NPHP1 gene

nephrocystin 1

Normal Function

The *NPHP1* gene provides instructions for making the nephrocystin-1 protein. This protein is thought to play a role in cell structures called cilia, which are microscopic, finger-like projections that stick out from the surface of cells. Cilia participate in signaling pathways that transmit information within and between cells and are important for the development and function of many types of cells and tissues. Nephrocystin-1 is found at the base of cilia in cells of the kidneys, respiratory tract, and the light-sensitive tissue at the back of the eye (the retina). Although the specific function of nephrocystin-1 is not well understood, it is thought to interact with a number of other proteins as part of a large protein complex that may be important for normal cilia function.

Health Conditions Related to Genetic Changes

Nephronophthisis

At least 23 mutations in the *NPHP1* gene have been found to cause a kidney disorder called nephronophthisis type 1. Type 1 is the most common type of nephronophthisis, accounting for approximately 20 percent of cases of the disorder. Nephronophthisis is characterized by inflammation and scarring of the kidneys and ultimately leads to a life-threatening failure of kidney function (end-stage renal disease or ESRD). In nephronophthisis type 1, ESRD usually occurs around age 13.

The most common genetic change in nephronophthisis type 1 is a large deletion on chromosome 2 that removes the whole *NPHP1* gene. Other deletions that remove all or most of the gene or a small portion of the gene can also be involved in this condition. Some mutations change single protein building blocks (amino acids) or lead to an abnormally short nephrocystin-1 protein. It is thought that people with nephronophthisis type 1 have little or no functional nephrocystin-1. The lack of this protein probably impairs the function of cilia in some way, which likely disrupts important chemical signaling pathways during development. Although researchers believe that defective cilia are responsible for the features of nephronophthisis, the mechanism remains unclear.

Joubert syndrome

MedlinePlus Genetics provides information about Joubert syndrome

Senior-Løken syndrome

MedlinePlus Genetics provides information about Senior-Løken syndrome

Other disorders

Mutations in the *NPHP1* gene can cause syndromes that include nephronophthisis among their features; such conditions are known as nephronophthisis-associated ciliopathies. Senior-Løken syndrome is characterized by the combination of nephronophthisis and breakdown of the retina (retinal degeneration). Joubert syndrome is a multisystem disorder that typically involves neurological problems and can include nephronophthisis, eye abnormalities, liver disease, and other abnormalities. As in nephronophthisis type1 (described above), *NPHP1* gene mutations probably impair cilia function. Defective cilia likely cause the features of these nephronophthisis-associated ciliopathies, although it remains unclear how these defects lead to the specific abnormalities of each condition. It is unknown why some individuals with *NPHP1* gene mutations develop the additional signs and symptoms of Senior-Løken syndrome or Joubert syndrome.

Other Names for This Gene

- JBTS4
- juvenile nephronophthisis 1 protein
- nephrocystin-1
- nephronophthisis 1 (juvenile)
- NPH1
- SLSN1

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of NPHP1 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=4867[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28NPHP1%5BTIAB%5D%29+OR+%28nephronophthisis+1%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+1800+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- NEPHROCYSTIN 1; NPHP1 (https://omim.org/entry/607100)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/4867)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=NPHP1[gene])

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Genomic Location

The *NPHP1* gene is found on chromosome 2 (https://medlineplus.gov/genetics/chromosome/2/).

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