MT-ND4L gene

mitochondrially encoded NADH 4L dehydrogenase

Normal Function

The *MT-ND4L* gene provides instructions for making a protein called NADH dehydrogenase 4L. 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

A mutation in the *MT-ND4L* gene has been identified in several families with Leber hereditary optic neuropathy. This mutation, which can be written as T10663C or Val65Ala, changes a single protein building block (amino acid) in the NADH dehydrogenase 4L protein. Specifically, it replaces the amino acid valine with the amino acid alanine at protein position 65.

Researchers have not determined how a mutation in the *MT-ND4L* gene can lead to the vision loss characteristic of Leber hereditary optic neuropathy. This genetic change appears to disrupt the normal activity of complex I in the mitochondrial inner membrane,

which may affect the production of ATP. It remains unclear, however, why the effects of this mutation are 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 features of Leber hereditary optic neuropathy.

Mitochondrial complex I deficiency

MedlinePlus Genetics provides information about Mitochondrial complex I deficiency

Other Names for This Gene

- Complex I, subunit ND4L
- mitochondrially encoded NADH 4L
- mitochondrially encoded NADH dehydrogenase 4L
- MTND4L
- NADH dehydrogenase 4L
- NADH dehydrogenase subunit 4L
- NADH-ubiquinone oxidoreductase chain 4L
- NADH-ubiquinone oxidoreductase, subunit ND4L
- NADH4L
- ND4L
- NU4LM_HUMAN

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of MT-ND4L (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=4539[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28MT-ND4L%5BTIAB%5D%29+OR+%28mitochondrially+encoded+NADH+4L%5BTIAB%5D%29%29+OR+%28%28MTND4L%5BTIAB%5D%29+OR+%28NADH+dehydrogenase+subunit+4L%5BTIAB%5D%29+OR+%28Complex+I,+subunit+ND4L%5BTIAB%5D%29+OR+%28NADH+dehydrogenase+4L%5BTIAB%5D%29+OR+%28NADH-ubiquinone+oxidoreductase+chain+4L%5BTIAB%5D%29+OR+%28NADH-ubiquinone+oxidoreductase,+subunit+ND4L%5BTIAB%5D%29+OR+%28NADH4L%5BTIAB%5D%29+OR+%28ND4L%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+3600+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- COMPLEX I, SUBUNIT ND4L; MTND4L (https://omim.org/entry/516004)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/4539)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=MT-ND4L[gene])

References

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- 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/)
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- Yu-Wai-Man P, Chinnery PF. Leber Hereditary Optic Neuropathy. 2000 Oct 26[updated 2021 Mar 11]. In: Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE,Bean LJH, Gripp KW, Amemiya A, editors. GeneReviews(R) [Internet].Seattle (WA): University of Washington, Seattle; 1993-2024. Available fromhttp://www.ncbi. nlm.nih.gov/books/NBK1174/ Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/ 20301353)

Genomic Location

The *MT-ND4L* gene is found on mitochondrial DNA (https://medlineplus.gov/genetics/chromosome/mitochondrial-dna/).

Last updated August 1, 2006