

## Alpha Hemoglobin DNA Sequence

### Background

There are currently over 800 hemoglobin variants catalogued, of which approximately 300 are due to mutations in the  $\alpha$ -globin gene. In addition, approximately 5% of  $\alpha$ -thalassemia is caused by point mutations. This test, which sequences the coding regions and introns of both the  $\alpha$ -globin 1 (HBA1) and  $\alpha$ -globin 2 (HBA2) genes in both directions, identifies hemoglobin variants that are not easily diagnosed by electrophoresis/HPLC and can determine the cause of non-deletional  $\alpha$ -thalassemia. The sensitivity of this test for detecting nucleotide substitutions, small insertions and deletions in the  $\alpha 1$  (HBA1) and  $\alpha 2$  (HBA2) genes is theoretically >95%.

Testing of a relative of an individual with a known  $\alpha$ -globin mutation is also available.

If testing for deletional  $\alpha$ -thalassemia is indicated, order "Alpha Thalassemia DNA Screen".

### Indications for Testing

- Identification of hemoglobin variants detected by electrophoresis or HPLC
- Differential diagnosis of microcytic anemia
- Evaluation of nondeletional Hemoglobin H disease
- Evaluation of a relative of an individual with a known  $\alpha$ -globin mutation.
- Prenatal diagnosis of nondeletional  $\alpha$ -thalassemia in pregnancies at risk for Hb H hydrops fetalis syndrome

### 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](http://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: "Alpha-hemoglobin DNA Sequence"
  - If requesting screening for a particular mutation known to occur in a family, request "Other: Alpha 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.

[www.labmed.washington.edu](http://www.labmed.washington.edu)

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**

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- Globin Gene Server: <http://globin.cse.psu.edu/>