MT-ND6 gene

mitochondrially encoded NADH dehydrogenase 6

Normal Function

The *MT-ND6* gene provides instructions for making a protein called NADH dehydrogenase 6. 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 variants (also called mutations) in the *MT-ND6* gene have been identified in people with Leber hereditary optic neuropathy. This condition is an inherited form of vision loss. Each of the MT-ND6 gene variants changes a single protein building block (amino acid) in the NADH dehydrogenase 6 protein. One common *MT-ND6* gene variant is responsible for about 14 percent of all cases of Leber hereditary optic neuropathy, and it is the most common cause of this disorder among people of French Canadian descent. This genetic change, written as T14484C or Met64Val, replaces the amino acid methionine with the amino acid valine at protein position 64. The T14484C variant is associated with a good long-term prognosis; affected people with this genetic change

have a 37 percent to 65 percent chance of some visual recovery.

Researchers are investigating how variants in the *MT-ND6* gene lead to Leber hereditary optic neuropathy. These genetic changes appear to prevent complex I from interacting normally with ubiquinone, which may affect the generation of ATP.

Variants another gene called *MT-ND4* may also increase the production within mitochondria of potentially harmful molecules called reactive oxygen species. It remains unclear, however, why the effects of these variants 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.

Leigh syndrome

A variant in the *MT-ND6* gene also has been identified in a small number of people with Leigh syndrome, a progressive brain disorder that typically appears in infancy or early childhood. Affected children 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 Leigh syndrome.

The *MT-ND6* gene variant that can cause Leigh syndrome, written as G14459A or Ala72Val, replaces the amino acid alanine with the amino acid valine at protein position 72. This genetic change also has been found in people with Leber hereditary optic neuropathy and a movement disorder called dystonia, which involves involuntary muscle contractions, tremors, and other uncontrolled movements. This variant appears to disrupt the normal assembly or activity of complex I in mitochondria. It is not known, however, how this *MT-ND6* gene alteration is related to the specific features of Leigh syndrome, Leber hereditary optic neuropathy, or dystonia. It also remains unclear why a single variant can cause such varied signs and symptoms in different people.

Mitochondrial complex I deficiency

MedlinePlus Genetics provides information about Mitochondrial complex I deficiency

Other Names for This Gene

- mitochondrially encoded NADH dehydrogenase 6
- MTND6
- NADH dehydrogenase 6
- NADH dehydrogenase subunit 6
- NADH-ubiquinone oxidoreductase chain 6
- NADH-ubiquinone oxidoreductase, subunit ND6
- ND6
- NU6M_HUMAN

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of MT-ND6 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=4541[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28MT-ND6%5BTIAB%5D%29+OR+%28mitochondrially+encoded+NADH+dehydrogenase+6%5BTIAB%5D%29%29+OR+%28%28MTND6%5BTIAB%5D%29+OR+%28NADH+dehydrogenase+subunit+6%5BTIAB%5D%29+OR+%28NADH+dehydrogenase+6%5BTIAB%5D%29+OR+%28NADH-ubiquinone+oxidoreductase+chain+6%5BTIAB%5D%29+OR+%28NADH-ubiquinone+oxidoreductase,+subunit+ND6%5BTIAB%5D%29+OR+%28ND6%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+1080+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- COMPLEX I, SUBUNIT ND6; MTND6 (https://omim.org/entry/516006)
- LEIGH SYNDROME; LS (https://omim.org/entry/256000)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/4541)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=MT-ND6[gene])

References

- Baracca A, Solaini G, Sgarbi G, Lenaz G, Baruzzi A, Schapira AH, Martinuzzi A, Carelli V. Severe impairment of complex I-driven adenosine triphosphate synthesisin leber hereditary optic neuropathy cybrids. Arch Neurol. 2005 May;62(5):730-6.doi: 10.1001/archneur.62.5.730. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/15883259)
- Carelli V, Ghelli A, Bucchi L, Montagna P, De Negri A, Leuzzi V, Carducci C,Lenaz G, Lugaresi E, Degli Esposti M. Biochemical features of mtDNA 14484(ND6/M64V) point mutation associated with Leber's hereditary optic neuropathy.Ann Neurol. 1999 Mar;45(3):320-8. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/10072046)
- Chinnery PF, Andrews RM, Turnbull DM, Howell NN. Leber hereditary opticneuropathy: Does heteroplasmy influence the inheritance and expression of theG11778A mitochondrial DNA mutation? Am J Med Genet. 2001 Jan 22;98(3):235-43.doi: 10.1002/1096-8628(20010122)98:33.0.co;2-o. Citation on PubMed (https://p

ubmed.ncbi.nlm.nih.gov/11169561)

- Fauser S, Leo-Kottler B, Besch D, Luberichs J. Confirmation of the 14568mutation in the mitochondrial ND6 gene as causative in Leber's hereditary opticneuropathy. Ophthalmic Genet. 2002 Sep;23(3):191-7. doi:10.1076/opge.23.3.191.7881. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/12324878)
- Gropman A, Chen TJ, Perng CL, Krasnewich D, Chernoff E, Tifft C, Wong LJ. Variable clinical manifestation of homoplasmic G14459A mitochondrial DNAmutation. Am J Med Genet A. 2004 Feb 1;124A(4):377-82. doi: 10.1002/ajmg.a.20456. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/14735585)
- Huoponen K. Leber hereditary optic neuropathy: clinical and molecular geneticfindings. Neurogenetics. 2001 Jul;3(3):119-25. doi: 10.1007/s100480100115. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/11523562)
- Kirby DM, Kahler SG, Freckmann ML, Reddihough D, Thorburn DR. Leigh diseasecaused by the mitochondrial DNA G14459A mutation in unrelated families. AnnNeurol. 2000 Jul;48(1):102-4. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/10894222)
- Lenaz G, Baracca A, Carelli V, D'Aurelio M, Sgarbi G, Solaini G. Bioenergeticsof mitochondrial diseases associated with mtDNA mutations. Biochim Biophys Acta.2004 Jul 23;1658(1-2):89-94. doi: 10.1016/j.bbabio.2004.03.013. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/15282179)
- Mitchell AL, Elson JL, Howell N, Taylor RW, Turnbull DM. Sequence variation inmitochondrial complex I genes: mutation or polymorphism? J Med Genet. 2006Feb;43(2):175-9. doi: 10.1136/jmg.2005.032474. Epub 2005 Jun 21. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/15972314) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2564640/)
- Tarnopolsky MA, Baker SK, Myint T, Maxner CE, Robitaille J, Robinson BH.Clinical variability in maternally inherited leber hereditary optic neuropathywith the G14459A mutation. Am J Med Genet A. 2004 Feb 1;124A(4):372-6. doi:10.1002/ajmg.a.20449. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/14735584)
- Valentino ML, Avoni P, Barboni P, Pallotti F, Rengo C, Torroni A, Bellan M,Baruzzi A, Carelli V. Mitochondrial DNA nucleotide changes C14482G and C14482A inthe ND6 gene are pathogenic for Leber's hereditary optic neuropathy. Ann Neurol. 2002 Jun;51(6):774-8. doi: 10.1002/ana.10193. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/12112086)

Genomic Location

The *MT-ND6* gene is found on mitochondrial DNA (https://medlineplus.gov/genetics/chromosome/mitochondrial-dna/).

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