

HARS2 gene

histidyl-tRNA synthetase 2, mitochondrial

Normal Function

The *HARS2* gene provides instructions for making an enzyme called mitochondrial histidyl-tRNA synthetase. This enzyme is important in the production (synthesis) of proteins in cellular structures called mitochondria, the energy-producing centers in cells. While most protein synthesis occurs in the fluid surrounding the nucleus (cytoplasm), some proteins are synthesized in the mitochondria.

During protein synthesis, in either the mitochondria or the cytoplasm, a type of RNA called transfer RNA (tRNA) helps assemble protein building blocks (amino acids) into a chain that forms the protein. Each tRNA carries a specific amino acid to the growing chain. Enzymes called aminoacyl-tRNA synthetases, including mitochondrial histidyl-tRNA synthetase, attach a particular amino acid to a specific tRNA. Mitochondrial histidyl-tRNA synthetase attaches the amino acid histidine to the correct tRNA, which helps ensure that histidine is added at the proper place in the mitochondrial protein.

Health Conditions Related to Genetic Changes

Perrault syndrome

At least two mutations in the *HARS2* gene have been found to cause Perrault syndrome. This rare condition is characterized by hearing loss in males and females with the disorder and abnormalities of the ovaries in affected females. The *HARS2* gene mutations involved in Perrault syndrome reduce the activity of mitochondrial histidyl-tRNA synthetase. A shortage of functional mitochondrial histidyl-tRNA synthetase prevents the normal assembly of new proteins within mitochondria. Researchers speculate that impaired protein assembly disrupts mitochondrial energy production. However, it is unclear exactly how *HARS2* gene mutations lead to hearing problems and ovarian abnormalities in affected individuals.

Other Names for This Gene

- HARS-related
- HARSL
- HARSR

- hisRS
- histidine transase
- histidine tRNA ligase 2, mitochondrial (putative)
- histidine-tRNA ligase homolog
- histidyl-tRNA synthetase 2
- histidyl-tRNA synthetase 2, mitochondrial (putative)
- HO3
- PRLTS2
- probable histidine--tRNA ligase, mitochondrial
- probable histidine--tRNA ligase, mitochondrial isoform 2
- probable histidine--tRNA ligase, mitochondrial isoform 3
- probable histidyl-tRNA synthetase, mitochondrial

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of HARS2 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=23438\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=23438[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28HARS2%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%29%29%29>)

Catalog of Genes and Diseases from OMIM

- HISTIDYL-tRNA SYNTHETASE 2; HARS2 (<https://omim.org/entry/600783>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/23438>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=HARS2\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=HARS2[gene]))

References

- Konovalova S, Tyynismaa H. Mitochondrial aminoacyl-tRNA synthetases in humandisease. Mol Genet Metab. 2013 Apr;108(4):206-11. doi:10.1016/j.ymgme.2013.01.010. Epub 2013 Jan 26. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.g>

ov/23433712)

- Pierce SB, Chisholm KM, Lynch ED, Lee MK, Walsh T, Opitz JM, Li W, Klevit RE, King MC. Mutations in mitochondrial histidyl tRNA synthetase HARS2 cause ovariandysgenesis and sensorineural hearing loss of Perrault syndrome. Proc Natl AcadSci U S A. 2011 Apr 19;108(16):6543-8. doi: 10.1073/pnas.1103471108. Epub 2011Apr 4. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/21464306>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3081023/>)
- Schwenzer H, Zoll J, Florentz C, Sissler M. Pathogenic implications of humanmitochondrial aminoacyl-tRNA synthetases. Top Curr Chem. 2014;344:247-92. doi:10.1007/128_2013_457. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/23824528>)

Genomic Location

The *HARS2* gene is found on chromosome 5 (<https://medlineplus.gov/genetics/chromosome/5/>).

Last updated December 1, 2014