PPT1 Gene

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palmitoyl-protein thioesterase 1

genes

1. Introduction

The *PPT1* gene provides instructions for making an enzyme called palmitoyl-protein thioesterase 1. This enzyme is found in structures called lysosomes, which are compartments within cells that break down and recycle different types of molecules. Palmitoyl-protein thioesterase 1 removes certain fats called long-chain fatty acids from specific proteins, typically a fatty acid called palmitate. Removing these fatty acids helps break the proteins down when they are no longer needed. Palmitoyl-protein thioesterase 1 is also thought to be involved in a variety of other cell functions, such as the development of synapses, which are the connections between nerve cells where cell-to-cell communication occurs.

2. Health Conditions Related to Genetic Changes

2.1. CLN1 disease

More than 65 mutations in the *PPT1* gene have been found to cause CLN1 disease. This condition impairs mental and motor development causing difficulty with walking, speaking, and intellectual function. In addition, affected children often develop recurrent seizures (epilepsy) and vision loss. Signs and symptoms of CLN1 disease typically appear by age 18 months but can begin later, sometimes in adulthood, in some individuals.

The *PPT1* gene mutations that cause CLN1 disease decrease or eliminate the production or function of palmitoyl-protein thioesterase 1. The most common mutation causing CLN1 disease worldwide, written as Arg151Ter or R151X, replaces the protein building block (amino acid) arginine with a premature stop signal in the instructions used to make the enzyme. This mutation results in an abnormally short, nonfunctional version of the enzyme. Another mutation causes most cases of the disorder in people of Finnish descent; this genetic change replaces arginine with the amino acid tryptophan at position 122 in the palmitoyl-protein thioesterase 1 enzyme (written as Arg122Trp or R122W).

PPT1 gene mutations that cause CLN1 disease lead to a shortage of functional enzyme, which impairs the removal of long-chain fatty acids from certain proteins. These partially broken down fats and proteins accumulate in

lysosomes. While accumulations of these substances occurs in cells throughout the body, nerve cells appear to be particularly vulnerable to damage caused by the abnormal cell materials. Early and widespread loss of nerve cells in CLN1 disease leads to severe signs and symptoms and death in childhood.

In the later-onset cases of CLN1 disease, *PPT1* gene mutations result in the production of a palmitoyl-protein thioesterase 1 enzyme that has a reduced level of normal function; however, protein function in these individuals is higher than in those who have the condition beginning in early childhood. As a result, long-chain fatty acids are removed from some proteins, allowing for a small amount of proteins to be broken down. Because it takes longer for these substances to accumulate in lysosomes and cause nerve cell death, the signs and symptoms of CLN1 disease in these individuals occur later in life.

3. Other Names for This Gene

- ceriod-lipofuscinosis, neuronal 1
- CLN1
- INCL
- palmitoyl-protein hydrolase 1
- PPT
- PPT-1
- PPT1_HUMAN

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