DARS1 gene

aspartyl-tRNA synthetase 1

Normal Function

The *DARS1* gene provides instructions for making an enzyme called aspartyl-tRNA synthetase. This enzyme is found in all cell types and plays an important role in the production (synthesis) of proteins. During protein synthesis, building blocks (amino acids) are connected together in a specific order, creating a chain of amino acids. A type of RNA called transfer RNA (tRNA) carries a specific amino acid to the growing chain. Enzymes called aminoacyl-tRNA synthetases, including aspartyl-tRNA synthetase, attach a particular amino acid to a specific tRNA. Aspartyl-tRNA synthetase attaches the amino acid aspartate to the correct tRNA, which helps ensure that aspartate is added at the proper place in proteins.

In addition to its role in protein synthesis, aspartyl-tRNA synthetase may have other functions that are not fully understood.

Health Conditions Related to Genetic Changes

Hypomyelination with brainstem and spinal cord involvement and leg spasticity

At least 16 mutations in the *DARS1* gene have been found to cause a condition called hypomyelination with brainstem and spinal cord involvement and leg spasticity (HBSL). This condition is characterized by abnormalities of the nervous system's white matter, usually involving particular regions of the spinal cord and brainstem (the region of the brain that connects to the spinal cord). The white matter consists of nerve fibers covered by a fatty substance called myelin, which insulates the fibers and promotes the rapid transmission of nerve impulses. In HBSL, the nervous system has a reduced ability to form myelin (hypomyelination). Affected individuals develop muscle stiffness (spasticity) in the legs that worsens over time and impairs walking.

Most of the mutations in the *DARS1* gene change single amino acids in the aspartyl-tRNA synthetase enzyme. These alterations occur in a region of the enzyme called the active site, where aspartate and the tRNA come together so the amino acid can be transferred. The altered enzyme has difficulty adding the amino acid to the tRNA, which in turn hinders the addition of aspartate to proteins. It is unclear how the gene mutations lead to the signs and symptoms of HBSL. Researchers do not understand why reduced activity of aspartyl-tRNA synthetase affects myelination or why specific parts of the

brainstem and spinal cord are involved.

Other Names for This Gene

- Asp tRNA Ligase
- Aspartate tRNA Ligase
- aspartate tRNA ligase 1, cytoplasmic
- Aspartyl tRNA Synthetase
- DARS
- Synthetase, Aspartyl-tRNA

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of DARS1 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=1615[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28DARS%5BTIAB%5D%29+OR+%28aspartyl-tRNA+synthetase%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+2160+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- ASPARTYL-tRNA SYNTHETASE 1; DARS1 (https://omim.org/entry/603084)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/1615)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=DARS1[gene])

References

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Genomic Location

The *DARS1* gene is found on chromosome 2 (https://medlineplus.gov/genetics/chromosome/2/).

Last updated February 1, 2019