

Heart Institute Diagnostic Lab

CAP#: 7518730

CLIA#: 36D2003208

Phone: (513) 803-1751

Fax: (513) 803-1748

Email: HeartDx@cchmc.org

Shipping Instructions

Please enclose a test requisition form with sample. All information must be complete before sample can be processed. Samples may be shipped at room temperature by overnight Federal Express to arrive Monday through Friday.

Ship To:Cincinnati Children's
Hospital Medical Center

Attn: Heart Institute Diagnostic Lab

240 Albert Sabin Way,
Room S4.381

Cincinnati, OH 45229-3039

***SURF1* Sequencing**

The *SURF1* gene encodes a protein that is important for the proper assembly and function of cytochrome c oxidase (COX, the complex of proteins that form Complex IV of the electron transport chain). The electron transport chain contains five large multi-subunit protein complexes that are important for the generation of energy in the form of ATP. The fourth complex of the electron transport chain, cytochrome c oxidase, is comprised of 13 subunits that are located within the inner mitochondrial membrane. Three of these subunits, which form the catalytic core of the complex, are encoded by mitochondrial DNA, while the remaining ten subunits are encoded by nuclear DNA. This complex cannot assemble correctly without *SURF1*. Mutations in the *SURF1* gene are the most common cause of Leigh syndrome with COX deficiency. The mutations are autosomal recessive and include nonsense, missense, and small insertion/deletion mutations. There is a common 2bp deletion 845-846delCT that is found in a high percentage of patients with Leigh disease. The *SURF1* gene contains 9 exons and is located at chromosome 9q34.

Clinically, patients with *SURF1* mutations commonly present in infancy. Leigh disease, a heterogeneous condition with progressive neurological symptoms, hypotonia, lactic acidosis, and characteristic findings on brain imaging, is the most common presentation. Seizures, strabismus, or ptosis may be present along with failure to thrive. COX activity is generally decreased or absent by histochemical staining or electron transport chain analysis and life expectancy is decreased. In patients with Leigh disease and COX deficiency, mutations in *SURF1* account for approximately 26% of cases.

Indication

Molecular confirmation of the diagnosis of Leigh syndrome or COX deficiency resulting from *SURF1* mutations.

Methodology:

All 9 exons of the *SURF1* gene, as well as the exon/intron boundaries and a portion of untranslated regions of the gene are amplified by PCR. Genomic DNA sequences from both forward and reverse directions are obtained by automatic fluorescent detection using an *ABI PRISM® 3730 DNA Analyzer*. Sequence variants different from National Center for Biotechnology Information GenBank references are further evaluated for genetic significance. If a mutation is identified, known familial mutation analysis will be available for additional family members.

Sensitivity & Accuracy:

Greater than 98.5% of the mutations in exon 2 of *SURF1* are detectable by sequence based methods. Sequencing does not detect deletions or duplications.

References:

1. Bohm M, Pronicka E, Karczarewicz E, Pronicki M, Piekutowska-Abramczuk D, Sykut-Cegielska J, Mierzewska H, Hansikova H, Vesela K, Tesarova M, Houstkova H, Houstek J, Zeman J. Retrospective, multicentric study of 180 children with cytochrome C oxidase deficiency. *Pediatric Research*. 2006;59:21-26.
2. Head RA, Brown RM, Brown GK. Diagnostic difficulties with common *SURF1* mutations in patients with cytochrome oxidase-deficient Leigh syndrome. *Journal of inherited metabolic disease*. 2004;27:57-65.
3. Piekutowska-Abramczuk D, Magner M, Popowska E, Pronicki M, Karczarewicz E, Sykut-Cegielska J, Kmiec T, Jurkiewicz E, Szymanska-Debinska T, Bielecka L, Krajewska-Walasek M, Vesela K, Zeman J, Pronicka E. *SURF1* missense mutations promote a mild Leigh phenotype. *Clinical Genetics*. 2009;76:195-204.

Specimen:

Peripheral blood in EDTA tube

Adult: 5-10mL

Child: 3-5mL

Infant: 1-3mL

For other specimen types, please contact Amy Shikany at 513-803-3317

Turnaround Time:

Full Mutation Analysis 2-4 weeks

Known Mutation Analysis 1-2 weeks

CPT Codes:

Full Gene Sequencing 81479

Additional Family Members 81403