UCHL1 gene
ubiquitin C-terminal hydrolase L1

Normal Function

The *UCHL1* gene provides instructions for making an enzyme called ubiquitin carboxyl-terminal esterase L1. This enzyme is found in nerve cells throughout the brain. Ubiquitin carboxyl-terminal esterase L1 is probably involved in the cell machinery that breaks down (degrades) unneeded proteins. In cells, damaged or excess proteins are tagged with molecules called ubiquitin. Ubiquitin serves as a signal to move these unneeded proteins into specialized structures known as proteasomes, where the proteins are degraded. The ubiquitin-proteasome system acts as the cell's quality control system by disposing of damaged, misshapen, and excess proteins.

Although the exact function of ubiquitin carboxyl-terminal esterase L1 is not fully understood, it appears to have two types of enzyme activity. One of these, called hydrolase activity, removes and recycles ubiquitin molecules from degraded proteins. This recycling step is important to sustain the degradation process. The other enzyme function, known as ligase activity, links together ubiquitin molecules for use in tagging proteins for disposal.

Health Conditions Related to Genetic Changes

Parkinson disease

A relatively common variation (polymorphism) in the *UCHL1* gene may reduce the risk of developing Parkinson disease, a condition characterized by progressive problems with movement and balance. The variation leads to a change in one of the building blocks (amino acids) used to make ubiquitin carboxyl-terminal esterase L1. Instead of serine at position 18 in the enzyme's chain of amino acids, people with the polymorphism have the amino acid tyrosine (written as Ser18Tyr or S18Y). This change is most common in Chinese and Japanese populations and occurs less frequently in European populations. The polymorphism reduces the ligase activity of ubiquitin carboxyl-terminal esterase L1 but has little effect on the hydrolase activity. Some studies suggest that having the S18Y polymorphism may help protect against Parkinson disease, particularly in young adults. However, other studies have not shown this effect. It remains unclear how this amino acid variation might reduce the risk of developing Parkinson disease.

A different change in the *UCHL1* gene may increase the risk of Parkinson disease. This mutation has been reported in two siblings with the disease. The mutation replaces the amino acid isoleucine with the amino acid methionine at position 93 in ubiquitin carboxyl-terminal esterase L1 (written as Ile93Met or I93M). The mutation
leads to decreased hydrolase activity, which may disrupt the ubiquitin-proteasome system. Instead of being degraded, unneeded proteins could accumulate to toxic levels that impair or kill nerve cells in the brain. The loss of these cells weakens communication between the brain and muscles, and ultimately the brain becomes unable to control muscle movement. It is unclear whether this UCHL1 gene mutation is a true risk factor for Parkinson disease, because it has been identified in only one family.

**Chromosomal Location**

Cytogenetic Location: 4p13, which is the short (p) arm of chromosome 4 at position 13

Molecular Location: base pairs 41,256,928 to 41,268,455 on chromosome 4 (Homo sapiens Updated Annotation Release 109.20200522, GRCh38.p13) (NCBI)

Credit: Genome Decoration Page/NCBI

**Other Names for This Gene**

- MSY1
- neuron cytoplasmic protein 9.5
- PARK5
- PGP9.5
- ubiquitin carboxyl-terminal esterase L1 (ubiquitin thiolesterase)
- ubiquitin thiolesterase
- UBL1
- UCHL-1
- UCHL1_HUMAN
Additional Information & Resources

Educational Resources

- Annual Reviews Collection: Overview of the Ubiquitin-Proteasome Degradation System
  https://www.ncbi.nlm.nih.gov/books/NBK2229/#A103
- Biochemistry (fifth edition, 2002): Protein Turnover is Tightly Regulated
  https://www.ncbi.nlm.nih.gov/books/NBK22397/
  https://www.ncbi.nlm.nih.gov/books/NBK9957/#A1233

Clinical Information from GeneReviews

- Parkinson Disease Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1223

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28UCHL1%5BTIAB%5D%29+OR+%28UCHL-1%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+3600+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- UBIQUITIN CARBOXYL-TERMINAL ESTERASE L1
  http://omim.org/entry/191342

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_UCHL1.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=UCHL1%5Bgene%5D
- HGNC Gene Symbol Report
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:7345
- NCBI Gene
Sources for This Summary

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15882803