MT-ND1 gene
mitochondrially encoded NADH:ubiquinone oxidoreductase core subunit 1

Normal Function

The *MT-ND1* gene provides instructions for making a protein called NADH dehydrogenase 1. This protein is part of a large enzyme complex known as complex I, which is active in mitochondria. Mitochondria are structures within cells that convert the energy from food into a form that cells can use. These cellular structures produce energy through a process called oxidative phosphorylation, which uses oxygen and simple sugars to create adenosine triphosphate (ATP), the cell's main energy source.

Complex I is one of several enzyme complexes necessary for oxidative phosphorylation. Within mitochondria, these complexes are embedded in a tightly folded, specialized membrane called the inner mitochondrial membrane. During oxidative phosphorylation, mitochondrial enzyme complexes carry out chemical reactions that drive the production of ATP. Specifically, they create an unequal electrical charge on either side of the inner mitochondrial membrane through a step-by-step transfer of negatively charged particles called electrons. This difference in electrical charge provides the energy for ATP production.

Complex I is responsible for the first step in the electron transport process, the transfer of electrons from a molecule called NADH to another molecule called ubiquinone. Electrons are then passed from ubiquinone through several other enzyme complexes to provide energy for the generation of ATP.

Health Conditions Related to Genetic Changes

Leber hereditary optic neuropathy

Several mutations in the *MT-ND1* gene are known to cause Leber hereditary optic neuropathy. Each of these mutations changes a single DNA building block (nucleotide) in the gene. One common *MT-ND1* mutation is responsible for about 13 percent of all cases of Leber hereditary optic neuropathy. This mutation replaces the nucleotide guanine with the nucleotide adenine at gene position 3460 (written as G3460A). This change is associated with moderately severe cases of Leber hereditary optic neuropathy; however, 20 percent to 40 percent of people with vision loss due to this mutation experience some recovery of vision.

Researchers are investigating how mutations in the *MT-ND1* gene lead to Leber hereditary optic neuropathy. These genetic changes appear to disrupt the normal activity of complex I in the mitochondrial inner membrane, which may affect the generation of ATP. *MT-ND1* mutations also may increase the production within mitochondria of potentially harmful molecules called reactive oxygen species. It
remains unclear, however, why the effects of these mutations are often limited to
the nerve that relays visual information from the eye to the brain (the optic nerve).
Additional genetic and environmental factors probably contribute to the vision loss
and other medical problems associated with Leber hereditary optic neuropathy.

Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes

*MT-ND1* mutations are a rare cause of mitochondrial encephalomyopathy, lactic
acidosis, and stroke-like episodes (MELAS). Most cases of MELAS are caused by
mutations in other mitochondrial genes, but a small number of cases resulting from
mutations in the *MT-ND1* gene have been reported. Fewer than five mutations,
each of which alters a single DNA building block (nucleotide) in the gene, have
been identified in affected individuals. These genetic changes reduce the activity
of complex I, which disrupts energy production within mitochondria. Although these
abnormalities have the greatest impact on tissues that require a lot of energy (such
as the brain and muscles), researchers have not determined how changes in the *MT-
ND1* gene lead to the specific signs and symptoms of MELAS.

Leigh syndrome

Mitochondrial complex I deficiency

Other disorders

A mutation in the *MT-ND1* gene has been reported in a few cases of adult-onset
dystonia. Dystonia is a movement disorder that involves involuntary tensing of the
muscles (muscle contractions), tremors, and other uncontrolled movements. The *MT-
ND1* mutation associated with these rare cases replaces the nucleotide adenine with
the nucleotide guanine at gene position 3796 (written as A3796G). Further studies
are needed to determine whether this genetic change combines with other genetic
and environmental factors to increase the risk of developing adult-onset dystonia.
Chromosomal Location

Other Names for This Gene

- mitochondrially encoded NADH dehydrogenase 1
- MTND1
- NADH dehydrogenase 1
- NADH dehydrogenase subunit 1
- NADH-ubiquinone oxidoreductase chain 1
- NADH-ubiquinone oxidoreductase, subunit ND1
• ND1
• NU1M_HUMAN

Additional Information & Resources

Educational Resources
• Mayo Clinic: North American Mitochondrial Disease Consortium Patient Registry and Biorepository (NAMDC) https://www mayo.edu/research/clinical-trials/cls-20409244
• The Neuromuscular Disease Center at Washington University: Complex I https://neuromuscular.wustl.edu/pathol/diagrams/mito.htm#complexI

Clinical Information from GeneReviews
• Leber Hereditary Optic Neuropathy https://www.ncbi.nlm.nih.gov/books/NBK1174
• MELAS https://www.ncbi.nlm.nih.gov/books/NBK1233
• Mitochondrial Disorders Overview https://www.ncbi.nlm.nih.gov/books/NBK1224

Scientific Articles on PubMed
• PubMed https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28MT-ND1%5BTIAB%5D %29+OR+%28mitochondrially+encoded+NADH+dehydrogenase+1%5BTIAB%5D %29%29+OR+%28%28MTND1%5BTIAB%5D%29+OR+%28NADH+dehydrogenase+subunit+1%5BTIAB%5D%29+OR+%28NADH+ubiquinone+oxidoreductase+chain+1%5BTIAB%5D %29+OR+%28NADH-ubiquinone+oxidoreductase,+subunit+ND1%5BTIAB%5D %29+OR+%28ND1%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D %29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla% 5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM
• COMPLEX I, SUBUNIT ND1 http://omim.org/entry/516000
Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_ND1.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=MT-ND1%5Bgene%5D
- HGNC Gene Symbol Report
- Mitomap: Coding and control region mutations
  https://www.mitomap.org/MITOMAP/MutationsCodingControl
- Mitomap: Leber hereditary optic neuropathy disease mutation database
  https://www.mitomap.org/MITOMAP/MutationsLHON
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:4535
- NCBI Gene
- UniProt
  https://www.uniprot.org/uniprot/P03886

Sources for This Summary

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Reviewed: November 2006
Published: July 16, 2019

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