Hemoglobin SC Mutation Analysis

Sickle cell disease (SCD) is a group of disorders that are characterized by chronic hemolytic anemia and vaso-occlusive events that may result in organ and tissue damage. SCD is caused by mutations in the β-globin gene (HBB) and are defined by the presence of hemoglobin S (HbS). Versiti offers testing to identify the presence of HbS.

HbS is caused by a single nucleotide substitution that changes a glutamic acid to valine at codon 6 (Glu6Val). Homozygosity for this mutation (HbSS) causes sickle cell anemia and accounts for 60-70% of SCD. The heterozygous state (HbAS) is known as sickle cell trait. The other forms of SCD include compound heterozygous states in which the HbS gene is co-inherited with another β-globin variant such as HbC (Glu6Lys), β+-thalassemia, β0 -thalassemia, D-Punjab (Glu121Gln) or O-Arab (Glu121Lys). The incidence of SCD in the African American population is between 1/250-1/600. The frequency of HbAS and HbAC in this population is approximately 8-10% and 3%, respectively. HbS is also common in SubSaharan Africa, India and the Middle East. SCD is an autosomal recessive disorder. Parents who are both carriers of HBB mutations that cause SCD are at risk of having affected children. After identifying the disease-causing alleles in the carrier parents, molecular prenatal testing can be offered for pregnancies at increased risk.

Indications for testing:

- Confirmation of diagnosis/hemoglobin electrophoresis
- Carrier Testing
- Prenatal Diagnosis

Test method:

Gene amplification and detection with FRET hybridization probes.

Assay sensitivity and limitations:

Analytical sensitivity is >99%. Other mutations in β-globin are not detected by this assay. Rare polymorphisms within primer or probe regions may interfere with detection of these gene variants. Clinical sensitivity for SCD is approximately 90%. HBB mutations such as alleles for β+-thalassemia, β0 - thalassemia, D-Punjab and O-Arab are not detected by this assay but may cause SCD when co-inherited with HbS. Testing of carrier parents is recommended.

Reporting of results:

Reference interval: Negative, Heterozygous (HbS and HbC), Compound Heterozygous (HbSC), Homozygous (HbS and HbC).

Specimen requirements:

Parental: 3-5 ml EDTA (lavender top) whole blood for carrier testing and maternal cell contamination studies.

Fetal: Amniotic fluid 7-15 ml amniotic fluid, 1ml cord blood, $5x10^6$ cultured amniotic cells (2-T25 flasks) or 2 ml EDTA (lavender top) whole blood. Backup cultures are highly recommended.

CVS: 5-10 mg with maternal tissue dissected or cultured CVS (2-T25 flasks).

A maternal sample should be provided for maternal cell contamination studies. Testing of parents is recommended prior to prenatal testing or results from previous testing may be provided.

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SHIP

Shipping requirements:

Ship at room temperature. Insert specimens and the test requisition form into plastic bags and seal. Insert into a Styrofoam container; seal and place into a sturdy cardboard box and tape securely; ship by an overnight carrier. Ship the package in compliance with your overnight carrier guidelines. Please contact your carrier for current biohazard shipping regulations.
Label with the following address:

Versiti Client Services
Molecular Oncology & Genetics Laboratory
638 N. 18th Street
Milwaukee, WI 53233
800-245-3117, ext. 6250

ORDER

Required forms:

Please complete all pages of the requisition form. Clinical history (including patient's ethnicity, clinical diagnosis, family history and relevant laboratory findings) is necessary for optimal interpretation of genetic test results and recommendations. Clinical and laboratory history can either be recorded on the requisition form or clinical and laboratory reports can be submitted with the sample.

CPT Codes/Billing/Turnaround time:

Test Code: 4624

CPT code: For recommended CPT codes please visit versiti.org/test-catalog

Turnaround time: 3-6 days

References:

1. Costa, C et al. A One Step Real-Time PCR for Rapid Prenatal Detection of Sickle Cell Disease and Detection of Maternal Contamination. Mol Diag 2003; 7(1)45-48.
2. Bender, MA
3. Sickle Cell Disease, GeneReview (2006) www.genetests.org

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