Test Definition: WAGDR

Alpha Globin Cluster Locus Deletion/Duplication, Blood

Overview

Useful For

Diagnosis of 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.

Genetics Test Information

This test is for genetic deletions and duplications only.

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)/Quantitative Polymerase Chain Reaction (qPCR)/Multiplex Ligation-Dependent Probe Amplification (MLPA)

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

Sequence variants, other than the alpha T-Saudi and hemoglobin Constant Spring 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.

Specimen Required

Patient Preparation: A previous bone marrow transplant from an allogeneic donor will interfere with testing. For instructions for testing patients who have received a bone marrow transplant, call 800-533-1710.

Specimen Type: Whole blood
Container/Tube:

Preferred: Lavender top (EDTA)
Acceptable: Yellow top (ACD)
Specimen Volume: 3 mL
Collection Instructions:
1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot**.

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)

Specimen Minimum Volume
Blood: 1 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
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 Barts hydrops fetalis, and almost invariably in utero fetal demise or early after birth, if left untreated. Samples with protein effects of intrauterine transfusion are increasingly common.

Less frequently, alpha-thalassemia results from single point alterations, such as hemoglobin Constant Spring (*HBA2*: c.427T >C).

Alpha-thalassemia occurs in all ancestral 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 Africans, and 1 in 30 to 1 in 50 for individuals of Mediterranean ancestry. Both deletional and nondeletional (caused by sequence alterations) forms of alpha-thalassemia are found in individuals with Mediterranean ancestry. Those of Arab ancestry can carry a fairly common sequence alteration, called alpha T-Saudi. Deletions in cis (two 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 hemoglobin H disease or hemoglobin Bart hydrops fetalis syndrome.

Reference Values

An interpretive report will be provided.

Interpretation

The interpretive report includes an overview of the findings as well as the associated clinical significance.

Cautions

Hemoglobin electrophoresis should usually be done prior to this test to exclude other diagnoses

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;42(12):922-931. doi:10.1136/jmg.2005.033597
2. Harteveld CL, Higgs DR. Alpha-thalassemia. Orphanet J Rare Dis. 2010;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
5. Musallam KM, Cappellini DM, Coates TD, et al. ?lpha-thalassemia: A practical overview. Blood Rev. 2024;64:101165.

doi.10.1016/j.blre.2023.101165

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. Thirty-three 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. A quantitative polymerase chain reaction-based assay is used to detect the presence of hemoglobin Constant Spring (*HBA2*: c.427T >C) and alphaT-Saudi (*HBA2*: c.*94A>G) point mutations. 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;30[12]:e57. doi:10.1093/nar/gnf056)

PDF Report

No

Day(s) Performed

Varies

Report Available

9 to 13 days

Specimen Retention Time

2 weeks (if available)

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.

Test Definition: WAGDR

Alpha Globin Cluster Locus Deletion/Duplication, Blood

CPT Code Information

81269

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
WAGDR	Alpha Globin Clustr Locus Del/Dup,B	90040-7

Result ID	Test Result Name	Result LOINC® Value
621362	Result Summary	50397-9
621363	Result	82939-0
621364	Interpretation	69047-9
621365	Additional Information	48767-8
621366	Specimen	31208-2
621367	Source	31208-2
621368	Method	85069-3
621804	Disclaimer	62364-5
621369	Released By	18771-6