ATP1A3 Gene

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ATPase Na+/K+ transporting subunit alpha 3

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1. Normal Function

The *ATP1A3* gene provides instructions for making one part (the alpha-3 subunit) of a protein known as Na+/K+ ATPase or the sodium pump. This protein uses energy from a molecule called adenosine triphosphate (ATP) to transport charged atoms (ions) into and out of cells. Specifically, it pumps sodium ions (Na+) out of cells and potassium ions (K+) into cells.

Na+/K+ ATPases that include the alpha-3 subunit are primarily found in nerve cells (neurons) in the brain and are critical for their normal function. The movement of sodium and potassium ions helps regulate the electrical activity of these cells and plays an important role in the signaling process that controls muscle movement. The activity of Na+/K+ ATPase also helps regulate cell size (volume).

Additionally, Na+/K+ ATPase helps regulate a process called neurotransmitter reuptake. Neurotransmitters are chemicals that transmit signals from one neuron to another. After a neurotransmitter has had its effect, it must be removed quickly from the space between the neurons. The reuptake of neurotransmitters is carefully controlled to ensure that signals are sent and received accurately throughout the nervous system.

2. Health Conditions Related to Genetic Changes

2.1. Alternating Hemiplegia of Childhood

Mutations in the *ATP1A3* gene are the primary cause of a neurological condition called alternating hemiplegia of childhood; at least 25 *ATP1A3* gene mutations have been found in affected individuals. This condition is characterized by recurrent episodes of temporary paralysis, often affecting one side of the body (hemiplegia). During some episodes, the paralysis alternates from one side to the other or affects both sides of the body at the same time.

Most *ATP1A3* gene mutations associated with alternating hemiplegia of childhood change single protein building blocks (amino acids) in the alpha-3 subunit of Na+/K+ ATPase. These genetic changes appear to impair the pump's ability to transport ions, although it is unclear how the mutations lead to the specific features of alternating hemiplegia of childhood.

2.2. Rapid-Onset Dystonia Parkinsonism

At least nine mutations in the *ATP1A3* gene have been identified in individuals and families with rapid-onset dystonia parkinsonism. Most of these mutations change single amino acids in the alpha-3 subunit of Na+/K+ ATPase. Changes in the protein's structure can reduce its activity or make it unstable. Studies suggest that the defective Na+/K+ ATPase is unable to transport sodium ions normally, which disrupts the electrical activity of neurons in the brain. However, it is unclear how a malfunctioning Na+/K+ ATPase causes the movement abnormalities characteristic of rapid-onset dystonia parkinsonism.

3. Other Names for This Gene

- AT1A3_HUMAN
- ATPase, Na+/K+ transporting, alpha 3 polypeptide
- DYT12
- MGC13276
- Na+/K+ -ATPase alpha 3 subunit

- Na+/K+ ATPase 3
- RDP
- sodium pump 3
- sodium-potassium-ATPase, alpha 3 polypeptide
- sodium/potassium-transporting ATPase alpha-3 chain

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