Test Definition: WBDD
Beta Globin Cluster Locus Del/Dup

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 mutations result in elevated hemoglobin (Hb) A2 and usually have slightly elevated Hb F levels

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

Evaluating microcytic neonatal anemia

Evaluating unexplained long standing microcytosis in the setting of normal iron studies and negative alpha-thalassemia testing/normal Hb A2 percentages

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

Confirming homozygosity vs hemizygosity of mutations 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 hereditary persistence of fetal hemoglobin.

Genetics Test Information

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

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

Testing Algorithm

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 (HPFH), delta-beta-thalassemias, and gamma-delta-beta-thalassemia

-Identifying beta-thalassemia conditions in cases where beta gene sequencing did not find a beta-thalassemia mutation

-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-
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beta-thalassemia

- Confirming homozygosity vs hemizygosity of mutations 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

Special Instructions

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

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 are highly recommended prior to this test to allow for more complete interpretation of results. See HBELC / Hemoglobin Electrophoresis Cascade, Blood or THEVP / Thalassemia and Hemoglobinopathy Evaluation.

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

Specimen Required

Specimen Type: Peripheral 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 specimen in the original tube.

Specimen Stability Information: Refrigerated (preferred)/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. Complete, print and send a *Thalassemia/Hemoglobinopathy Patient Information* sheet (T358) with the specimen (in Special Instructions). Document the reason for suspecting a large beta cluster locus deletion along with the Hb F percentage and RBC indices for the patient.

**Specimen Minimum Volume**

2 mL

**Reject Due To**

All specimens will be evaluated by Mayo Clinic Laboratories for test suitability

**Specimen Stability Information**

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**Clinical and 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 (LCR) 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 (Hb) 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 mutation, such as Hb S 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**

An interpretive report will be provided.

**Cautions**

Nondeletional subtypes of beta-thalassemia or hereditary persistence of fetal hemoglobin (HPFH) 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**


**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) and Time(s) Test Performed**

Wednesday; 10 a.m., Friday; 2 p.m.

**Analytic Time**

5 days

**Maximum Laboratory Time**

28 days

**Specimen Retention Time**

Whole Blood: 2 weeks; DNA: 3 months

**Performing Laboratory Location**

Rochester

**Fees and Codes**

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

LOINC® Information

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