

Beta Globin Sequencing

TO DETERMINE AFFECTED OR CARRIER STATUS FOR A BETA GLOBINOPATHY OR BETA THALASSEMIA

Disease Overview

- Beta globin chain mutations can result in the formation of a structurally abnormal protein (hemoglobinopathy) or decrease the amount of protein produced (thalassemia).
- Other beta chain mutations impair the developmental switch from fetal to adult hemoglobin, resulting in hereditary persistence of fetal hemoglobin.
- Some beta globin variants have no clinical effect, while others may result in microcytic anemia, hemolytic anemia, cyanosis due to reduced oxygen affinity, or erythrocytosis due to increased oxygen affinity.
- Interactions between beta globin chains with different mutations may either alleviate or exacerbate the effects of the individual variants.

Epidemiology

- Approximately 5 percent of the world's population carries clinically important hemoglobin mutations.
- Annually, 300,000 individuals are born with a severe hemoglobinopathy.
- Beta thalassemias are most commonly observed in individuals from Southern Europe, Northern Africa, and India.

Genetics

- The overwhelming majority of affected individuals have an autosomal recessive disorder caused by homozygosity or compound heterozygosity for a beta chain variant.
- Greater than 300 hemoglobin variants have been described.

Indications for Ordering

- To confirm the diagnosis of a beta thalassemia or beta globinopathy especially when a definitive diagnosis cannot be made by HPLC or gel electrophoresis.
- For clinical symptoms of a hemoglobinopathy.
- For a positive family history of a beta thalassemia or hemoglobinopathy.
- To confirm a specific beta globin mutation in parents prior to prenatal diagnosis.
- Prenatal diagnosis of beta globin mutations previously documented in parents.

Interpretation

- For optimal test interpretation, provide information regarding patient symptoms, family history of beta globin variant, and ethnicity.
- Individuals with a single beta globin variant may be a carrier of a structurally abnormal beta globin, carrier of beta thalassemia, or a silent mutation.
- Individuals with two beta chain variants are variably affected, ranging from infantile lethality to no clinical effects, depending on the specific mutations identified.

Methodology

Bi-directional sequencing of the three beta globin exons, intron/exon borders, proximal promoter, 5' and 3' untranslated regions and intronic mutations IVS-II-654, IVS-II-705, IVS-II-745.

Limitation

Mutations within the primer/probe regions could affect this assay. Large beta globin deletions or fusion genes will not be detected.

Related Tests

- Beta Globin Gene Mutations for HbS, HbC, & HbE by PCR (0051421)
- Beta Globin Gene Mutations for HbS, HbC, & HbE by PCR, Fetal (0051422)

References

1. Bunn HF and Forget BG. *Hemoglobin: molecular, genetic, and clinical aspects*. 1986. Philadelphia: WB Saunders Co.
2. Hoffman R, et al, eds. *Hematology: basic principles and practice*. 1991. New York: Churchill Livingstone.
3. Thomas MW, McInnes RR, and Willard HF. *The hemoglobinopathies: models of molecular disease*. Genetics in Medicine, 5th edition. 1991. Philadelphia: WB Saunders Co., 247-270.

Test Information

0050388 **Beta Globin Gene Sequencing, Fetal**
0050578 **Beta Globin Gene Sequencing**

For specific collection, transport, and testing information, refer to the ARUP Web site at www.aruplab.com.