Prima Cancer Genetics

MEDGENOME

Thalassemia Mutation Testing

Beta-thalassemia

Beta-thalassemia (β-thalassemia) is characterized by reduced synthesis of the hemoglobin subunit beta (hemoglobin beta chain) that results in microcytic hypochromic anemia, an abnormal peripheral blood smear with nucleated red blood cells, and reduced amounts of hemoglobin A (HbA) on hemoglobin analysis.

Beta-thalassemia (OMIM#613985) can be caused by homozygous or compound heterozygous mutations in the HBB gene (OMIM*141900).

Prevalence

Beta Thalassemia poses a significant health burden in India.The average prevalence of Beta Thalassemia Carriers is 3-4%. Estimates indicate that there would be around 100,000 patients with Beta Thalassemia Syndrome, however, exact numbers are not available due to absence of National Registries of patients.

Genetic testing for beta-thalassemia

The complete coding region sequencing of *HBB* gene can detect all the common point mutations (SNVs) and small indels as well as novel and rare mutations. The most common mutations reported in Indian population are IVS1-5, IVS1-1 G>T, codon 41/42 (-TCTT), Codon 8/9 (+G), 619-bp deletion, c.*110T>C (promoter mutation) and $Xmn1^{G}_{\gamma}$ polymorphism (HBG2 c.-211C>T) accounting for more than 90% of the thalassemia carriers are covered.

Gene	Test Method	Proportion of Pathogenic Variants Detectable by This Method
HBB	Sequence analysis by NGS (point mutations/small indels in coding regions and splice junctions)	~90%
HBB	Gene-targeted deletion/duplication analysis	~10%

List of common mutations covered

Variant	cDNA position	Covered by our test
IVS1-5	c.92+5G>C	Sanger / NGS
Codon41/42(-TCTT)	c.125_128delTCTT	Sanger / NGS
Codon 30 (G>C)	c.92G>C	Sanger / NGS
IVS1-1 (G>T/A)	c.92+1G>A	Sanger / NGS
619-bp deletion	-	MLPA
Codon 8/9(+G)	c.27dupG	Sanger / NGS
codon 15 (G>A)	c.47 G>A	Sanger / NGS
Codon 16 (-C)	c.51delC	Sanger / NGS
poly A site (T>C)	c.*110T>C	Sanger / NGS
Codon 15 (-T)	c.46delT	Sanger / NGS

- Sanger sequencing / NGS is highly recommended for *HBB* sequencing followed by MLPA analysis.
- The *HBB* is 100% covered in our NGS.

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Alpha-Thalassemia

Alpha-thalassemia (α-thalassemia) has two clinically significant forms: hemoglobin Bart hydrops fetalis (Hb Bart) syndrome, caused by deletion of all four α-globin genes; and hemoglobin H (HbH) disease, most frequently caused by deletion of three α-globin genes.

Hb Bart syndrome, the more severe form, is characterized by fetal onset of generalized edema, pleural and pericardial effusions, and severe hypochromic anemia, in the absence of ABO or Rh blood group incompatibility. Additional clinical features include marked hepatosplenomegaly, extramedullary erythropoiesis, hydrocephalus, and cardiac and urogenital defects. Death usually occurs in the neonatal period.

HbH disease is characterized by microcytic hypochromic hemolytic anemia, splenomegaly, mild jaundice, and sometimes thalassemia-like bone changes. Individuals with HbH disease may develop gallstones and experience acute episodes of hemolysis in response to oxidant drugs and infections.

Alpha-thalassemia (OMIM#604131) is caused by mutations in the HBA1 (OMIM*141800) and HBA2 OMIM*141850) genes.

Genetic testing for Alpha-thalassemia

Gene	Test Method	Proportion of Pathogenic Variants Detectable by This Method
HBA1 and *HBA2*	Targeted deletion analysis	~85%
HBA1 and *HBA2*	Sequence analysis	~15%

List of common mutations covered

Variant	Covered by our test
Common two α-globin-gene deletion	MLPA
Common single α-globin-gene deletion	MLPA
c.2T>C	Sanger / NGS
c.94_95delAG	Sanger / NGS
c.95+2_95+6delTGAGG	Sanger / NGS
c.207C>G	Sanger / NGS
c.207C>A	Sanger / NGS
c.223G>C	Sanger / NGS
c.[339C>G; 340_351delCTCCCCGCCGAG]	Sanger / NGS
c.377T>C	Sanger / NGS
c.*94A>G	Sanger / NGS

- MLPA analysis is highly recommended for HBA1 and HBA2 deletions followed by Sanger sequencing / NGS

Get in touch

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