MT-TS1 gene

mitochondrially encoded tRNA serine 1 (UCN)

Normal Function

The *MT-TS1* gene provides instructions for making a particular type of RNA, a molecule that is a chemical cousin of DNA. This type of RNA, called transfer RNA (tRNA), helps assemble protein building blocks known as amino acids into full-length, functioning proteins. The *MT-TS1* gene provides instructions for a specific form of tRNA that is designated as $tRNA^{Ser(UCN)}$. During protein assembly, this molecule attaches to a particular amino acid, serine (Ser), and inserts it into the appropriate locations in the growing protein.

The $tRNA^{Ser(UCN)}$ molecule is present in cellular structures called mitochondria. These structures convert energy from food into a form that cells can use. Through a process called oxidative phosphorylation, mitochondria use oxygen, simple sugars, and fatty acids to create adenosine triphosphate (ATP), the cell's main energy source. The $tRNA^{Ser(UCN)}$ molecule is involved in the assembly of proteins that carry out oxidative phosphorylation.

Health Conditions Related to Genetic Changes

Myoclonic epilepsy with ragged-red fibers

Mutations in the *MT-TS1* gene have been found in a few people with variant forms of myoclonic epilepsy with ragged-red fibers (MERRF). In these cases, affected individuals typically have muscle twitches (myoclonus), muscle weakness (myopathy), difficulty coordinating movement (ataxia), hearing loss, seizures, and intellectual impairment. Two mutations in the *MT-TS1* gene have been found to cause these symptoms. One mutation replaces the DNA building block (nucleotide) thymine with the nucleotide cytosine at gene position 7512 (written as T7512C). The other mutation inserts an extra cytosine at position 7472 (written as 7472insC). Researchers have not determined how these genetic changes cause variant forms of MERRF.

Nonsyndromic hearing loss

Palmoplantar keratoderma with deafness

Some of the *MT-TS1* gene mutations responsible for hearing loss can cause additional signs and symptoms in affected individuals. For example, one mutation causes a skin condition called palmoplantar keratoderma with deafness. In addition

to hearing loss, this condition causes skin on the palms of the hands and the soles of the feet to become thick, scaly, and calloused.

The genetic change that results in this combination of features replaces the nucleotide adenine with the nucleotide guanine at position 7445 in the *MT-TS1* gene (written as A7445G). This mutation likely disrupts the normal production of the $tRNA^{Ser(UCN)}$ molecule. As a result, less $tRNA^{Ser(UCN)}$ is available to assemble proteins within mitochondria. These changes reduce the production of proteins needed for oxidative phosphorylation, which may impair the ability of mitochondria to make ATP. It is unclear why the effects of the mutation are limited to cells in the inner ear and the skin in this condition.

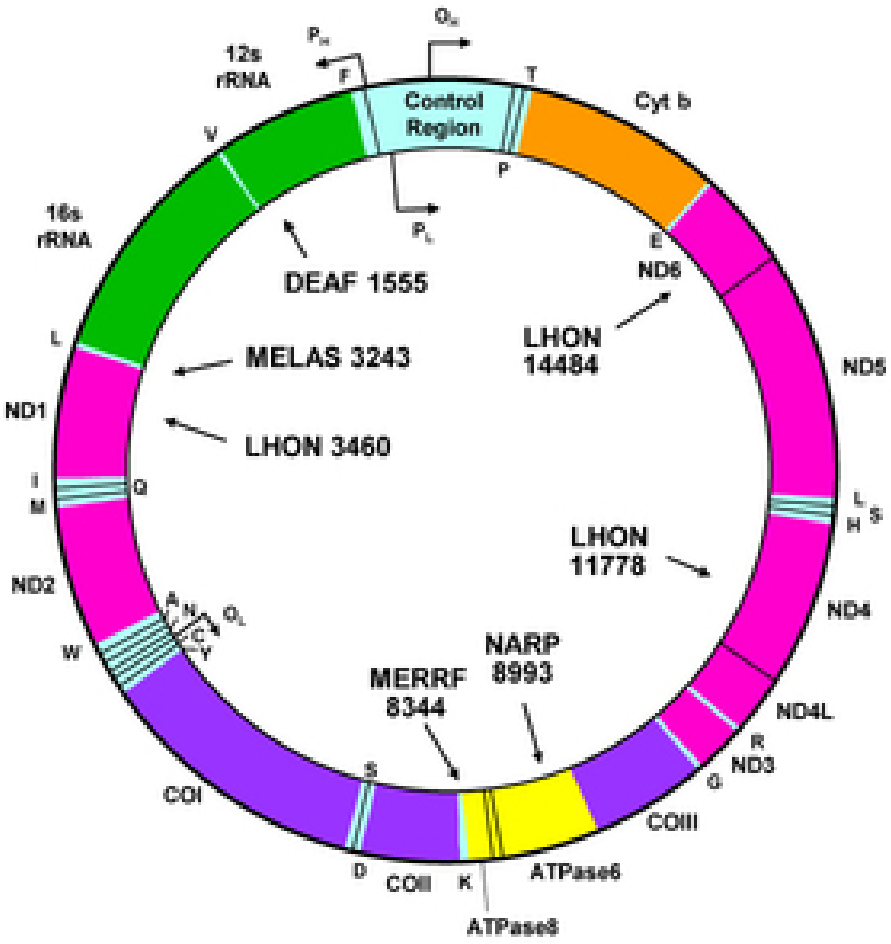
Other disorders

In some families, mutations in the *MT-TS1* gene cause health problems unrelated to hearing loss. For example, one mutation has been identified in people with muscle pain, weakness, and extreme fatigue associated with exercise (exercise intolerance). The genetic change that causes these symptoms replaces the nucleotide adenine with the nucleotide guanine at position 7497 in the *MT-TS1* gene (written as A7497G).

It is unclear why changes in the *MT-TS1* 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. Researchers believe that other genetic and environmental factors help determine whether a *MT-TS1* gene mutation leads to isolated hearing loss, hearing loss associated with other signs and symptoms, or features unrelated to hearing.

Chromosomal Location

Molecular Location: base pairs 7,446 to 7,514 on mitochondrial DNA (Homo sapiens Annotation Release 109, GRCh38.p12) (NCBI)



Other Names for This Gene

- MTTS1
- tRNA serine 1 (UCN)
- TRNS1 tRNA

Additional Information & Resources

Educational Resources

- Madame Curie Bioscience Database: Mitochondrial Translation System
  https://www.ncbi.nlm.nih.gov/books/NBK6292/#A27945
- Mayo Clinic: North American Mitochondrial Disease Consortium Patient Registry and Biorepository (NAMDC)
  https://www.mayo.edu/research/clinical-trials/cls-20409244
- Neuromuscular Disease Center, Washington University: MERRF
  https://neuromuscular.wustl.edu/mitosyn.html#merrf
- Neuromuscular Disease Center, Washington University: Mitochondrial Deafness
  https://neuromuscular.wustl.edu/mitosyn.html#deaf
- The Cell: A Molecular Approach (second edition, 2000): The Genetic System of Mitochondria
  https://www.ncbi.nlm.nih.gov/books/NBK9896/#A1629

Clinical Information from GeneReviews

- Hereditary Hearing Loss and Deafness Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1434
- MERRF
  https://www.ncbi.nlm.nih.gov/books/NBK1520
- Mitochondrial Disorders Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1224
- Nonsyndromic Hearing Loss and Deafness, Mitochondrial
  https://www.ncbi.nlm.nih.gov/books/NBK1422

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28MTTS1%5BTIAB%5D%29+OR+%28%28Mitochondrial+Diseases%5BMAJR%5D%29+AND+%28hearing+loss%5BMH%5D%29+AND+%28tRNA%5BTIAB%5D%29%29+OR+%28%28tRNA%5BTIAB%5D%29+AND+%28ser%28UCN%29%29%29+OR+%28A7445G%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- TRANSFER RNA, MITOCHONDRIAL, SERINE, 1
  http://omim.org/entry/590080

Research Resources

- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=MT-TS1%5Bgene%5D
- Hereditary Hearing Loss Homepage
  https://hereditaryhearingloss.org/
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:7497
- Mitomap: rRNA/tRNA mutations
  https://www.mitomap.org/MITOMAP/MutationsRNA
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:4574
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/4574

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