MT-ATP6 gene

mitochondrially encoded ATP synthase 6

Normal Function

The *MT-ATP6* gene provides information for making a protein that is essential for normal mitochondrial function. 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.

The MT-ATP6 protein forms one part (subunit) of a large enzyme called ATP synthase. This enzyme, which is also known as complex V, is responsible for the final step of oxidative phosphorylation. Specifically, one segment of ATP synthase allows positively charged particles, called protons, to flow across a specialized membrane inside mitochondria. Another segment of the enzyme uses the energy created by this proton flow to convert a molecule called adenosine diphosphate (ADP) to ATP.

Health Conditions Related to Genetic Changes

Leigh syndrome

Mutations in the *MT-ATP6* gene have been found in approximately 10 percent of people with Leigh syndrome. Leigh syndrome is a progressive brain disorder that usually appears in infancy or early childhood. Affected children may experience delayed development, muscle weakness, problems with movement, or difficulty breathing.

MT-ATP6 gene mutations associated with Leigh syndrome change one DNA building block (nucleotide) in the *MT-ATP6* gene. The most common genetic change replaces the nucleotide thymine with the nucleotide guanine at position 8993 (written as T8993G). The mutations that cause Leigh syndrome impair the function or stability of the ATP synthase complex, inhibiting ATP production and impairing oxidative phosphorylation.

Although the exact mechanism is unclear, researchers believe that impaired oxidative phosphorylation can lead to cell death because of decreased energy available in the cell. Certain tissues that require large amounts of energy, such as the brain, muscles, and heart, seem especially sensitive to decreases in cellular energy. Cell death in the brain and in other sensitive tissues likely cause the characteristic signs and symptoms of Leigh syndrome.

Mitochondrial complex V deficiency

MedlinePlus Genetics provides information about Mitochondrial complex V deficiency

Neuropathy, ataxia, and retinitis pigmentosa

Some of the mutations that cause Leigh syndrome are also responsible for a similar, but less severe, condition called neuropathy, ataxia, and retinitis pigmentosa (NARP). A small number of mutations in the *MT-ATP6* gene have been identified in people with NARP. Each of these mutations changes one nucleotide in the *MT-ATP6* gene. As in Leigh syndrome, the most common genetic change associated with NARP replaces the nucleotide thymine with the nucleotide guanine at position 8993 (written as T8993G). The mutations that cause NARP alter the structure or function of ATP synthase, reducing the ability of mitochondria to produce ATP. Although the precise effects of these mutations are unclear, researchers continue to investigate how changes in the *MT-ATP6* gene interfere with ATP production and lead to muscle weakness, vision loss, and the other features of NARP.

Most of the body's cells contain thousands of mitochondria, each with one or more copies of mitochondrial DNA. The severity of some mitochondrial disorders is associated with the percentage of mitochondria in each cell that has a particular genetic change. People with Leigh syndrome due to an *MT-ATP6* gene mutation tend to have a very high percentage of mitochondria with the mutation (from more than 90 percent to 95 percent). The less-severe features of NARP result from a lower percentage of mitochondria with the mutation, typically 70 percent to 90 percent. Because these two conditions result from the same genetic changes and can occur in different members of a single family, researchers believe that they may represent a spectrum of overlapping features instead of two distinct syndromes.

Charcot-Marie-Tooth disease

MedlinePlus Genetics provides information about Charcot-Marie-Tooth disease

Other disorders

A condition called familial bilateral striatal necrosis, which is similar to Leigh syndrome (described above), can also result from changes in the *MT-ATP6* gene. In the few reported cases with these mutations, affected children have delayed development, problems with movement and coordination, weak muscle tone (hypotonia), and an unusually small head size (microcephaly). Researchers have not determined why *MT-ATP6* mutations result in this combination of signs and symptoms in children with bilateral striatal necrosis.

Other Names for This Gene

- ATP synthase 6
- ATP synthase F0 subunit 6
- ATP6

- ATP6_HUMAN
- ATPase protein 6
- ATPase-6
- ATPASE6
- mitochondrially encoded ATP synthase 6
- MTATP6
- Su6m

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of MT-ATP6 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=4508[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28MT-ATP6%5BTIAB%5D%29+OR+%28%28MTATP6%5BTIAB%5D%29+OR+%28ATP+synthase+F0+subunit+6%5BTIAB%5D%29+OR+%28ATP6%5BTIAB%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

- STRIATONIGRAL DEGENERATION, INFANTILE, MITOCHONDRIAL (https://omim.org/entry/500003)
- ATP SYNTHASE 6; MTATP6 (https://omim.org/entry/516060)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/4508)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=MT-ATP6[gene])

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Genomic Location

The *MT-ATP6* gene is found on mitochondrial DNA (https://medlineplus.gov/genetics/chromosome/mitochondrial-dna/).

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