ATP1A3 gene

ATPase Na+/K+ transporting subunit alpha 3

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 critical for normal function of nerve cells in the brain (neurons). 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 chemical messengers 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.

Health Conditions Related to Genetic Changes

Alternating hemiplegia of childhood

Variants (also called mutations) in the *ATP1A3* gene are the primary cause of a neurological condition called alternating hemiplegia of childhood. This condition is characterized by recurrent episodes of temporary paralysis that often affects only 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 variants 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 variants lead to the specific features of alternating hemiplegia of childhood.

Rapid-onset dystonia parkinsonism

Multiple variants in the *ATP1A3* gene have been found to cause a rare movement disorder called rapid-onset dystonia parkinsonism. This disorder is characterized by the abrupt appearance of signs and symptoms over a period of hours to days. Most of the *ATP1A3* gene variants that cause this disorder 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 seen in people with rapid-onset dystonia parkinsonism.

Other disorders

Variants in the *ATP1A3* gene can cause a group of features: cerebellar ataxia, areflexia, pes cavus, optic atrophy, and sensorineural hearing loss. This specific presentation is known as CAPOS syndrome (the abbreviation comes from the first letter of each feature) . Affected individuals usually develop signs and symptoms of CAPOS syndrome in infancy or early childhood during or following an illness that causes a fever.

To date, all instances of CAPOS syndrome have been caused by the same variant in the *ATP1A3* gene. This change replaces the amino acid glutamic acid with the amino acid lysine at position 818 in the alpha-3 subunit of Na+/K+ ATPase (written as Glu818Lys or E818K). This genetic change appears to impair the pump's ability to transport ions, although it is unclear how the variant causes the specific features of CAPOS syndrome.

Other Names for This Gene

- AT1A3_HUMAN
- ATPase, Na+/K+ transporting, alpha 3 polypeptide
- Na+/K+ -ATPase alpha 3 subunit
- Na+/K+ ATPase 3
- sodium pump 3
- sodium-potassium-ATPase, alpha 3 polypeptide
- sodium/potassium-transporting ATPase alpha-3 chain

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of ATP1A3 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=478[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28ATP1A3%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- ATPase, Na+/K+ TRANSPORTING, ALPHA-3 POLYPEPTIDE; ATP1A3 (https://omim.org/entry/182350)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/478)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=ATP1A3[gene])

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Genomic Location

The *ATP1A3* gene is found on chromosome 19 (https://medlineplus.gov/genetics/chromosome/19/).

Last updated April 23, 2024