SCNN1G gene

sodium channel epithelial 1 subunit gamma

Normal Function

The *SCNN1G* gene provides instructions for making one piece, the gamma subunit, of a protein complex called the epithelial sodium channel (ENaC). The channel is composed of alpha, beta, and gamma subunits, each of which is produced from a different gene. These channels are found at the surface of certain cells called epithelial cells in many tissues of the body, including the kidneys, lungs, and sweat glands. The ENaC channel transports sodium into cells.

In the kidney, ENaC channels open in response to signals that sodium levels in the blood are too low, which allows sodium to flow into cells. From the kidney cells, this sodium is returned to the bloodstream (a process called reabsorption) rather than being removed from the body in urine. In addition to regulating the amount of sodium in the body, the flow of sodium ions helps control the movement of water in tissues. For example, ENaC channels in lung cells help regulate the amount of fluid in the lungs.

Health Conditions Related to Genetic Changes

Liddle syndrome

At least 5 mutations in the *SCNN1G* gene can cause a condition known as Liddle syndrome. People with Liddle syndrome have high blood pressure (hypertension) and low levels of potassium in their blood (hypokalemia), often beginning in childhood. Mutations in the *SCNN1G* gene associated with Liddle syndrome lead to the production of an abnormally short gamma subunit protein. These changes affect an important region of the gamma subunit protein involved in signaling for its breakdown (degradation). As a result of the mutations, the protein is not degraded, and more ENaC channels remain at the cell surface. The increase in channels at the cell surface allows the reabsorption of excess sodium (followed by water), which leads to hypertension. Reabsorption of sodium into the blood is linked with removal of potassium from the blood, so excess sodium reabsorption leads to hypokalemia.

Pseudohypoaldosteronism type 1

Mutations in the *SCNN1G* gene are involved in a condition called pseudohypoaldosteronism type 1 (PHA1). This condition typically begins in infancy and

is characterized by low levels of sodium (hyponatremia) and high levels of potassium (hyperkalemia) in the blood, and severe dehydration due to the loss of excess sodium and fluid in urine. In particular, *SCNN1G* gene mutations are involved in autosomal recessive PHA1, a severe form of the condition that does not improve with age.

Most mutations in the *SCNN1G* gene lead to an abnormally short gamma subunit protein. These mutations result in reduced or absent ENaC channel activity. As a result, sodium reabsorption is impaired, leading to hyponatremia and other signs and symptoms of autosomal recessive PHA1. The reduced function of ENaC channels in lung epithelial cells leads to excess fluid in the lungs and recurrent lung infections.

Other disorders

Some people with cystic fibrosis-like syndrome have a mutation or a normal gene variation (polymorphism) in the *SCNN1G* gene. People with cystic fibrosis-like syndrome (also known as atypical cystic fibrosis or bronchiectasis with or without elevated sweat chloride type 3) have signs and symptoms that resemble those of cystic fibrosis, including breathing problems and lung infections. However, changes in the gene most commonly associated with cystic fibrosis, *CFTR*, cannot explain development of the condition. It is thought that a mutation or gene variation in the *SCNN1G* gene can disrupt sodium transport and fluid balance, which leads to the signs and symptoms of cystic fibrosis-like syndrome.

Other Names for This Gene

- amiloride-sensitive epithelial sodium channel gamma subunit
- amiloride-sensitive sodium channel gamma-subunit
- amiloride-sensitive sodium channel subunit gamma
- BESC3
- ENaC gamma subunit
- ENaCg
- ENaCgamma
- epithelial Na(+) channel subunit gamma
- gamma-ENaC
- gamma-NaCH
- nonvoltage-gated sodium channel 1 subunit gamma
- SCNEG
- SCNNG_HUMAN
- sodium channel, non voltage gated 1 gamma subunit
- sodium channel, non-voltage-gated 1, gamma subunit
- sodium channel, nonvoltage-gated 1, gamma

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of SCNN1G (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=6340[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28SCNN1G%5BTIAB%5D%29+OR+%28%28ENaC+gamma+subunit%5BTIAB%5D%29+OR+%28ENaCgamma%5BTIAB%5D%29+OR+%28gamma-ENaC%5BTIAB%5D%29+OR+%28PHA1%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1440+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- SODIUM CHANNEL, EPITHELIAL 1, GAMMA SUBUNIT; SCNN1G (https://omim.org/entry/600761)
- BRONCHIECTASIS WITH OR WITHOUT ELEVATED SWEAT CHLORIDE 3; BESC3 (https://omim.org/entry/613071)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/6340)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=SCNN1G[gene])

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Genomic Location

The *SCNN1G* gene is found on chromosome 16 (https://medlineplus.gov/genetics/chromosome/16/).

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