

Disease Information

Autosomal recessive disorders of hemoglobin are among the most common genetic disorders worldwide. More than 400 different mutations have been described in *HBB*, the gene for beta globin.¹ Beta globin mutations can result in sickle cell anemia, in which structurally abnormal beta globin is produced, or beta thalassemias, in which hemoglobin synthesis is diminished or absent. Beta globin mutations can also impair the developmental transition from fetal to adult hemoglobin. Sickle cell mutations are detected frequently in African, Mediterranean, Middle Eastern, and Indian ethnicities as well as in individuals from the Caribbean and parts of Central and South America. In the US, 1 out of 12 African Americans have sickle cell trait and 1 out of 500 newborns are affected with the disease.² Beta thalassemias are common in individuals of Asian, Filipino, Mediterranean, Middle Eastern, or African descent, with each group showing population specific mutations. Genetic counseling is recommended for an adequate interpretation of results for patients and their families.

Testing Benefits & Indications

This test is to clarify and/or confirm a suspected diagnosis of beta thalassaemia, sickle cell disease, or sickle-beta thalassemia disease. Hemoglobinopathies are typically diagnosed by HPLC or gel electrophoresis, but these methods may not always conclusively identify abnormal hemoglobin variants. Common mutation panels may provide an incomplete diagnosis by missing mutations due to the high number of mutations existing in *HBB*. Therefore, analysis of the entire gene with the Ambry Test:

- provides a useful second-tier test to enable a precise diagnosis
- defines the mutations for possible future prenatal diagnosis
- allows determination of carrier status in relatives

Test Description

The Ambry Test: Beta Thalassemia Plus is a full gene sequence analysis of the *HBB* gene. The following regions are analyzed by PCR-based double-stranded automated sequencing in sense and antisense directions: exons 1-3, 5' UTR sequence up to and including the mutation at -101 from the transcription site, the complete intron 1 (IVS1), 20 bp into intron 2 (IVSII) and about 230 bp of the 3' end of intron 2 (IVSII-645) for a total of 444 bp exon sequence plus at least 498 bp intronic sequence. In addition, PCR covering a 619 bp fragment that includes much of the 3' end of IVSII, all of exon 3, and the 3' end of the gene is performed to analyze for the del619 East Indian deletion. Other gross deletions of *HBB* are not detected. Specific mutation analysis for individual *HBB* mutations known to be in the family is also available.

Mutation Detection Rate

This test detects 97-99% of disease-causing mutations.

Turn-Around-Time

Gene sequence analysis	10 - 21 days
Specific mutation analysis	10 - 14 days

Specimen Requirements

Blood: Collect 3-5 cc from adult or 2 cc minimum from child into EDTA purple-top tube (first choice) or ACD yellow-top tube (second choice). Store at room temperature or refrigerate. Ship at room temperature.

Blood Spot: Minimum of one complete spot approximately 0.5 inch in diameter on S&S 903 collection paper or similar. Store in a clean plastic bag at room temperature. Ship at room temperature.

Saliva: Collect 2 ml into Oragene™ DNA Self-Collection container. Store and ship at room temperature.

DNA: Send 20 µg in TE at 50-100 ng/µl. Store frozen and ship on ice or dry ice.

Prenatal: Prenatal testing is available. Please call an Ambry Genetic Counselor to discuss your case.

CPT Codes

Full gene analysis or specific mutation analysis 83891, 83894, 83898, 83904, 83909, 83912

References

¹Allison Ashley-Koch A et al. *Am J Genet.* 2000; 151:839-845.

²Centers for Disease Control and Prevention at http://www.cdc.gov/ncbddd/sicklecell/hcp_data.htm. Accessed May 12, 2008.