MT-ND5 gene
mitochondrially encoded NADH:ubiquinone oxidoreductase core subunit 5

Normal Function

The MT-ND5 gene provides instructions for making a protein called NADH dehydrogenase 5. 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

Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes

Mutations in the MT-ND5 gene are responsible for a small percentage of all cases of mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS). These mutations alter single DNA building blocks (nucleotides) in the gene. A particular mutation has been identified in at least five people with the characteristic features of MELAS; this mutation replaces the nucleotide guanine with the nucleotide adenine at gene position 13513 (written as G13513A). Most of the MT-ND5 mutations that cause MELAS have been shown to 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-ND5 gene lead to the specific signs and symptoms of MELAS.

Mutations in the MT-ND5 gene also have been identified in patients with the major features of MELAS in combination with other mitochondrial diseases. For example,
researchers have found MT-ND5 mutations in several individuals with the signs of MELAS and some features of Leigh syndrome, a progressive brain disorder that typically appears in infancy or early childhood. In other cases, people with MELAS and a change in the MT-ND5 gene have developed sudden, progressive vision loss characteristic of an eye disease called Leber hereditary optic neuropathy. A few individuals have been reported with signs and symptoms of all three of these mitochondrial conditions—MELAS, Leigh syndrome, and Leber hereditary optic neuropathy.

It is unclear why changes in the MT-ND5 gene can cause such a large variety of signs and symptoms. Even within a single family, affected individuals may have different health problems caused by the same genetic change.

Leigh syndrome

Mitochondrial complex I deficiency

Other disorders

Mutations in the MT-ND5 gene have been identified in at least 10 people with Leigh syndrome. Children with this condition may experience vomiting, seizures, delayed development, muscle weakness, and problems with movement. Heart disease, kidney problems, and difficulty breathing can also occur in people with this disorder. A few affected children with MT-ND5 mutations have had additional features that are not typical of Leigh syndrome, including slow growth before birth (intrauterine growth retardation) and distinctive facial features.

The MT-ND5 mutations responsible for Leigh syndrome change single nucleotides in the gene. These genetic changes disrupt the activity of complex I, impairing the ability of mitochondria to produce energy. It is not known, however, how mutations in the MT-ND5 gene are related to the specific features of Leigh syndrome.
Chromosomal Location
Molecular Location: base pairs 12,337 to 14,148 on mitochondrial DNA (Homo sapiens Annotation Release 109, GRCh38.p12) (NCBI)

Other Names for This Gene
• mitochondrially encoded NADH dehydrogenase 5
• MTND5
• NADH dehydrogenase subunit 5
• NADH-ubiquinone oxidoreductase chain 5
• NADH-ubiquinone oxidoreductase, subunit ND5
• NADH5
• ND5
• NU5M_HUMAN

Additional Information & Resources

Educational Resources
• Basic Neurochemistry (sixth edition, 1999): Diseases of Mitochondrial Metabolism
  https://www.ncbi.nlm.nih.gov/books/NBK27914/
• Biochemistry (fifth edition, 2002): Oxidative Phosphorylation
  https://www.ncbi.nlm.nih.gov/books/NBK21208/
• Mayo Clinic Mitochondrial Disease Biobank
  https://www.mayo.edu/research/centers-programs/mitochondrial-disease-biobank/overview
• The Neuromuscular Disease Center at Washington University: Complex I
  https://neuromuscular.wustl.edu/pathol/diagrams/mito.htm#complexI

Clinical Information from GeneReviews
• MELAS
  https://www.ncbi.nlm.nih.gov/books/NBK1233
• Mitochondrial Disorders Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1224
• Mitochondrial DNA-Associated Leigh Syndrome and NARP
  https://www.ncbi.nlm.nih.gov/books/NBK1173

Scientific Articles on PubMed
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  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28MT-ND5%5BTIAB%5D%29+OR+%28mitochondrially+encoded+NADH+dehydrogenase+5%5BTIAB%5D%29+OR+%28%28MTND5%5BTIAB%5D%29+OR+%28NADH+dehydrogenase+subunit+5%5BTIAB%5D%29+OR+%28NADH5%5BTIAB%5D%29+OR+%28ND5%5BTIAB%5D%29+OR+%28NADH-ubiquinone+oxidoreductase+chain+5%5BTIAB%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29+OR+%28Human%5Bmh%5D+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1440+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM
• COMPLEX I, SUBUNIT ND5
  http://omim.org/entry/516005
• LEIGH SYNDROME
  http://omim.org/entry/256000
Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_ND5.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=MT-ND5%5Bgene%5D
- HGNC Gene Family: NADH:ubiquinone oxidoreductase core subunits
  https://www.genenames.org/cgi-bin/genefamilies/set/1149
- HGNC Gene Symbol Report
  https://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=7461
- Mitomap: Coding and Control Region Mutations
  https://www.mitomap.org/MITOMAP/MutationsCodingControl
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:4540
- NCBI Gene
- UniProt
  https://www.uniprot.org/uniprot/P03915

Sources for This Summary

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  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11198278
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