SCNN1A gene

sodium channel epithelial 1 subunit alpha

Normal Function

The *SCNN1A* gene provides instructions for making one piece, the alpha 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 take sodium into cells in response to signals that sodium levels in the body are too low. From the kidney cells, this sodium is returned to the bloodstream rather than being removed from the body (a process called reabsorption). 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

Pseudohypoaldosteronism type 1

At least a dozen mutations in the *SCNN1A* gene cause 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. In particular, *SCNN1A* gene mutations are involved in autosomal recessive PHA1, a severe form of the condition that does not improve with age.

Most mutations in the *SCNN1A* gene result in a shortened alpha subunit protein of the ENaC channel. Other mutations delete a small piece of DNA or change a single protein building block (amino acid) in the alpha subunit protein. *SCNN1A* gene mutations lead to 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 *SCNN1A* gene. People with cystic fibrosis-like syndrome (also known as atypical cystic fibrosis or bronchiectasis with or without elevated sweat chloride type 2) 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 *SCNN1A* 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

- alpha-ENaC
- alpha-NaCH
- amiloride-sensitive epithelial sodium channel alpha subunit
- amiloride-sensitive sodium channel subunit alpha
- BESC2
- ENaCa
- ENaCalpha
- epithelial Na(+) channel subunit alpha
- FLJ21883
- nasal epithelial sodium channel alpha subunit
- nonvoltage-gated sodium channel 1 subunit alpha
- SCNEA
- SCNN1
- SCNNA_HUMAN
- sodium channel, non voltage gated 1 alpha subunit
- sodium channel, non-voltage-gated 1 alpha subunit
- sodium channel, nonvoltage-gated 1 alpha

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of SCNN1A (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=6337[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28SCNN1A%5BTIAB%5D%29+OR+%28%28alpha-ENaC%5BTIAB%5D%29+OR+%28alpha-NaCH%5BTIAB%5D%29+OR+%28amiloride-sensitive+epithelial+sodium+channel+alpha+subunit%5BTI

AB%5D%29+OR+%28ENaCa%5BTIAB%5D%29+OR+%28ENaCalpha%5BTIAB%5D%29+OR+%28SCNN1%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, ALPHA SUBUNIT; SCNN1A (https://omim.org/entry/600228)
- BRONCHIECTASIS WITH OR WITHOUT ELEVATED SWEAT CHLORIDE 2; BESC2 (https://omim.org/entry/613021)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/6337)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=SCNN1A[gene])

References

- Azad AK, Rauh R, Vermeulen F, Jaspers M, Korbmacher J, Boissier B, Bassinet L, Fichou Y, des Georges M, Stanke F, De Boeck K, Dupont L, Balascakova M, Hjelte L,Lebecque P, Radojkovic D, Castellani C, Schwartz M, Stuhrmann M, Schwarz M, Skalicka V, de Monestrol I, Girodon E, Ferec C, Claustres M, Tummler B, CassimanJJ, Korbmacher C, Cuppens H. Mutations in the amiloride-sensitive epithelialsodium channel in patients with cystic fibrosis-like disease. Hum Mutat. 2009Jul;30(7):1093-103. doi: 10.1002/humu.21011. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/19462466)
- Canessa CM, Schild L, Buell G, Thorens B, Gautschi I, Horisberger JD, RossierBC. Amiloride-sensitive epithelial Na+ channel is made of three homologoussubunits. Nature. 1994 Feb 3;367(6462):463-7. doi: 10.1038/367463a0. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/8107805)
- Chang SS, Grunder S, Hanukoglu A, Rosler A, Mathew PM, Hanukoglu I, Schild L, Lu Y, Shimkets RA, Nelson-Williams C, Rossier BC, Lifton RP. Mutations insubunits of the epithelial sodium channel cause salt wasting with hyperkalaemicacidosis, pseudohypoaldosteronism type 1. Nat Genet. 1996 Mar;12(3):248-53. doi:10.1038/ng0396-248. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/8589714)
- Chen SY, Bhargava A, Mastroberardino L, Meijer OC, Wang J, Buse P, FirestoneGL, Verrey F, Pearce D. Epithelial sodium channel regulated byaldosterone-induced protein sgk. Proc Natl Acad Sci U S A. 1999 Mar2;96(5):2514-9. doi: 10.1073/pnas.96.5.2514. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/10051674) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC26816/)
- Masilamani S, Kim GH, Mitchell C, Wade JB, Knepper MA. Aldosterone-

mediatedregulation of ENaC alpha, beta, and gamma subunit proteins in rat kidney. J ClinInvest. 1999 Oct;104(7):R19-23. doi: 10.1172/JCI7840. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/10510339) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC408561/)

- Mutesa L, Azad AK, Verhaeghe C, Segers K, Vanbellinghen JF, Ngendahayo L, Rusingiza EK, Mutwa PR, Rulisa S, Koulischer L, Cassiman JJ, Cuppens H, Bours V. Genetic analysis of Rwandan patients with cystic fibrosis-like symptoms: identification of novel cystic fibrosis transmembrane conductance regulator andepithelial sodium channel gene variants. Chest. 2009 May;135(5):1233-1242. doi: 10.1378/chest.08-2246. Epub 2008 Nov 18. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/19017867)

Genomic Location

The *SCNN1A* gene is found on chromosome 12 (https://medlineplus.gov/genetics/chromosome/12/).

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