Cincinnati Children's
Heart Institute

Heart Institute Diagnostic Lab
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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

SCO2 Sequencing

The *SCO2* gene encodes a protein that is important for regulating the copper level of a cell. It is also required 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 *SCO2*. Mutations in the *SCO2* gene product are one cause of Leigh syndrome. Mutations in *SCO2* have been identified in patients with fatal, infantile hypertrophic cardiomyopathy with encephalopathy. The mutations are autosomal recessive and include nonsense, missense, and small duplication mutations. The *SCO2* gene contains 2 exons and is located at chromosome 22q13.33.

Clinically, patients with *SCO2* mutations commonly present in infancy. Common symptoms include rapidly progressive hypertrophic cardiomyopathy, hypotonia, stridor and/or respiratory distress, and mild to moderate lactic acidosis. Seizures, strabismus, or ptosis may be present along with failure to thrive. A spinal muscular atrophy-like phenotype has been described. COX activity is generally decreased or absent by histochemical staining or electron transport chain analysis, but this is not an invariable finding. Children usually die within the first year of life. In patients with COX deficiency, mutations in *SCO2* account for approximately 5% of cases.

Indication

Molecular confirmation of the diagnosis of severe infantile hypertrophic cardiomyopathy and/or encephalopathy resulting from *SCO2* mutations.

Methodology:

Exon 2, the only protein coding exon of the *SCO2* 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 *SCO2* are detectable by sequence based methods. Sequencing does not detect deletions or duplications.

References:

1. Bohm M, Pronicka E, Karczmarewicz 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. Jaksch M, Horvath R, Horn N, Auer DP, Macmillan C, Peters J, Gerbitz KD, Kraegeloh-Mann I, Muntau A, Karcagi V, Kalmanchey R, Lochmuller H, Shoubridge EA, Freisinger P. Homozygosity (e140k) in *SCO2* causes delayed infantile onset of cardiomyopathy and neuropathy. *Neurology*. 2001;57:1440-1446.
3. Papadopoulou LC, Sue CM, Davidson MM, Tanji K, Nishino I, Sadlock JE, Krishna S, Walker W, Selby J, Glerum DM, Coster RV, Lyon G, Scalais E, Lebel R, Kaplan P, Shanske S, De Vivo DC, Bonilla E, Hirano M, DiMauro S, Schon EA. Fatal infantile cardioencephalomyopathy with cox deficiency and mutations in *SCO2*, a cox assembly gene. *Nature Genetics*. 1999;23:333-337.

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