PRRT2 Gene

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proline rich transmembrane protein 2

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1. Normal Function

The *PRRT2* gene provides instructions for making the proline-rich transmembrane protein 2 (PRRT2). The function of this protein is unknown, although it is thought to be involved in signaling in the brain. Studies show that it interacts with another protein called SNAP25, which is involved in signaling between nerve cells (neurons) in the brain. SNAP25 helps control the release of neurotransmitters, which are chemicals that relay signals from one neuron to another.

2. Health Conditions Related to Genetic Changes

2.1. Familial hemiplegic migraine

At least two mutations in the *PRRT2* gene have been identified in people with familial hemiplegic migraine. This condition is characterized by migraine headaches with a pattern of neurological symptoms known as aura. In familial hemiplegic migraine, the aura includes temporary numbness or weakness on one side of the body (hemiparesis).

One *PRRT2* gene mutation that is found in multiple people with familial hemiplegic migraine inserts an extra DNA building block (nucleotide) in the gene. (This change is written as 649dupC.) Both known mutations alter the blueprint used for making the protein and lead to production of an abnormally short PRRT2 protein that is quickly broken down. As a result, affected individuals have a shortage of PRRT2 protein. Researchers speculate that this shortage affects the function of the SNAP25 protein, leading to abnormal signaling between neurons, although the mechanism that causes familial hemiplegic migraine is unknown. It is thought that the changes in signaling in the brain lead to development of the severe headaches characteristic of the disorder.

2.2. Familial paroxysmal kinesigenic dyskinesia

More than 10 mutations in the *PRRT2* gene have been found to cause a neurological disorder called familial paroxysmal kinesigenic dyskinesia. This condition is characterized by episodes of involuntary jerking or shaking of the body that are triggered by sudden motion, such as standing up quickly or being startled. The 649dupC mutation (described above) is the most common genetic change in familial paroxysmal kinesigenic dyskinesia. Most *PRRT2* gene mutations involved in this condition, including 649dupC, lead to an abnormally short protein that is quickly broken down. As a result, affected individuals have less PRRT2 protein than normal. Researchers speculate that a shortage of PRRT2 affects the function of the SNAP25 protein, leading to abnormal signaling between neurons. Altered neuronal activity could underlie the movement problems characteristic of familial paroxysmal kinesigenic dyskinesia, but the exact mechanism is unknown.

2.3. Other disorders

PRRT2 gene mutations have been found to cause other neurological conditions, including benign familial infantile seizures (BFIS) and infantile convulsions and choreoathetosis (ICCA). BFIS is characterized by recurrent seizures that begin in infancy and usually disappear by age 2. ICCA is characterized by both benign infantile seizures like those that occur in BFIS and episodes of involuntary movements like those that occur in familial paroxysmal kinesigenic dyskinesia (described above). The 649dupC mutation that causes both familial paroxysmal kinesigenic dyskinesia and familial hemiplegic migraine can also cause BFIS and ICCA. It is unclear how this mutation can cause one condition in some people and a different condition in others.

Although they have been described as separate disorders, researchers speculate that paroxysmal kinesigenic dyskinesia, BFIS, ICCA, and familial hemiplegic migraine may represent a spectrum of related disorders. In some families with a *PRRT2* gene mutation, affected individuals have different conditions; for example, one may have paroxysmal kinesigenic dyskinesia and another may have familial hemiplegic migraine. Sometimes, an affected individual has the features of more than one of these related conditions. In addition, the 649dupC mutation that can cause both familial paroxysmal kinesigenic dyskinesia and familial hemiplegic migraine is also involved in BFIS and ICCA. It is unclear how this mutation can cause a variety of disorders. A combination of environmental and genetic factors may influence the pattern of signs and symptoms an affected individual develops.

3. Other Names for This Gene

- dispanin subfamily B member 3
- DKFZp547J199
- DSPB3
- EKD1
- FLJ25513
- IFITMD1
- interferon induced transmembrane protein domain containing 1
- PKC
- proline-rich transmembrane protein 2
- PRRT2_HUMAN

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