CLN3 Gene

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1. Normal Function

The *CLN3* gene provides instructions for making a protein that is found in tissues throughout the body, yet its function is unclear. The CLN3 protein is found in many compartments within cells, but its role in lysosomes is most well-studied. Lysosomes are cellular compartments that digest and recycle different types of molecules. The CLN3 protein spans the membrane surrounding lysosomes, helping to facilitate communication between it and the rest of the cell.

Studies have associated the CLN3 protein with many cellular processes, including recycling of worn-out cell parts and unneeded proteins (autophagy), maintenance of the relative acidity (pH) of lysosomes, the movement of molecules from the cell surface into the cell (endocytosis), transportation (trafficking) of proteins to where they are needed in the cell, self-destruction of cells (apoptosis), cell growth and division (proliferation), and maintenance of the body's water balance (osmoregulation). It is uncertain which of these varied functions is the primary role of the CLN3 protein, or if these processes instead represent downstream effects.

2. Health Conditions Related to Genetic Changes

2.1. CLN3 Disease

More than 65 mutations in the *CLN3* gene have been found to cause CLN3 disease. CLN3 disease is an inherited disorder that begins in childhood and primarily affects the nervous system. People with this condition develop worsening vision impairment, intellectual disability, movement problems, speech difficulties, and seizures.

One *CLN3* gene mutation, found in the vast majority of cases, deletes about 1,000 DNA building blocks (base pairs) in the gene. This mutation, which is usually called the 1 kilobase (kb) deletion, often occurs in both copies of the *CLN3* gene. The 1 kb deletion removes a piece of the *CLN3* gene and leads to the production of an abnormally short protein. As a result, the abnormal CLN3 protein is broken down or may interfere with normal cellular processes. Other mutations reduce the amount of normal protein or impair its function. It is not known how loss of this protein causes the signs and symptoms of CLN3 disease.

CLN3 disease is characterized by the accumulation of proteins and other substances in lysosomes. These accumulations occur in cells throughout the body; however, nerve cells seem to be particularly vulnerable to their effects. The accumulations can cause cell damage leading to cell death. The progressive death of nerve cells in the brain and other tissues leads to the neurological signs and symptoms of CLN3 disease. However, it is unclear how mutations in the *CLN3* gene are involved in the buildup of substances in lysosomes.

2.2. Other Disorders

Mutations in the *CLN3* gene can cause vision impairment without the other signs and symptoms of CLN3 disease (described above), which is known as CLN3-associated isolated retinal degeneration. In affected individuals, vision impairment is caused by a breakdown of the light-sensitive tissue at the back of the eye (retinal degeneration). People with CLN3-associated isolated retinal degeneration typically have decreased sharpness of vision (visual acuity) and increased sensitivity to light (photophobia). There are two types of this condition, which are distinguished by the age at which vision problems begin. The early-onset form begins in late childhood or adolescence, and the late-onset form begins in early to mid-adulthood.

Research suggests that the *CLN3* gene mutations that cause CLN3-associated isolated retinal degeneration are less severe than those that cause CLN3 disease. As a result, a partially functional CLN3 protein is produced, which leads to the development of visual problems in affected individuals without the neurological features characteristic of CLN3 disease.

3. Other Names for This Gene

- BATTENIN
- BTN1
- BTS
- ceroid-lipofuscinosis, neuronal 3
- CLN3_HUMAN
- JNCL
- MGC102840

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