CACNB4 Gene

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calcium voltage-gated channel auxiliary subunit beta 4

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1. Normal Function

The *CACNB4* gene belongs to a family of genes that provide instructions for making calcium channels. These channels, which transport positively charged calcium atoms (calcium ions) into cells, play a key role in a cell's ability to generate and transmit electrical signals. Calcium ions are involved in many different cellular functions, including cell-to-cell communication, the tensing of muscle fibers (muscle contraction), and the regulation of certain genes.

Calcium channels are each made up of a large alpha-1 (α1) subunit, which forms the hole (pore) through which calcium ions can flow. Each channel also includes several smaller subunits, which regulate the channel's activity and interact with various proteins inside and outside the cell. The *CACNB4* gene provides instructions for making a regulatory subunit called beta-4 (β4). This subunit is most often associated with calcium channels in the brain, particularly the part of the brain that is involved in coordinating movements (the cerebellum).

In the brain, calcium channels play an essential role in communication between nerve cells (neurons). These channels help control the release of neurotransmitters, which are chemicals that relay signals from one neuron to another. Researchers believe that calcium channels are also involved in the survival of neurons and the ability of these cells to change and adapt over time (plasticity).

2. Health Conditions Related to Genetic Changes

2.1. Episodic Ataxia

Researchers have identified at least one mutation in the *CACNB4* gene that is likely to cause episodic ataxia. This mutation, which was found in a French-Canadian family with episodic ataxia type 5 (EA5), changes a single protein building block (amino acid) in the calcium channel β4 subunit. Specifically, it replaces the amino acid cysteine with the amino acid phenylalanine at position 104 (written as Cys104Phe or C104F). Scientists speculate that this genetic change may alter the ability of the β4 subunit to interact with other proteins and in some way disrupt the normal function of calcium channels in the brain. It is unclear how these effects may lead to episodes of uncoordinated movement and the other signs and symptoms of episodic ataxia.

2.2. Juvenile Myoclonic Epilepsy

Juvenile myoclonic epilepsy

2.3. Other Disorders

Mutations in the *CACNB4* gene have been associated with epilepsy in a small number of families. One of these mutations prematurely stops protein production at position 482 (written as Arg482Ter or R482X). This mutation results in an abnormally shortened β4 subunit that is missing a region critical for interaction with the larger α1 subunit. Calcium channels made with the altered β4 subunit close more quickly than usual, reducing the flow of calcium ions into the cell. Impaired calcium ion transport likely disrupts communication between nerve cells, causing seizures in people with this genetic change.

Another *CACNB4* mutation, Cys104Phe, appears to cause epilepsy in at least one family. This genetic change (described above) has also been found in an unrelated family with episodic ataxia. Researchers are uncertain why this single mutation appears to underlie two different neurological conditions. They suspect that other genetic and environmental

factors may be involved.

3. Other Names for This Gene

- CAB4
- CACB4_HUMAN
- CACNLB4
- calcium channel, voltage-dependent, beta 4 subunit
- dihydropyridine-sensitive L-type, calcium channel beta-4 subunit
- EA5
- EJM
- EJM4
- voltage dependent calcium channel beta 4 subunit

References

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