DNAJC5 Gene

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DnaJ Heat Shock Protein Family (Hsp40) Member C5

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1. Normal Function

The *DNAJC5* gene provides instructions for making a protein called cysteine string protein alpha (CSPα). This protein is found near nerve cells in the brain, where it plays a role in the transmission of nerve impulses. Specifically, CSPα is part of a group (complex) of proteins that is found on the membrane of sac-like structures called synaptic vesicles. Synaptic vesicles are found close to the ends of nerve cells and contain chemical messengers that transmit signals from one nerve cell to another. CSPα is involved in recycling proteins that are involved in nerve impulse transmission by re-folding misshapen proteins so that they can be used in additional transmissions.

2. Health Conditions Related to Genetic Changes

2.1 CLN4 Disease

At least two mutations in the *DNAJC5* gene have been found to cause CLN4 disease. CLN4 disease is an inherited disorder that primarily affects the nervous system. This condition usually begins in adulthood with problems with movement and intellectual function that worsen over time.

One of the *DNAJC5* gene mutations replaces the protein building block (amino acid) leucine with the amino acid arginine at position 115 in the CSPα protein (written as L115R). The other mutation deletes the amino acid leucine at position 116 in the protein (written as L116del). Affected individuals have one of these mutations in one copy of the *DNAJC5* gene in each cell, which leads to the production of an altered protein that cannot associate with the membrane of synaptic vesicles. The resulting reduction in protein recycling leads to a shortage (deficiency) of functional proteins, which impairs the efficiency of nerve impulse transmission. The abnormal CSPα protein may also bind to the functional CSPα protein that is produced from the normal copy of the *DNAJC5* gene and prevent it from associating with synaptic vesicles, further impairing impulse transmission. Without communication between nerve cells, neurological functions are impaired, contributing to the features of CLN4 disease.

CLN4 disease is characterized by the accumulation of proteins and other substances in lysosomes, which are compartments in the cell that digest and recycle materials. 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 contributes to the decline of neurological function in CLN4 disease. However, it is unclear how mutations in the *DNAJC5* gene are involved in the buildup of substances in lysosomes.

3. Other Names for This Gene

- CLN4
- CLN4B
- CSP
- cysteine string protein alpha
- DnaJ (Hsp40) homolog, subfamily C, member 5

- dnaJ homolog subfamily C member 5
- DNAJC5A
- DNJC5_HUMAN
- FLJ00118
- FLJ13070

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