disorders that may not be detected using any of the single tests alone.

Method Name

CTS02, OLI02: Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry (MALDI-TOF MS)
MPS02, SAU02: Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS)
BG721: Medical Interpretation

NY State Available

Yes

Specimen

Specimen Type

Urine

Ordering Guidance

This test is the recommended screening test for the initial workup of a suspected lysosomal disorder (LD) when the patient's clinical features are not suggestive of any specific LD.

Necessary Information

1. Patient's age is required.
2. Biochemical Genetics Patient Information (T602) is recommended. This information aids in providing a more thorough interpretation of results. Send information with specimen.

Specimen Required

Patient Preparation:
1. Do not administer low-molecular weight heparin before specimen collection.
2. Baby wipes or wipes containing soaps or lotions should **not** be used before specimen collection because these may interfere with results.
Supplies: Urine Container, 60 mL (T313)
Container/Tube: Clean, plastic urine container with no metal cap or glued insert
Specimen Volume: 12 mL
Pediatric Volume: 3.5 mL
Collection Instructions:
1. Collect a random urine specimen **(early morning preferred)**.
2. No preservative.

Forms

1. Biochemical Genetics Patient Information (T602)
2. If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

Specimen Minimum Volume

3.5 mL

Reject Due To

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

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Urine	Refrigerated (preferred)	15 days	
	Frozen	90 days	

Clinical & Interpretive

Clinical Information

Lysosomal disorders (LD) are a diverse group of inherited diseases characterized by the intracellular accumulation of macromolecules leading to cell damage and organ dysfunction. Approximately 50 LD have been described with a wide phenotypic spectrum and ranging in severity from neonatal lethal to later onset variants.

Although classification is not always straightforward, LD are generally categorized according to the type of storage material that accumulates in the cells and tissues. Major categories include mucopolysaccharidoses, oligosaccharidoses, mucolipidoses, and sphingolipidoses. In many cases, accumulating analytes can be detected in urine. Screening for these disorders typically begins with an analysis to detect disease-specific metabolite patterns or profiles indicative of a LD. The combined analysis of disease-specific markers for LD in multiple tests can allow for the identification of additional disorders that may not be characterized using any of the single tests alone.

Disorders detectable by this approach include the oligosaccharidoses: alpha-mannosidosis, aspartylglucosaminuria, beta-mannosidosis, fucosidosis, Schindler disease, and sialidosis; the sphingolipidoses: GM1 gangliosidosis, Sandhoff disease, galactosialidosis, saposin B deficiency, metachromatic leukodystrophy, multiple sulfatase deficiency, Fabry disease, and Gaucher disease; the mucopolysaccharidoses (MPS) excluding MPS IX (hyaluronidase deficiency); the glycogen storage disorder Pompe disease, free sialic storage disorder, and the mucolipidoses types II and III. Additionally, other disorders such as congenital disorder of glycosylation (CDG) type IIb and deglycosylation disorders such as NGLY1-CDG may also be detected.

The MPS are a subset of lysosomal disorders caused by the deficiency of any one of the enzymes involved in the stepwise degradation of dermatan sulfate, heparan sulfate, keratan sulfate, and/or chondroitin sulfate (glycosaminoglycans: GAG). Undegraded or partially degraded GAG (also called mucopolysaccharides) are stored in lysosomes and excreted in the urine. Accumulation of GAG in lysosomes interferes with normal functioning of cells, tissues, and organs resulting in the clinical features observed in MPS disorders. There are 11 known enzyme deficiencies that result in MPS. In addition, abnormal GAG storage is observed in multiple sulfatase deficiency and in I-cell disease. Finally, an abnormal excretion of GAG in urine is observed occasionally in other disorders including active bone diseases, connective tissue disease, hypothyroidism, urinary dysfunction, and oligosaccharidoses.

The oligosaccharidoses are a subset of lysosomal disorders caused by the deficiency of any one of the lysosomal enzymes involved in the degradation of complex oligosaccharide chains. They are characterized by the abnormal

accumulation of incompletely degraded oligosaccharides in cells and tissues and the corresponding increase of related free oligosaccharides in the urine. Clinical features can include bone abnormalities, coarse facial features, corneal cloudiness, organomegaly, muscle weakness, hypotonia, developmental delay, and ataxia. Age of onset ranges from early infancy to adult and can even present prenatally.

The sphingolipidoses are a subset of lysosomal disorders caused by a defect in any one of the enzymes that degrade complex ceramide containing lipids. They are characterized by the excessive accumulation of sphingolipids in the tissues, particularly in the central nervous system, resulting in progressive neurodegeneration and developmental regression. In 2 conditions, Fabry disease and Gaucher disease type I, there is only systemic involvement. In many cases, sphingolipidoses can be detected by through oligosaccharide analysis in urine.

Sialic acid (SA), or N-acetyl-neuraminic acid, is a component of carbohydrates, glycoproteins, and gangliosides, which are important for the human nervous system. SA can be measured in urine as free sialic acid or in a conjugated form bound to oligosaccharides. Sialic acid disorders are a subset of lysosomal disorders caused by defective protein transport or enzyme deficiency that result in multisystem organ disease. Analysis of free and total sialic acid and their ratio in urine can detect the following conditions: free sialic acid storage disorder, sialuria, N-acetylneuraminate pyruvate lyase deficiency, sialidosis, and galactosialidosis.

Because of the similarity of features across disorders and their phenotypic variability, clinical diagnosis of LD can be challenging; therefore, the combined analysis of multiple urine screening tests is an important tool for the initial workup of an individual suspected of having a lysosomal disorder. Abnormal results can be followed up with the appropriate enzyme or molecular analysis.

Reference Values

Dermatan Sulfate:
< or =1.00 mg/mmol creatinine

Heparan Sulfate:
< or =4 years: < or =0.50 mg/mmol creatinine
> or =5 years: < or =0.25 mg/mmol creatinine

Chondroitin-6 Sulfate:
< or =24 months: < or =10.00 mg/mmol creatinine
25 months-10 years: < or =2.50 mg/mmol creatinine
> or =11 years: < or =1.50 mg/mmol creatinine

Keratan Sulfate:
< or =12 months: < or =2.00 mg/mmol creatinine
13-24 months: < or =1.50 mg/mmol creatinine
25 months-4 years: < or =1.00 mg/mmol creatinine
5-18 years: < or =0.50 mg/mmol creatinine
> or =19 years: < or =0.30 mg/mmol creatinine

Free Sialic Acid:
< or =4 weeks: < or =208 mmol/mol creatinine

5 weeks-12 months: < or =104 mmol/mol creatinine
13 months-18 years: < or =100 mmol/mol creatinine
> or =19 years: < or =38 mmol/mol creatinine

Total Sialic Acid:
< or =4 weeks: < or =852 mmol/mol creatinine
5 weeks-12 months: < or =656 mmol/mol creatinine
13 months-18 years: < or =335 mmol/mol creatinine
> or =19 years: < or =262 mmol/mol creatinine

Total/Free Ratio:
< or =4 weeks: 1.94-18.68
5 weeks-12 months: 2.34-13.85
13 months-18 years: 2.63-9.18
> or =19 years: 3.35-15.81

Ceramide Trihexosides:
Negative

Sulfatides:
Negative

Oligosaccharides:
Negative
An interpretive report will be provided.

Interpretation

When abnormal results are detected with characteristic patterns, a detailed interpretation is given, including an overview of the results and their significance, a correlation to available clinical information, elements of differential diagnosis, recommendations for additional biochemical testing, and in vitro confirmatory studies (enzyme assay and molecular test).

Abnormal results are not sufficient to conclusively establish a diagnosis of a particular disease. Specific enzymatic or molecular assays is recommended to confirm positive results.

Cautions

In rare instances, a normal excretion of ceramide trihexosides may be seen in individuals with Fabry disease. If Fabry disease is clinically suspected, see Fabry Disease Testing Algorithm for additional testing recommendations.

Not all lysosomal disorders are detectable through urine screening.

Clinical Reference

1. Lysosomal Disorders. In: Valle DL, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019:part 16. Accessed June 9, 2025. Available at https://ommbid.mhmedical.com/book.aspx?bookID=2709#225069419
2. Pino G, Conboy E, Tortorelli S, et al. Multiplex testing for the screening of lysosomal storage disease in urine:

Sulfatides and glycosaminoglycan profiles in 40 cases of sulfatiduria. Mol Genet Metab. 2020;129(2):106-110. doi:10.1016/j.ymgme.2019.10.009
3. Kingma SDA, Bodamer OA, Wijburg FA. Epidemiology and diagnosis of lysosomal storage disorders; challenges of screening. Best Pract Res Clin Endocrinol Metab. 2015;29(2):145-157. doi:10.1016/j.beem.2014.08.004

Performance

Method Description

Ceramide trihexosides and sulfatides are determined by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) analysis. Urine specimens are centrifuged, and most of the supernatant is discarded from the pellet. Reagent including internal standards is added, and then ceramide trihexosides and sulfatides are extracted. After centrifugation, the bottom layer is spotted onto a MALDI plate, matrix is added and allowed to air dry. The plate is then analyzed using a MALDI TOF/TOF 5800 Analyzer.(Unpublished Mayo method)

Dermatan sulfate (DS), heparan sulfate (HS), keratan sulfate (KS) and chondroitin-6-sulfate (C6S) are enzymatically digested from urine. The reaction mixture is centrifuged and analyzed by liquid chromatography tandem mass spectrometry (LC-MS/MS). The ratio of the extracted peak area of DS, HS, KS and C6S to internal standard as determined by LC-MS/MS is used to calculate the concentration of DS, HS, KS and C6S in the sample.(Unpublished Mayo method)

Oligosaccharides in urine samples are extracted using Oasis HLB and carbograph columns and lyophilized overnight. Oligosaccharides are permethylated, the tubes centrifuged, and the supernatant removed. The supernatant is quenched with water, neutralized with acetic acid, extracted, eluted, and again lyophilized overnight. Specimens are resuspended, mixed 1:1 with a matrix solution, spotted onto a MALDI plate and allowed to air dry. The plate is then analyzed using a MALDI TOF/TOF 5800 Analyzer.(Xia B, Asif G, Arthur L, et al. Oligosaccharide analysis in urine by MALDI-TOF mass spectrometry for the diagnosis of lysosomal storage diseases. Clin Chem 2013;59[9]:1357-1368, Hall PL, Lam C, Alexander JJ. Urine oligosaccharide screening by MALDI-TOF for the identification of NGLY1 deficiency. Mol Genet Metab. 2018;124[1]:82-86)

Sialic acid in urine samples is measured twice to obtain free sialic acid and total sialic acid values. Free sialic acid is dried down and butylated in 3M hydrochloric acid in butanol. Total sialic acid is hydrolyzed with hydrochloric acid and butylated in 3M hydrochloric acid in butanol. Both samples are reconstituted in eluent and analyzed by LC-MS/MS. The free and total sialic acid samples are quantitated using an internal standard calibration curve.(Tebani A, Schlemmer D, Imbard A, et al. Measurement of free and total sialic acid by isotopic dilution liquid chromatography tandem mass spectrometry method. J. Chromatogr. B Analyt Technol Biomed Life Sci. 2011;879[31]:3694-3699, Li J, Wu T, Zhang X, et al. Clinical application of liver diseases diagnosis using ultrahigh-sensitive liquid chromatography-mass spectrometry for sialic acids detection. J. Chromatogr. A. 2022;1666:462837)

PDF Report

No

Day(s) Performed

Varies

Report Available

8 to 14 days

Specimen Retention Time

1 month

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

83789
83864
84377
84275

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
LSDS	Lysosomal Disorders Scrn, U	105125-9

Result ID	Test Result Name	Result LOINC® Value
606773	Lysosomal Disorders Interpretation	94423-1
606772	Reviewed By	18771-6
621077	Dermatan Sulfate	94692-1
621078	Heparan Sulfate	94693-9
621079	Chondroitin-6 Sulfate	94690-5
621080	Keratan Sulfate	92806-9
621074	Free Sialic Acid	In Process
621075	Total Sialic Acid	In Process
621076	Total/Free Sialic Acid Ratio	In Process
621081	Ceramide Trihexosides	34680-9
621082	Sulfatides	34646-0
621083	Oligosaccharides	49284-3