Test Definition: WASEQ

Alpha Globin Gene Sequencing, B

Overview

Useful For

Diagnosing nondeletional alpha thalassemia

Testing for nondeletional alpha thalassemia in a symptomatic individual

Follow-up testing to an abnormal hemoglobin electrophoresis that identified an alpha globin chain variant

Genetics Test Information

A hemoglobin electrophoresis evaluation (HBELC / Hemoglobin Electrophoresis Cascade, Blood) is always indicated prior to alpha globin gene sequencing because these conditions can be complex and protein data allows accurate and rapid classification of the patient phenotype.

Not the preferred first-tier molecular test for carrier screening or diagnosis of alpha thalassemia. This test is used to identify nondeletional alpha-thalassemia variants when there is a strong clinical suspicion and ATHAL / Alpha-Globin Gene Analysis, Varies, is negative. This test can also identify alpha globin variants that can result in variable phenotypes, such as erythrocytosis, chronic hemolytic anemia, and many that are clinically benign.

Testing Algorithm

This test is a second-tier test in the evaluation of alpha thalassemia carrier determination, hemoglobin H disease confirmation, and alpha globin variant identification.

Special Instructions

- Thalassemia/Hemoglobinopathy Patient Information
- Informed Consent for Genetic Testing
- Informed Consent for Genetic Testing (Spanish)

Method Name

Polymerase Chain Reaction (PCR) and Sanger Sequencing Analysis

NY State Available

Yes

Specimen

Specimen Type

Varies

Advisory Information

For first-tier testing for alpha thalassemia detection, order THEVP / Thalassemia and Hemoglobinopathy Evaluation, Serum and Whole Blood.

For first-tier testing for an alpha globin variant, order HBELC / Hemoglobin Electrophoresis Cascade, Blood.

If genetic testing is desired, the first-tier genetic test assesses large deletional alpha thalassemia alterations. Order ATHAL / Alpha-Globin Gene Analysis, Varies.

Necessary Information

1. Patient's age is required.

2. Include recent transfusion information.

Specimen Required

Submit only 1 of the following specimens:

Specimen Type: Peripheral blood

Container/Tube:

Preferred: Lavender top (EDTA)

Acceptable:Â Yellow top (ACD), green top (sodium heparin)

Specimen Volume: 4 mL

Collection Instructions:

1. Invert several times to mix blood.

2. Send specimen in the original tube.

Specimen Stability Information: Refrigerate 30 days(preferred)/Ambient 14 days

Specimen Type: Extracted DNA from whole blood

Container/Tube: 1.5- to 2-mL tube

Specimen Volume: Entire specimen

Collection Instructions: Label specimen as extracted DNA from blood and provide indication of volume and concentration of the DNA

Specimen Stability Information:Â Frozen (preferred)/Refrigerate/Ambient

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. Thalassemia/Hemoglobinopathy Patient Information (T358) in Special Instructions.

Specimen Minimum Volume

Blood: 1 mL
Extracted DNA: 50 mcL at 50 ng/mcL concentration

Reject Due To

Gross hemolysis	OK
Moderately to severely clotted	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

Clinical and Interpretive

Clinical Information

Alpha globin gene sequencing detects alpha globin variants and nondeletional alpha thalassemia variants.

Alpha thalassemia is the most common monogenic condition in the world. It is estimated that up to 5% of the world's population carries at least 1 alpha thalassemia variant and, in the United States, approximately 30% of African Americans are thought to carry an alpha thalassemia variant. Alpha thalassemia variations are most common in individuals of Southeastern Asian, African, Mediterranean, Indian, and Middle-Eastern descent, but they can be found in persons from any ethnic group.

Four alpha globin genes are normally present, 2 copies on each chromosome 16. Alpha thalassemia variants result in decreased alpha globin chain production. In general, alpha thalassemia is characterized by hypochromic, microcytic anemia and varies clinically from asymptomatic (alpha thalassemia silent carrier and alpha thalassemia trait) to lethal hemolytic anemia (hemoglobin: Hb Barts hydrops fetalis).

Large deletions of the alpha globin genes account for approximately 90% of alpha thalassemia alterations, and these variations will not be detected by alpha globin gene sequencing. Other variants, such as point variants or small deletions within the alpha globin genes, account for most of the remaining 10% of alpha thalassemia variations. These nondeletional subtypes can be detected by alpha globin gene sequencing. The most common nondeletional alpha thalassemia variant is Hb Constant Spring (Hb CS).

The majority of alpha globin chain variants are clinically and hematologically benign; however some cause erythrocytosis and chronic hemolytic anemia. Hemoglobin electrophoresis may not be able to confirm their identity. In these instances alpha globin gene sequencing can be useful.

Reference Values

An interpretive report will be provided.

Interpretation

An interpretive report will be provided.

Cautions

This assay will not detect large deletions or duplications within the alpha globin genes. Therefore, test results should be interpreted in the context of hemoglobin electrophoresis, clinical findings, family history, and other laboratory data. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.

Rare genetic 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.

Clinical Reference

1. Harteveld CL, Higgs DR: Alpha-thalassemia. Orphanet J Rare Dis 2010;5:13

2. Hoyer JD, Hoffman DR: The Thalassemia and hemoglobinopathy syndromes. In Clinical Laboratory Medicine. Second edition. Edited by KD McMlatchey. Philadelphia, Lippincott Williams and Wilkins. 2002, pp 866-895

Performance

Method Description

Genomic DNA is extracted from whole blood. The *HBA1* and *HBA2* genes are amplified by PCR. The PCR product is then purified and sequenced in both directions using fluorescent dye-terminator chemistry. Sequencing products are separated on an automated sequencer and trace files analyzed for variations in all exons, introns and the polyadenylation site. Results are correlated with routine studies to identify unusual alpha globin variants.(Reddy PL, Bowie LJ: Sequence-based diagnosis of hemoglobinopathies in the clinical laboratory. Clin Lab Med 1997;17[1]:85-96; Traeger-Synodinos J, Harteveld CL: Advances in technologies for screening and diagnosis of hemoglobinopathies. Biomarkers Med 2014;8[1]:115-127)

PDF Report

No

Day(s) and Time(s) Test Performed

Monday through Friday; Varies

Analytic Time

2 days

Maximum Laboratory Time

10 days

Specimen Retention Time

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

81259-HBA1/HBA2; full sequence

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
WASEQ	Alpha Globin Gene Sequencing, B	87730-8

Result ID	Test Result Name	Result LOINC Value
61362	Alpha Globin Gene Sequencing, B	87730-8
43921	Interpretation	69047-9