

MITO PROFILE

COMPLEX 1 INFORMATION

PROVIDED BY THE UNITED MITOCHONDRIAL DISEASE FOUNDATION

Complex 1 Deficiency or NADH-quinone oxidoreductase deficiency, NADH:Q (1) oxidoreductase deficiency, NADH-Coenzyme Q Reductase Deficiency

Inside the mitochondrion is a group of proteins that carry electrons along four chain reactions (Complexes I-IV), resulting in energy production. This chain is known as the Electron Transport Chain. A fifth group (Complex V) churns out the ATP. Together, the electron transport chain and the ATP synthase form the respiratory chain and the whole process is known as oxidative phosphorylation or OXPHOS.

Complex I, the first step in this chain, is the most common site for mitochondrial abnormalities, representing as much as one third of the respiratory chain deficiencies. Often presenting at birth or in early childhood, Complex I deficiency is usually a progressive neuro-degenerative disorder and is responsible for a variety of clinical symptoms, particularly in organs and tissues that require high energy levels, such as brain, heart, liver, and skeletal muscles. A number of specific mitochondrial disorders have been associated with Complex I deficiency including: Leber's hereditary optic neuropathy (LHON), MELAS, MERRF, and Leigh Syndrome (LS).

There are three major forms of Complex I deficiency:

- 1) Fatal infantile multisystem disorder – characterized by poor muscle tone, developmental delay, heart disease, lactic acidosis, and respiratory failure.
- 2) Myopathy (muscle disease) – starting in childhood or adulthood, and characterized by weakness or exercise intolerance.
- 3) Mitochondrial encephalomyopathy (brain and muscle disease) – beginning in childhood or adulthood and involving variable symptom combinations which may include: eye muscle paralysis, pigmentary retinopathy (retinal color changes with loss of vision), hearing loss, sensory neuropathy (nerve damage involving the sense organs), seizures, dementia, ataxia (abnormal muscle coordination), and involuntary movements. This form of Complex I deficiency may cause Leigh Syndrome and MELAS.

Most cases of Complex I deficiency result from autosomal recessive inheritance (combination of defective nuclear genes from both the mother and the father). Less frequently, the disorder is maternally inherited or sporadic and the genetic defect is in the mitochondrial DNA.

As with all mitochondrial diseases, there is no cure for Complex I deficiency. A variety of treatments, which may or may not be effective, can include such metabolic therapies as: riboflavin, thiamine, biotin, co-enzyme Q10, carnitine, and the ketogenic diet. Therapies for the infantile multisystem form have been unsuccessful.

The clinical course and prognosis for Complex I patients is highly variable and may depend on the specific genetic defect, age of onset, organs involved, and other factors.

RESOURCES FOR COMPLEX I INFORMATION

Mitochondrial Complex I Deficiency, OMIM article

Available through UMDF website www.umdf.org, then *Mito Info*, then *disease descriptions*. Click on *Complex I* and follow the links for other resources.

Complex I Home Page - <http://www.scripps.edu/mem/biochem/CI/> (also available through UMDF website link)

Mitochondrial Pathways, Oxidative Phosphorylation Neuromuscular Disease Center, Washington University, St. Louis, Missouri

<http://www.neuro.wustl.edu/neuromuscular/pathol/diagrams/mito.htm>

Facts about Mitochondrial Myopathies, MDA Publications. Available through UMDF website www.umdf.org, then *Library*, then *Various pdf articles*

Numerous "Ask the Mito Doc" Complex I questions and answers can be found via the UMDF website www.umdf.org, then *Mito Doc* link