Overview

Useful For
Diagnosis of alpha-thalassemia
Prenatal diagnosis of deletional alpha-thalassemia
Carrier screening for individuals from high-risk populations for alpha-thalassemia

Genetics Test Information
Deletions and duplications, hemoglobin Constant Spring (HbCS), and alpha-thalassemia Saudi point mutations only.

Profile Information

<table>
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<tr>
<th>Test ID</th>
<th>Reporting Name</th>
<th>Available Separately</th>
<th>Always Performed</th>
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<tbody>
<tr>
<td>ATHL</td>
<td>Alpha-Globin Gene Analysis (ATHL)</td>
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Reflex Tests

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<tr>
<td>CULAF</td>
<td>Amniotic Fluid Culture/Genetic Test</td>
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<tr>
<td>MATCC</td>
<td>Maternal Cell Contamination, B</td>
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Testing Algorithm
For prenatal specimens only: If amniotic fluid (nonconfluent cultured cells) is received, amniotic fluid culture/genetic test will be added and charged separately. 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

**Shipping Instructions**
Specimen preferred to arrive within 96 hours of draw.

**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:

**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

Due to the complexity of prenatal testing, consultation with the laboratory is required for all prenatal testing. Prenatal specimens can be sent Monday through Thursday and **must be received by 5 p.m. CST on Friday** in order to be processed appropriately. All prenatal specimens must be accompanied by a maternal blood specimen. Order MATCC / Maternal Cell Contamination, Molecular Analysis on the maternal specimen.

**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) in Special Instructions

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

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Clinical and 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 mutations. 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 mutations. The most common nondeletion mutation is hemoglobin Constant Spring (HbCS) \((HBA2: c.427T >C)\). Point mutations other than HbCS and alpha-thalassemia Saudi are not detected by this assay.

Alpha-thalassemia occurs in all ethnic groups but is especially common 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 mutations) 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.

Hemoglobin Constant Spring and alpha-thalassemia Saudi are the only nondeletion types of alpha-thalassemia that will be detected by this assay. This test is not useful for diagnosis or confirmation of beta-thalassemia or hemoglobinopathies.

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 polymorphisms 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.

This assay cannot be performed on chorionic villus specimens.

**Clinical Reference**


Method Description

This is a direct mutation analysis. Deletions within the alpha-globin locus and the hemoglobin Constant Spring and alpha-thalassemia Saudi point mutations 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 PCR-based assay is used to detect the presence of the alpha-3.7 and alpha-4.2 deletions. (Schouten JP, McElgunn CJ, Waaijer R, et al: Relative quantification of 40 nucleic acid sequences by multiplex ligation-dependent probe amplification. Nucleic Acids Res 2002 Jun 15;30[12]:e57)

PDF Report

No

Day(s) and Time(s) Test Performed

Batched 2 times per week

Analytic Time

8 days

Maximum Laboratory Time

12 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

CPT Code Information

81269

Reflex Tests
Test Definition: ATHAL
Alpha-Globin Gene Analysis

CULAF / Amniotic Fluid Culture for Genetic Testing

Tissue culture for amniotic fluid (if appropriate)

Cryopreservation (if appropriate)

Maternal Cell Contamination, Molecular Analysis

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

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