SLC25A4 gene

solute carrier family 25 member 4

Normal Function

The *SLC25A4* gene provides the instructions for making a protein called adenine nucleotide translocase type 1 (ANT1). ANT1 functions in mitochondria, which are structures within cells that convert the energy from food into a form that cells can use. This process, called oxidative phosphorylation, converts adenosine diphosphate (ADP) into adenosine triphosphate (ATP), the cell's main energy source. ANT1 forms a channel in the inner membrane of mitochondria. This channel allows ADP into mitochondria and ATP out of mitochondria to be used as energy for the cell. ANT1 may also be a part of another structure in the inner membrane called the mitochondrial permeability transition pore. This structure allows various molecules to pass into mitochondria and is thought to play a role in the self-destruction (apoptosis) of the cell.

Health Conditions Related to Genetic Changes

Progressive external ophthalmoplegia

At least five mutations in the *SLC25A4* gene have been reported to cause an eye condition called progressive external ophthalmoplegia. This disorder weakens the muscles that control eye movement and causes the eyelids to droop (ptosis). When caused by *SLC25A4* gene mutations, progressive external ophthalmoplegia is inherited in an autosomal dominant pattern, which means one copy of the gene in each cell is mutated. These mutations impair the movement of ADP and ATP into and out of mitochondria; however, it is not well understood what role these changes play in the cause of the condition.

Mitochondria each contain a small amount of DNA, known as mitochondrial DNA (mtDNA), which is essential for the normal function of these structures. Although the mechanism is unclear, mutations in the *SLC25A4* gene result in large deletions of genetic material from mtDNA in muscle tissue. Researchers have not determined how deletions of mtDNA lead to the specific signs and symptoms of progressive external ophthalmoplegia, although the features of the condition are probably related to impaired oxidative phosphorylation. It has been suggested that eye muscles are commonly affected by mitochondrial defects because they are especially dependent on oxidative phosphorylation for energy.

Other disorders

Mutations in the *SLC25A4* gene can also cause a disorder characterized by myopathy and hypertrophic cardiomyopathy. Myopathy is weakness of the muscles used for movement, and cardiomyopathy is a thickening of the heart muscle that forces the heart to work harder to pump blood. This disorder is inherited in an autosomal recessive pattern, which means both copies of the *SLC25A4* gene in each cell are mutated. The mutations associated with this disorder prevent production of ANT1 channels. As in progressive external ophthalmoplegia (described above), the mutations result in deletions of mtDNA, although the mechanism is unclear. Researchers are unsure how deletions of mtDNA lead to myopathy and hypertrophic cardiomyopathy.

Other Names for This Gene

- AAC1
- adenine nucleotide translocator 1 (skeletal muscle)
- ADP,ATP carrier protein 1
- ADP,ATP carrier protein, heart/skeletal muscle
- ADP/ATP translocase 1
- ADT1_HUMAN
- ANT
- ANT 1
- ANT1
- heart/skeletal muscle ATP/ADP translocator
- PEO2
- PEO3
- solute carrier family 25 (mitochondrial carrier; adenine nucleotide translocator), member 4
- T1

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of SLC25A4 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=291[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28SLC25A4%5BTIAB%5D%29+OR+%28%28ADP/ATP+translocase+1%5BTIAB%5D%29+OR+%28ANT1%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+AN

D+%22last+1800+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- SOLUTE CARRIER FAMILY 25 (MITOCHONDRIAL CARRIER, ADENINE NUCLEOTIDE TRANSLOCATOR), MEMBER 4; SLC25A4 (https://omim.org/entry/103220)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/291)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=SLC25A4[gene])

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Genomic Location

The *SLC25A4* gene is found on chromosome 4 (https://medlineplus.gov/genetics/chromosome/4/).

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