UCHL1 Gene

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Ubiquitin C-terminal hydrolase L1.

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1. 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.

2. Health Conditions Related to Genetic Changes

2.1. 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.

3. Other Names for This Gene

- MSY1
- neuron cytoplastic protein 9.5
- PARK5

- PGP9.5
- ubiquitin carboxyl-terminal esterase L1 (ubiquitin thiolesterase)
- ubiquitin thiolesterase
- UBL1
- UCHL-1
- UCHL1_HUMAN

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