MAYO CLINIC LABORATORIES

Test Definition: ATHAL

Alpha-Globin Gene Analysis, Varies

Overview

Useful For

Diagnosis of alpha-thalassemia

Prenatal diagnosis of deletional alpha-thalassemia

Carrier screening for individuals from high-risk populations for alpha-thalassemia

This test is **not useful for** diagnosis or confirmation of beta-thalassemia or hemoglobinopathies.

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
ATHL	Alpha-Globin Gene Analysis (ATHL)	No	Yes

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
CULAF	Amniotic Fluid Culture/Genetic Test	Yes	No
MATCC	Maternal Cell Contamination, B	Yes	No
CULFB	Fibroblast Culture for Genetic Test	Yes	No
_STR1	Comp Analysis using STR (Bill only)	No, (Bill only)	No
_STR2	Add'l comp analysis w/STR (Bill Only)	No, (Bill only)	No

Genetics Test Information

This test is for genetic deletions and duplications only.

Testing Algorithm

For prenatal specimens only: If amniotic fluid (nonconfluent cultured cells) is received, amniotic fluid culture will be added at an additional charge.

For any prenatal specimen that is received, maternal cell contamination studies will be added.

Special Instructions

- Molecular Genetics: Congenital Inherited Diseases Patient Information
- Informed Consent for Genetic Testing

- Informed Consent for Genetic Testing (Spanish)

Method Name
Dosage Analysis by Polymerase Chain Reaction (PCR)/Multiplex Ligation-Dependent Probe Amplification (MLPA)/Luminex Technology

NY State Available
Yes

Specimen

Specimen Type
Varies

Ordering Guidance
This assay **cannot** be performed on chorionic villus specimens.

Point alterations are **not** detected by this assay. For detection of single point and other nondeletion variants, order WASEQ / Alpha Globin Gene Sequencing, Varies if clinically indicated.

Additional Testing Requirements
All prenatal specimens must be accompanied by a maternal blood specimen; order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on the maternal specimen.

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. For instructions for testing patients who have received a bone marrow transplant, call 800-533-1710

Submit only 1 of the following specimens:

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 whole blood specimen in original tube. **Do not** aliquot.
Specimen Stability Information: Ambient (preferred) 4 days/Refrigerated

Prenatal Specimens
Due to its complexity, consultation with the laboratory is required for all prenatal testing; call 800-533-1710 to speak to a genetic counselor.

Specimen Type: Amniotic fluid
Container/Tube: Amniotic fluid container
Specimen Volume: 20 mL
Specimen Stability Information: Refrigerated (preferred)/Ambient

Acceptable:
Specimen Type: Confluent cultured cells
Container/Tube: T-25 flask
Specimen Volume: 2 Flasks
Collection Instructions: Submit confluent cultured cells from another laboratory.
Specimen Stability Information: Ambient (preferred)/Refrigerated

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: Congenital Inherited Diseases Patient Information (T521)
3.If not ordering electronically, complete, print, and send a Benign Hematology Test Request (T755) with the specimen.

Specimen Minimum Volume

Blood: 1 mL; Amniotic Fluid: 10 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
Varies	Varies		

Clinical & Interpretive

Clinical Information

The thalassemias are a group of inherited conditions characterized by decreased synthesis of one or more of the globin chains, resulting in an imbalance in the relative amounts of the alpha and beta chains. The excess normal chains precipitate in the cell, damaging the membrane and leading to premature red blood cell destruction. Additionally, the defect in hemoglobin synthesis produces a hypochromic, microcytic anemia. The frequency of thalassemia is due to the protective advantage against malaria that it gives carriers. Consequently, thalassemias are prevalent in populations from equatorial regions in the world where malaria is endemic.

Alpha-thalassemia is caused by decreased synthesis of alpha-globin chains. Four alpha-globin genes are normally present (2 on each chromosome 16). One, 2, 3, or 4 alpha-globin genes may be deleted or, less commonly, contain variants. Deletions account for approximately 90% of disease-causing alleles in alpha thalassemia. Phenotypically, these deletions result in 4 categories of disease expression:
-Deletion of 1 alpha-chain: Silent carrier state, with a normal phenotype
-Deletion of 2 alpha-chains: Alpha-thalassemia trait (alpha-1 thalassemia), with mild hematologic changes but no major clinical difficulties
-Deletion of 3 alpha-chains: Hemoglobin H disease, which is extremely variable but usually includes anemia due to hemolysis, jaundice, and hepatosplenomegaly
-Deletion of all 4 alpha-chains: Hemoglobin Bart, with hydrops fetalis and almost invariably in utero demise

Less frequently, alpha-thalassemia results from single point alterations, such as hemoglobin Constant Spring (*HBA2*: c.427T >C). Note: these point alterations are **not** detected by this assay.

Alpha-thalassemia occurs in all ethnic groups but is especially common in individuals of Southeast Asian and African ancestry. It is also frequent in individuals of Mediterranean ancestry. The carrier frequency is estimated to be 1 in 20 for Southeast Asians, 1 in 30 for African Americans, and 1 in 30 to 1 in 50 for individuals of Mediterranean ancestry. Both deletional and nondeletional (caused by point alterations) forms of alpha-thalassemia are found in individuals with Mediterranean ancestry. Deletions in cis (deletions on the same chromosome) are rare in African or Mediterranean populations but are prevalent in Asian populations. Couples in which both partners carry deletions in cis are at risk of having a child with the fatal hemoglobin Bart hydrops fetalis syndrome.

Reference Values

An interpretive report will be provided.

Interpretation

An interpretive report will be provided.

Cautions

Hemoglobin electrophoresis should usually be done prior to this test to exclude other diagnoses or to identify nondeletion types of alpha-thalassemia.

In addition to disease-related probes, the multiplex ligation-dependent probe amplification technique utilizes probes localized to other chromosomal regions as internal controls. In certain circumstances, these control probes may detect other diseases or conditions for which this test was not specifically intended. Results of the control probes are not normally reported. However, in cases where clinically relevant information is identified, the ordering physician will be informed of the result and provided with recommendations for any appropriate follow-up testing.

Rare alterations (ie, polymorphisms) exist that could lead to false-negative or false-positive results. If the 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 the interpretation of results may occur if information given is inaccurate or incomplete.

Clinical Reference

1. Harteveld CL, Voskamp A, Phylipsen M, et al: Nine unknown rearrangements in 16p13.3 and 11p15.4 causing alpha-

and beta-thalassaemia characterized by high resolution multiplex ligation-dependent probe amplification. J Med Genet. 2005 Dec;42(12):922-931. doi: 10.1136/jmg.2005.033597
2. Harteveld CL, Higgs DR: Alpha-thalassemia. Orphanet J Rare Dis. 2010 May;5:13. doi: 10.1186/1750-1172-5-13
3. Bunn HF, Forget BG: Hemoglobin: Molecular, Genetic and Clinical Aspects. 2nd ed. WB Saunders Company; 1986
4. Weatherall DJ, Higgs DR, Clegg JB, Hill AS, Nicholls R: Heterogeneity and origins of the alpha-thalassemias. Birth Defects Origi Artic Ser. 1987;23(5A):3-14

Performance

Method Description

This test is a direct variant analysis assay. Deletions and duplications within the alpha-globin locus are identified by a multiplex ligation-dependent probe amplification assay. Fifteen probes that hybridize throughout the alpha-globin locus from the HS40 promoter region through the 3'HVR region are utilized in order to maximize the information needed to map the approximate location of nearly all DNA deletions that occur. In addition, a polymerase chain reaction-based assay is used to detect the presence of the alpha-3.7 and alpha-4.2 deletions.(Schouten JP, McElgunn CJ, Waaijer R, Zwijnenburg D, Diepvens F, Pals G: Relative quantification of 40 nucleic acid sequences by multiplex ligation-dependent probe amplification. Nucleic Acids Res. 2002 Jun 15;30[12]:e57. doi: 10.1093/nar/gnf056.)

PDF Report

No

Day(s) Performed

Monday, Wednesday

Report Available

9 to 13 days

Specimen Retention Time

Whole Blood: 2 weeks (if available); Extracted DNA: 3 months

Performing Laboratory Location

Rochester

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

81269
88235-Tissue culture for amniotic fluid (if appropriate)
88240-Cryopreservation (if appropriate)
81265-Comparative analysis using Short Tandem Repeat (STR) markers; patient and comparative specimen (eg, pre-transplant recipient and donor germline testing, post-transplant non-hematopoietic recipient germline [eg, buccal swab or other germline tissue sample] and donor testing, twin zygosity testing or maternal cell contamination of fetal cells (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
ATHAL	Alpha-Globin Gene Analysis	90040-7

Result ID	Test Result Name	Result LOINC® Value
52834	Result Summary	50397-9
52835	Result	82939-0
52836	Interpretation	69047-9
54871	Additional Information	48767-8
52837	Specimen	31208-2
52838	Source	31208-2
52839	Method	85069-3
52840	Released By	18771-6