WNK1 Gene

Subjects: Genetics & Heredity
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Definition

WNK lysine deficient protein kinase 1.

1. Normal Function

The *WNK1* gene provides instructions for making multiple versions (isoforms) of the WNK1 protein. The different WNK1 isoforms are important in several functions in the body, including blood pressure regulation and pain sensation.

One isoform produced from the *WNK1* gene is the full-length version, called the L-WNK1 protein, which is found in cells throughout the body. A different isoform, called the kidney-specific WNK1 protein or KS-WNK1, is found only in kidney cells. The L-WNK1 and KS-WNK1 proteins act as kinases, which are enzymes that change the activity of other proteins by adding a cluster of oxygen and phosphorus atoms (a phosphate group) at specific positions.

The L-WNK1 and KS-WNK1 proteins regulate channels in the cell membrane that control the transport of sodium or potassium into and out of cells. In the kidneys, sodium channels help transport sodium into specialized cells, which then transfer it into the blood. This transfer helps keep sodium in the body through a process called reabsorption. Potassium channels handle excess potassium that has been transferred from the blood into kidney cells. The channels transport potassium out of the cells in a process called secretion, so that it can be removed from the body in urine.

The L-WNK1 protein increases sodium reabsorption and decreases potassium secretion, whereas the KS-WNK1 protein has the opposite effect. Sodium and potassium are important for regulating blood pressure, and a balance of L-WNK1 protein and KS-WNK1 protein in the kidneys helps maintain the correct levels of sodium and potassium for healthy blood pressure.

Another isoform produced from the *WNK1* gene, called the WNK1/HSN2 protein, is found in the cells of the nervous system, including nerve cells that transmit the sensations of pain, temperature, and touch (sensory neurons). The WNK1/HSN2 protein appears to regulate channels in the cell membrane that can transport negatively charged chlorine atoms (chloride ions). These channels maintain the proper amount of chloride inside cells, which is important for controlling the activation (excitation) of the neurons.

2. Health Conditions Related to Genetic Changes

2.1. Hereditary Sensory and Autonomic Neuropathy Type II

Mutations in the *WNK1* gene are responsible for one type of hereditary sensory and autonomic neuropathy type II (HSAN2) called HSAN2A. People with HSAN2A lose the ability to feel pain or sense hot and cold. More than a dozen mutations in the *WNK1* gene have been identified in people with HSAN2A. All of these mutations lead to an abnormally shortened WNK1/HSN2 protein that is probably nonfunctional. People with HSAN2A have a reduction in the number of sensory neurons; however, the role that the abnormal WNK1/HSN2 protein plays in that loss is unclear. The loss of sensory neurons results in the signs and symptoms of HSAN2A.

WNK1 gene mutations involved in HSAN2A do not appear to affect the L-WNK1 or KS-WNK1 isoforms.

2.2. Pseudohypoaldosteronism Type 2

At least two mutations in the *WNK1* gene have been found to cause pseudohypoaldosteronism type 2 (PHA2), a condition characterized by high blood pressure (hypertension) and high levels of potassium in the blood (hyperkalemia). The mutations involved in this condition delete large numbers of DNA building blocks (nucleotides) from the *WNK1* gene. These deletions lead to increased activity of the *WNK1* gene and excess L-WNK1 protein. An increase in L-WNK1 protein abnormally increases sodium reabsorption and blocks potassium secretion, resulting in hypertension and hyperkalemia.

WNK1 gene mutations involved in PHA2 do not appear to affect the KS-WNK1 or WNK1/HSN2 isoforms.

2.3. Other Disorders

Studies have associated normal variations in the *WNK1* gene with an increased risk of high blood pressure (hypertension) in people without PHA2 (described above). A combination of genetic variations and environmental factors likely influence the development of this complex condition.

3. Other Names for This Gene

- HSAN2
- HSN2
- KDP
- p65
- PPP1R167
- PRKWNK1
- prostate-derived sterile 20-like kinase
- protein kinase with no lysine 1
- protein kinase, lysine deficient 1
- PSK
- serine/threonine-protein kinase WNK1
- WNK1_HUMAN

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Keywords

genes