MAYO CLINIC LABORATORIES

Test Definition: WBDD

Beta-Globin Cluster Locus, Deletion/Duplication, Varies

Overview

Useful For

Determining the etiology of hereditary persistence of fetal hemoglobin (HPFH) or delta-beta thalassemia

Diagnosing less common causes of beta thalassemia; these large deletional beta thalassemia variants result in elevated hemoglobin (Hb) A2 and usually have slightly elevated HbF levels

Distinguishing homozygous Hb S disease from a compound heterozygous HbS/large beta-globin cluster deletion disorder (ie, HbS/beta zero thalassemia, Hb S/delta-beta zero thalassemia, HbS/HPFH, HbS/gamma-delta-beta thalassemia)

Diagnosing complex thalassemias where the beta-globin gene and one or more of the other genes in the beta-globin cluster have been deleted

Evaluating and classifying unexplained increased HbF percentages

Evaluating microcytic neonatal anemia

Evaluating unexplained long standing microcytosis in the setting of normal iron studies and negative alpha thalassemia testing/normal HbA2 percentages

Confirming gene fusion hemoglobin variants such as Hb Lepore and Hb P-Nilotic

Confirming homozygosity vs hemizygosity of variants in the beta-like genes (*HBB*, *HBD*, *HBG1*, *HBG2*)

This test is **not useful** for diagnosis or confirmation of alpha thalassemia, the most common beta thalassemias, or hemoglobin variants. It also does not detect nondeletional HPFH.

Genetics Test Information

This test can be used to identify a variety of conditions (see Highlights) that involve large deletions of the beta-globin gene cluster. These alterations will not be detected by DNA sequencing of the beta-globin gene.

Testing Algorithm

A hemoglobin electrophoresis evaluation (HBEL1 / Hemoglobin Electrophoresis Evaluation, Blood) is always indicated prior to beta-globin cluster locus deletion and duplication testing as these conditions can be complex and protein data allows accurate classification of the patient phenotype.

Special Instructions

- Informed Consent for Genetic Testing
- Metabolic Hematology Patient Information
- Informed Consent for Genetic Testing (Spanish)

Highlights

This test is recommended to identify a variety of conditions involving large deletions or duplications within the beta-globin gene cluster locus region including:
-Identifying large deletions causing increased hemoglobin (Hb) F levels such as hereditary persistence of fetal hemoglobin, delta-beta thalassemias, and gamma-delta-beta thalassemia
-Identifying beta thalassemia conditions in cases where beta gene sequencing did not find a beta thalassemia variant
-Confirming gene fusion hemoglobin variants such as Hb Lepore and Hb P-Nilotic
-Investigating newborns with unexplained microcytic anemia that is suspected to be caused by epsilon-gamma-delta-beta thalassemia
-Confirming homozygosity vs hemizygosity of variants in the beta-like genes (*HBB*, *HBD*, *HBG1*, *HBG2*)
-Investigating individuals older than 12 months of age with unexplained microcytosis and normal hemoglobin electrophoresis for whom more common causes of microcytosis such as iron deficiency and alpha thalassemia have been excluded

Method Name

Polymerase Chain Reaction (PCR) Analysis/Multiplex Ligation-Dependent Probe Amplification (MLPA)

NY State Available

Yes

Specimen

Specimen Type

Varies

Additional Testing Requirements

Hemoglobin electrophoresis studies performed at Mayo Clinic Laboratories are highly recommended prior to this test to allow for more complete interpretation of results. See HBEL1 / Hemoglobin Electrophoresis Evaluation, Blood or THEV1 / Thalassemia and Hemoglobinopathy Evaluation, Blood and Serum.

Shipping Instructions

Specimens must arrive within 4 days (96 hours) of collection.

Necessary Information

Metabolic Hematology Patient Information (T810) is required; see Special Instructions. Send a completed form with the specimen. Document the reason for suspecting a large beta cluster locus deletion along with the hemoglobin F percentage and red blood cell indices for the patient.

Specimen Required

Specimen Type: Whole blood
Collection Container/Tube:
Preferred: Lavender top (EDTA)
Acceptable: Yellow top (ACD)

Specimen Volume: 4 mL
Collection Instructions:
1. Invert several times to mix blood.
2. Send whole blood specimen in the original tube. **Do not aliquot.**
Specimen Stability Information: Refrigerated: 30 days; Ambient: 8 hours

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. If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:
Metabolic Hematology Patient Information (T810) **is required.**
Benign Hematology Test Request (T755)

Specimen Minimum Volume

2 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

Large deletions involving the beta-globin cluster locus on chromosome 11 manifest with widely variable clinical phenotypes. Up to 10% of beta-thalassemia cases (dependent on ethnicity) are caused by large deletions in the beta-globin cluster. Other thalassemias including delta-beta thalassemia, gamma-delta-beta-thalassemia, and epsilon-gamma-delta-beta-thalassemia, also result from functional loss of genes or the locus control region that controls globin gene expression. In addition, hereditary persistence of fetal hemoglobin (HPFH) is caused by deletions of variable size along the beta-globin cluster locus. Most, but not all, of the large deletion beta-globin cluster disorders are associated with variably elevated hemoglobin F percentages that persist after 2 years of age. In addition, most manifest in microcytosis. A notable exception is HPFH, which can have normal to minimal decreased mean corpuscular volume (MCV) values. The correct classification of these deletions is important as they confer variable predicted phenotypes and some are more protective than others when found in combination with a second beta-globin variant, such as HbS or beta thalassemia. In addition, identification of these deletions can explain lifelong microcytosis in the setting of normal iron studies and negative alpha thalassemia molecular results.

Reference Values

An interpretive report will be provided.

Interpretation

The alterations will be provided with the classification, if known. Further interpretation requires correlation with protein studies and red blood cell indices.

Cautions

Nondeletional subtypes of beta thalassemia or hereditary persistence of fetal hemoglobin are not detected by this assay.

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.

Clinical Reference

1. Hein MS, Oliveira JL, Swanson KC, et al. Large Deletions Involving the Beta Globin Gene Complex: Genotype-Phenotype Correlation of 119 cases. Blood. 2015;126:3374
2. Kipp BR, Roellinger SE, Lundquist PA, Highsmith WE, Dawson DB. Development and clinical implementation of a combination deletion PCR and multiplex ligation-dependent probe amplification assay for detecting deletions involving the human alpha-globin gene cluster. J Mol Diagn. 2011;13(5):549-57. doi:10.1016/j.jmoldx.2011.04.001
3. Rund D, Rachmilewitz E: Beta-thalassemia. N Engl J Med. 2005;353(11):1135-1146
4. Nussbaum R, McInnes R, Willard H: Principles of molecular disease: Lessons from the hemoglobinopathies. In: Thompson and Thompson Genetics in Medicine. 7th ed. Saunders Elsevier; 2007:323-342
5. Wood WG: Hereditary persistence of fetal hemoglobin and delta beta thalassemia. In: Disorders of Hemoglobin. Cambridge University Press; 2001:356-388

Performance

Method Description

Multiplex ligation-dependent probe amplification (MLPA) is utilized to test for the presence of large deletions in the beta-globin gene.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Wednesday, Friday

Report Available

25 to 30 days

Specimen Retention Time

Whole Blood: 2 weeks; 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

81363-HBB (hemoglobin, beta, beta-globin) (eg, beta thalassemia), duplication/deletion analysis

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
WBDD	Beta Globin Cluster Locus Del/Dup	In Process

Result ID	Test Result Name	Result LOINC® Value
48361	Beta Globin Cluster Locus Del/Dup	50397-9
48438	Specimen	31208-2
48362	Interpretation	69047-9
48360	Reviewed by	18771-6