Test Definition: XALDZ

X-ALD, Full Gene Analysis

Overview

Useful For

Confirming a diagnosis of X-linked adrenoleukodystrophy

Identifying a variant in the *ABCD1* gene

Genetics Test Information

Testing includes full gene sequencing of the *ABCD1* gene.

Reflex Tests

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

Testing Algorithm

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

See Newborn Screen Follow-up for X-Linked Adrenoleukodystrophy in Special Instructions.

For more information, see Newborn Screening Act Sheet X-linked Adrenoleukodystrophy: Increased Very Long Chain Fatty Acids 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 X-linked Adrenoleukodystrophy: Increased Very Long Chain Fatty Acids
- Newborn Screen Follow-up for X-Linked Adrenoleukodystrophy
- 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

The preferred first-tier screening test for X-linked adrenoleukodystrophy is POX / Fatty Acid Profile, Peroxisomal (C22-C26), Serum.

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

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

Supplies: Fibroblast Biopsy Transport Media (T115)

Specimen Type: Skin biopsy

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 (T493)

Specimen Volume:2 to 5 Blood spots on collection card

Collection Instructions:

1. An alternative blood collection option for a patient >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)

-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

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

Clinical and Interpretive

Clinical Information

X-linked adrenoleukodystrophy (X-ALD) is a peroxisomal disease characterized by magnetic resonance imaging (MRI) findings in the white matter, adrenocortical insufficiency, and abnormal plasma concentrations of very long chain fatty acids. The phenotypic expression of X-ALD varies widely. The phenotypes can be subdivided into 3 main categories: childhood cerebral form, adrenomyeloneuropathy (AMN), and Addison disease only. The childhood cerebral form has onset of symptoms between ages 4 and 8, beginning with attention deficit hyperactivity disorder-like symptoms with progressive cognitive, behavior, vision, hearing, and motor deterioration. AMN usually presents in males in their late twenties as progressive paraparesis, sexual dysfunction, sphincter disturbances, and abnormalities in adrenocortical function. The Addison only phenotype typically presents by age 7.5 with adrenocortical insufficiency without significant neurological involvement. Most of these patients eventually develop AMN. Some female carriers may experience mild AMN symptoms with a later age of onset.

The phenotype cannot be predicted by very long chain fatty acids (VLCFA) plasma concentration or by the nature of the genetic variant. The same variant can be associated with each of the known phenotypes. Different phenotypes often occur within a family.

POX / Fatty Acid Profile, Peroxisomal (C22-C26), Serum testing is the preferred first-tier screening method for X-ALD. This is abnormal in 99% of affected males and 85% of carrier females. Sequencing of the *ABCD1* gene is available to confirm the diagnosis of X-ALD, improve carrier detection, and assist with prenatal diagnosis.

Reference Values

An interpretive report will be provided.

Interpretation

All detected alterations are evaluated according to American College of Medical Genetics and Genomics 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 have a diagnosis of X-linked adrenoleukodystrophy (X-ALD) may have a variant that is not identified by this method (eg, large deletions/duplications, promoter alterations, deep intronic alterations). The absence of variants, therefore, does not eliminate the possibility of the diagnosis of X-ALD. For testing asymptomatic individuals it is important to first document the presence of an *ABCD1* gene variant in an affected family member.

In some cases, DNA alterations of undetermined significance may be identified.

Rare alterations 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

1. Richards S, Aziz N, Bale S, et al: Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med. 2015 May;17(5):405-424

2. Moser HW, Mahmood A, Raymond GV: X-linked adrenoleukodystrophy. Nat Clin Pract Neurol. 2007 Mar;3(3):140-151

3. Wang Y, Busin R, Reeves C, et al: X-linked adrenoleukodystrophy: ABCD1 de novo mutations and mosaicism. Mol Genet Metab. 2011 Sep-Oct;104(1-2):160-166

4. Kemp S, Berger J, Aubourg P: X-linked adrenoleukodystrophy: Clinical, metabolic, genetic and pathophysiological aspects. Biochim Biophys Acta. 2012 Sept;1822(9):1465-1474

Performance

Method Description

Bidirectional sequence analysis is performed to test for the presence of a variant in all coding regions and intron/exon boundaries of the *ABCD1* 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

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

81405-*ABCD1* (ATP-binding cassette, sub-family D [ALD] member 1) (eg, adrenoleukodystrophy) full gene sequence

88233-Tissue culture, skin or solid tissue biopsy (if appropriate)

88240-Cryopreservation (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
XALDZ	X-ALD, Full Gene Analysis	95782-9

Result ID	Test Result Name	Result LOINC Value
53561	Result Summary	50397-9
53562	Result	82939-0
53563	Interpretation	69047-9
53564	Additional Information	48767-8
53565	Specimen	31208-2
53566	Source	31208-2
53567	Released By	18771-6