MT-ND5 gene

mitochondrially encoded NADH dehydrogenase 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

Leigh syndrome

Variants (also called mutations) in the *MT-ND5* gene have been identified a few 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 children with Leigh syndrome caused by *MT-ND5* gene variants 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* gene variants responsible for Leigh syndrome change single DNA building

blocks (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 variants in the *MT-ND5* gene are related to the specific features of Leigh syndrome.

Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes

Variants in the *MT-ND5* gene are responsible for a small percentage of all cases of mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS). This condition affects many of the body's systems, particularly the brain and nervous system (encephalo-) and muscles (myopathy).

The *MT-ND5* gene variants that cause MELAS alter single nucleotides in the gene. Most people with MELAS caused by MT-ND5 gene variants have the variant that replaces the nucleotide guanine with the nucleotide adenine at gene position 13513 (written as G13513A).

Most commonly, *MT-ND5* gene variants 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.

Variants 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* gene variants 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.

Mitochondrial complex I deficiency

MedlinePlus Genetics provides information about Mitochondrial complex I deficiency

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

Tests Listed in the Genetic Testing Registry

- Tests of MT-ND5 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=4540[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28MT-ND5%5BTIAB%5D%29+OR+%28mitochondrially+encoded+NADH+dehydrogenase+5%5BTIAB%5D%29%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%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+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; MTND5 (https://omim.org/entry/516005)
- LEIGH SYNDROME, NUCLEAR; NULS (https://omim.org/entry/256000)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/4540)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=MT-ND5[gene])

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Genomic Location

The *MT-ND5* gene is found on mitochondrial DNA (https://medlineplus.gov/genetics/chromosome/mitochondrial-dna/).

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