Test Definition: SAU

Sialic Acid, Free and Total, Random, Urine

Overview

Useful For

Screening for sialic acid disorders

Genetics Test Information

This is a screening test to detect patients with sialic acid disorders such as free sialic acid storage disorder, sialidosis and galactosialidosis.

Quantitation of free and total sialic acid and the ratio of these are provided.

Special Instructions

- Biochemical Genetics Patient Information

Method Name

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

NY State Available

Yes

Specimen

Specimen Type

Urine

Ordering Guidance

This is a recommended screening test for patients suspected to have a diagnosis of free sialic acid storage disease. Urine oligosaccharides are also recommended for patients with a suspected diagnosis of sialidosis or galactosialidosis.

Necessary Information

Patient's age is required.

Specimen Required

Supplies: Sarstedt Aliquot Tube, 5mL (T914)
Container/Tube: Plastic, 5-mL tube
Specimen Volume: 1 mL
Pediatric Volume: 0.5 mL
Collection Instructions: Collect a random urine specimen **(early morning preferred).**

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

0.5 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)	90 days	
	Frozen	90 days	

Clinical & Interpretive

Clinical Information

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 (NPL) deficiency, sialidosis, and galactosialidosis.

Free sialic acid storage disorder (FSASD) is a rare lysosomal disorder caused by a defect in sialin, a sialic acid membrane exporter also known as SLC17A5. This defect results in increased stored free sialic acid in the lysosomes. Individuals with FSASD demonstrate the hallmark feature of progressive neurologic issues such as hypotonia, cerebellar ataxia, short stature, and cognitive impairment. Brain imaging may show central hypomyelination, cerebellar atrophy, and thinning of the corpus callosum. Infants and children with more severe disease may also have coarse facial features and organomegaly, such as enlarged liver and heart. A congenital form of the disease has been reported in which patients present with nonimmune hydrops fetalis. Historically, FSASD was divided into several conditions based on early to later age at disease presentation and severity: infantile free sialic acid storage disease, intermediate severe Salla disease, and Salla disease. These conditions are now considered to represent the spectrum of FSASD. There are no approved therapies for FSASD at present. Urine sialic acid analysis will show elevated free sialic acid and a high ratio of total to free sialic acid in individuals with FSASD. FSASD is an autosomal recessive condition caused by disease-causing variants in the *SLC17A5* gene.

There are two additional rare disorders that show elevated free sialic acid: sialuria and N-acetylneuraminate pyruvate lyase (NPL) deficiency. Sialuria is an autosomal recessive disorder caused by disease-causing variants in the *GNE* gene that results in onset of symptoms such as organomegaly and developmental delay in infancy. NPL deficiency is also inherited in an autosomal recessive manner due to disease-causing variants in the *NPL* gene. Individuals with NPL deficiency develop progressive cardiomyopathy and mild skeletal myopathy in childhood. There are no approved therapies for these conditions, so treatment is supportive.

Sialidosis is caused by a deficiency of the neuraminidase enzyme, which results in accumulation of sialyloligosaccharides in lysosomes. Individuals with sialidosis can present with a continuum of clinical features ranging from severe disease (type II) to a milder and more slowly progressive course (type I). These clinical features range from early developmental delay, coarse facial features, short stature, dysostosis multiplex, and hepatosplenomegaly to late onset cherry-red spot myoclonus syndrome. Seizures, hyperreflexia, and ataxia have been reported in more than 50% of later onset patients. A congenital form of the disease has been reported in which patients present with fetal hydrops or neonatal ascites. Urine sialic acid analysis will show a low ratio of total to free sialic acid in individuals with sialidosis, as they have increased excretion of conjugated SA. Analysis of urine oligosaccharides (OLIGU / Oligosaccharide Screen, Random, Urine) is also recommended for patients with a suspected diagnosis of sialidosis. Sialidosis is an autosomal recessive condition caused by disease-causing variants in the *NEU1* gene.

Galactosialidosis also presents with a continuum of clinical features ranging from severe and rapidly progressive disease to a milder and more slowly progressive course; clinical features of the early infantile type include fetal hydrops, edema, ascites, visceromegaly, dysostosis multiplex, coarse facies, and cherry red spot(s) in the retina. Most patients have milder presentations, which include ataxia, myoclonus, angiokeratoma, cognitive and neurologic decline. Urine sialic acid will show a low ratio of total to free sialic acid in individuals with galactosialidosis, as they have increased excretion of conjugated SA. Analysis of urine oligosaccharides is also recommended for patients with a suspected diagnosis of galactosialidosis. Galactosialidosis is an autosomal recessive condition caused by disease-causing variants in the *CTSA* gene.

Patients with an abnormal urine sialic acid result suggestive of any of the sialic acid disorders should have follow up confirmatory testing with the appropriate enzyme or molecular test.

Reference Values

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

An interpretive report will also be provided.

Interpretation

An elevated result of total/free sialic acid ratio may be indicative of sialidosis or galactosialidosis.

A decreased result of total/free sialic acid ratio may be indicative of free sialic acid storage disorder.

Abnormal results or clinical suspicion should be confirmed with biochemical or molecular genetic analysis.

Cautions

Mild elevations of urinary free sialic acid may occur due to other causes, including sepsis, renal disease, hemolytic uremic syndrome and type 2 diabetes mellitus.

Clinical Reference

1.Adams D, Wasserstein M. Free Sialic Acid Storage Disorders. In: Adam MP, Mirzaa GM, Pagon RA, et al, eds. GeneReviews [Internet]. University of Washington, Seattle;1993-2023. Updated January 23, 2020. Accessed June 10, 2025.Available at: www.ncbi.nlm.nih.gov/books/NBK1470/

2. Huizing M, Hackbarth ME, Adams DR, et al. Free sialic acid storage disorder: Progress and promise. Neurosci Lett. 2021;755:135896. doi:10.1016/j.neulet.2021.135896

3. Khan A, Sergi C. Sialidosis: A review of morphology and molecular biology of a rare pediatric disorder. Diagnostics (Basel). 2018;8(2):29. Published 2018 Apr 25. doi:10.3390/diagnostics8020029

4. Annunziata I, d'Azzo A. Galactosialidosis: historic aspects and overview of investigated and emerging treatment options. Expert Opin Orphan Drugs. 2017;5(2):131-141. doi:10.1080/21678707.2016.1266933

Performance

Method Description

Sialic acid is measured twice to give a free sialic acid and a total sialic acid value.

Free sialic acid is measured by drying down a 10 mcL aliquot from a random urine collection, reconstitution in 3M hydrochloric acid (HCl) in butanol to give the respective butyl ester. The butyl-ester sialic acid is reconstituted in eluent and submitted for liquid chromatography tandem mass spectrometry analysis.

Total sialic acid is measured by hydrolyzing a 10 mcL aliquot from a random urine collection with HCl. The hydrolyzed sialic acid is then converted to the respective butyl ester with 3M HCl in butanol. The butyl ester sialic acid is reconstituted in eluent and submitted for liquid chromatography tandem mass spectrometry analysis.

Both free and total sialic acid is quantitated using a commercially available stable isotope labeled internal standard from calibration over a concentration range 2.0 to 2000 mcM.(Tebani A, Schlemmer D, Imbard A, Rigal O, Porquet D, Benoist JF. 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. doi:10.1016/j.jchromb.2011.10.009; Li J, Wu T, Zhang X, Du Y, Wei B, Wang J. Clinical application of liver diseases diagnosis using ultrahigh-sensitive liquid chromatography-mass spectrometry for sialic acids detection. J Chromatogr A. 2022;1666:462837. doi:10.1016/j.chroma.2022.462837)

PDF Report

No

Day(s) Performed
Thursday

Report Available
5 to 11 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
84275

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
SAU	Sialic Acid, Free and Total, U	104657-2

Result ID	Test Result Name	Result LOINC® Value
621069	Free Sialic Acid	104658-0
621070	Total Sialic Acid	104659-8
621071	Total/Free Sialic Acid Ratio	104660-6
621072	Interpretation	94423-1
621073	Reviewed By	18771-6