

Beta Hemoglobin DNA Sequence

Background

There are currently over 800 hemoglobin variants catalogued, of which approximately 500 are due to mutations in the β -globin gene. In addition, approximately 95% of β -thalassemia is caused by point mutations. This test, which sequences the coding regions and introns of the β -globin gene (*HBB*) in both directions, identifies hemoglobin variants that are not easily diagnosed by electrophoresis/HPLC and can determine the cause of β -thalassemia. The sensitivity of this test for detecting nucleotide substitutions, small insertions and deletions in the β -globin gene (*HBB*) is theoretically >95%.

Testing of a relative of an individual with a known β -globin mutation is also available.

Indications for Testing

- Identification of hemoglobin variants detected by electrophoresis or HPLC
- Differential diagnosis of microcytic anemia
- Molecular characterization of β -thalassemia mutations
- Evaluation of a relative of an individual with a known β -globin mutation.
- Prenatal diagnosis of potentially severe β -thalassemia

Genetic Counseling

Genetic counseling can be useful to patients and families considering genetic testing. The laboratory can provide referrals to genetics clinics in the patient's locale or a listing can be found at www.genetests.org

Ordering

1. Obtain blood samples from patient(s).
 - If prenatal, call Genetics Lab with information on type of fetal sample and expected date of receipt
2. Fill out a Clinical Lab Request - Genetics for each patient
(available at <http://depts.washington.edu/labweb/Divisions/MolDiag/MolDiagGen/index.htm>).
 - Request: "Beta-hemoglobin DNA Sequence

For testing a relative of an individual with a known mutation, request "Other: Beta hemoglobin mutation" and provide information on the specific mutation.
3. Provide items needed for test interpretation:
 - Reason for ordering test (e.g. carrier detection, prenatal diagnosis)
 - Clinical history
 - Family history/pedigree, ethnic background
 - Hematologic data (RBC indices, hemoglobin electrophoresis, quantitative HbA₂, BCB inclusion body study, and iron studies)
4. Call Laboratory Medicine Community Services at (206)598-6066 to arrange the best method of shipment.

Sample Requirements and Specimen Handling

Whole blood - EDTA (purple top) - adults - 10 mL, children - 5 mL.
Samples should be received within 72 hours of collection.
Samples may be refrigerated until shipped.
For prenatal diagnosis specimens, consult laboratory.
Heparin (green top) tubes are not acceptable.

Test Frequency and Reporting

Test results usually within 1-2 weeks of specimen receipt. A written interpretative report is issued.

References

- Huisman, T. H. J., Carver, M. F. H., and Efremov, G. D. (1996). A Syllabus of Hemoglobin Variants (Augusta, GA: The Sickle Cell Anemia Foundation).
- Old JM. Screening and genetic diagnosis of haemoglobin disorders. Blood Reviews 17:43-54, 2003.
- Globin Gene Server: <http://globin.cse.psu.edu/>