

Alpha-Thalassemia: *HBA1* and *HBA2* Deletion Analysis

Test Code: AT

Turnaround time: 3 weeks

CPT Codes: 81257 x1

Condition Description

Alpha-thalassemias are caused by a decrease in the amount of alpha-globin production, relative to beta-globin production. The primary cause of alpha-thalassemia is alpha-globin gene deletions, which account for approximately 90% of mutations. Point mutations within the alpha-globin genes account for the remaining 10% of mutations.

There are two hemoglobin alpha chain genes, *HBA1* and *HBA2*, in the alpha-globin gene cluster located at the end of the short arm of chromosome 16. Because of the repetitive nature of this gene cluster, the alpha-globin genes are prone to deletion. Typically, individuals have 4 functional alpha-globin genes, 2 copies on each chromosome 16. An individual with one alpha-globin gene mutation and three functional alpha-globin genes is a silent carrier. An individual who carries two alpha-globin gene mutations and two functional alpha-globin genes is a carrier of the alpha-thalassemia trait, and may be unaffected or only mildly affected. Individuals who have only one functional alpha-globin gene have HbH disease. In newborns, HbH disease may present with microcytic, hypochromic hemolytic anemia, hepatosplenomegaly, mild jaundice, and sometimes thalassemia-like bone changes. However, the phenotype is highly variable and individuals with HbH disease may not present until adulthood after hematologic analysis as an asymptomatic individual. Deletion of all four alpha-globin results in the accumulation of Hb Barts and hydrops fetalis, which is fatal in utero or shortly after birth.

The highest frequency of alpha-thalassemia deletions occurs in populations from equatorial regions in the world where malaria is endemic. Individuals with African and Mediterranean ancestry are at a higher risk of carrying a mutation in which a single alpha-globin gene is deleted from chromosome 16. The carrier frequency is estimated to be 1 in 30 for African Americans and 1 in 30-50 for Mediterranean populations. Individuals with Mediterranean ancestry also have a higher risk of carrying other non-deletion alpha-globin gene mutations, not detected by this analysis. The two gene deletions in which both *HBA1* and *HBA2* are removed from the same chromosome 16, referred to as *cis* deletions, are rare in African or Mediterranean populations. Two gene *cis* deletions are more prevalent in Asian populations, with the carrier frequency among individuals of Southeast Asian ancestry estimated to be greater than 1 in 20. Couples who carry the Southeast Asian two gene deletion are at risk of having a child with the fatal Hb Bart form of alpha-thalassemia, which has a frequency of 0.5-5 births per 1000 in Southeast Asian populations. Couples who are carriers of the Filipino and Thailand deletions, larger deletions which encompass the embryonic zeta globin gene as well as *HBA1* and *HBA2*, will be detected by this assay. Carrier screening by molecular analysis can assist with prenatal and preconception counseling for individuals of higher risk ethnic populations.

[Click here](#) for the GeneReviews summary on this condition.

Genes

[HBA1](#), [HBA2](#)

Indications

Testing is indicated for:

- Patients with symptoms of alpha-thalassemia or microcytic anemia.
- Family members of an affected patient who are at risk to be carriers of alpha-thalassemia.
- Carrier screening for individuals of Asian, African, and Mediterranean background.

Methodology

Copy number changes in the *HBA1* and *HBA2* genes are detected using multiplex ligation polymerase chain reaction amplification (MLPA). This assay identifies the hemoglobin Constant Spring (HbCS) mutation, as well as common deletions associated with alpha-thalassemia, including the 3.7, 4.2, Southeast Asian, Filipino, and Thailand deletions.

Detection

This assay will detect the pathogenic variants specified above, accounting for over 90% of alpha-thalassemia cases. The presence of less common deletions may also be detected by MLPA.

Reference Range

Qualitative assay.

Specimen Requirements

Submit only 1 of the following specimen types

Type: Whole Blood (EDTA)

Specimen Requirements:

EDTA (Purple Top)

Infants and Young Children (2 years of age to 10 years old: 3-5 ml

Older Children & Adults: 5-10 ml

Autopsy: 2-3 ml unclotted cord or cardiac blood

Specimen Collection and Shipping:

Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

Type: DNA, Isolated**Specimen Requirements:**

Microtainer

3µg

Isolation using the Perkin Elmer™ Chemagen™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping:

Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

Related Tests

Prenatal Custom Diagnostics is available to couples who are confirmed carriers of alpha-globin gene deletions. Please contact the laboratory genetic counselor to arrange testing prior to collecting a prenatal specimen.