

FATAL INFANTILE CARDIOENCEPHALOMYOPATHY DUE TO CYTOCHROME C OXIDASE DEFICIENCY SCO2 GENE SEQUENCING

Cytochrome c oxidase (COX), also known as Complex IV, is the terminal enzyme of the mitochondrial respiratory chain. Deficiency of this enzyme can have a wide range of effects, from isolated myopathy to severe multisystem disease, with onset from infancy to adulthood. COX deficiency can be caused by mutations in several nuclear-encoded and mitochondrial-encoded genes. When caused by mutations in the *SCO2* gene (OMIM 604272), COX deficiency is associated with fatal infantile cardioencephalomyopathy (OMIM 604377), an autosomal recessive disorder.

Fatal infantile cardioencephalomyopathy is characterized by hypertrophic cardiomyopathy, encephalopathy, lactic acidosis, hypotonia, respiratory distress and/or stridor, developmental delay, spasticity or seizures, and decreased extraocular movements. Muscle biopsy shows COX deficiency and neurogenic changes.

Fatal infantile cardioencephalomyopathy can also present with a phenotype resembling spinal muscular atrophy (SMA), including hypotonia, respiratory distress, and SMA-like changes in the muscle and/or spinal cord (Pronicki, 2010; Salviati, 2002; Tarnopolsky, 2004). Heart involvement is not necessarily present at the onset of the disease.

All patients reported in the literature have been identified as either homozygotes for the common E140K mutation, or compound heterozygotes with E140K and another mutation. Homozygous E140K mutations are reported as having a delayed onset and slower clinical progression (Salviati, 2002).

Testing:

Testing is performed by sequencing the entire coding region (exon 2) and surrounding intronic regions of *SCO2*. This will detect point mutations, small deletions, and small insertions. It will not detect a partial or whole gene deletion or duplication.

Turnaround time: 10 - 14 business days

CPT codes and cost: 81479: \$ 200

BILLING: *We do not bill third party payers (insurance companies)* for samples received from external sources. **The person or institution(e.g., Clinical Lab; Send-out Lab; Physician Office) sending the sample is responsible for full payment of the invoices within 30 days of receipt of the invoice.** If the patient is on Medical assistance, please contact the lab **prior** to sample submission. Direct patient billing will be accepted **only** when a valid credit card form is received with the patient sample.

Online Resources

United Mitochondrial Disease Foundation – <http://www.umdf.org>

Fatal Infantile Cardioencephalomyopathy on OMIM - <http://www.ncbi.nlm.nih.gov/omim/604377>

SCO2 gene on OMIM - <http://www.ncbi.nlm.nih.gov/omim/604272>

References:

Pronicki M, et al. A homozygous mutation in the SCO2 gene causes a spinal muscular atrophy like presentation with stridor and respiratory insufficiency. Eur J Paediatr Neurol. 2010;14(3):253-60.

Salviati L, et al. Cytochrome c oxidase deficiency due to a novel SCO2 mutation mimics Werdnig-Hoffmann disease. Arch Neurol. 2002;59(5):862-5.

Tarnopolsky MA, et al. Novel SCO2 mutation (G1521A) presenting as a spinal muscular atrophy type I phenotype. Am J Med Genet A. 2004;125A(3):310-4.



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Molecular Diagnostic Laboratory

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Card holder signature:	Authorized payment amount:

For Direct Patient Billing

Prepayment for the testing services is required prior to beginning our testing. Please complete this form and include this paperwork with the shipment of the patient sample.

Billing questions can be addressed to: Denise Axsmith
Senior Budget/Financial Analyst
Nemours/A.I. duPont Hospital for Children
daxsmith@nemours.org
Phone: 302.651.6802
Fax: 302.651.6881