NPHS1 gene

NPHS1 adhesion molecule, nephrin

Normal Function

The *NPHS1* gene provides instructions for making a protein called nephrin. Nephrin is primarily found in the kidneys, which are organs that filter waste products from the blood and remove them in urine. Specifically, nephrin is found in cells called podocytes, which are located in specialized kidney structures called glomeruli. Nephrin is located at the cell surface in the area between two podocytes called the slit diaphragm. The slit diaphragm is known as a filtration barrier because it captures proteins in blood so that they remain in the body while allowing other molecules like sugars and salts to be excreted in urine. Nephrin proteins on one cell interact with nephrin proteins on adjacent podocytes, forming a zipper-like structure. This structure allows the passage of small molecules through the slit diaphragm while preventing larger molecules like proteins from passing through. Nephrin proteins are essential for forming the slit diaphragm, anchoring the slit diaphragm to podocytes, and filtering blood.

Nephrin is also involved in cell signaling. It relays signals from outside the cell to inside the cell. Additionally, nephrin proteins on the surface of adjacent cells send and receive signals, allowing podocytes to communicate with one another.

Health Conditions Related to Genetic Changes

Congenital nephrotic syndrome

At least 250 mutations in the *NPHS1* gene have been found to cause congenital nephrotic syndrome. This condition is a kidney disorder that begins in infancy and typically leads to irreversible kidney failure (end-stage renal disease) by early childhood.

NPHS1 gene mutations account for all cases of congenital nephrotic syndrome of the Finnish type. This form of the condition is found in people of Finnish ancestry. Two specific mutations, both of which result in an abnormally short, nonfunctional nephrin protein, account for nearly all cases. The first mutation, known as $Finn_{major}$, is written as L41fsX90 and is responsible for 78 percent of cases. The second mutation, known as $Finn_{minor}$, is written as R1109X and is responsible for 16 percent of cases.

NPHS1 gene mutations can also cause congenital nephrotic syndrome in non-Finnish individuals. Most of these mutations result in an abnormal nephrin protein that is

trapped inside the cell and cannot get to the podocyte cell surface. A shortage of functional nephrin at the podocyte cell surface impairs the formation of normal slit diaphragms. Without a functional slit diaphragm, molecules pass through the kidneys abnormally and are excreted in urine. The filtering ability of the kidneys worsens from birth, eventually leading to end-stage renal disease.

Other Names for This Gene

- CNF
- nephrin
- nephrin precursor
- nephrosis 1, congenital, Finnish type (nephrin)
- NPHN
- NPHS1 nephrin
- renal glomerulus-specific cell adhesion receptor

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of NPHS1 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=4868[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28NPHS1%5BTIAB%5D%29+OR+%28nephrin%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+1080+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- NEPHRIN; NPHS1 (https://omim.org/entry/602716)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/4868)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=NPHS1[gene])

References

- Fogo AB, Lusco MA, Najafian B, Alpers CE. AJKD Atlas of Renal Pathology: Congenital Nephrotic Syndrome of Finnish Type. Am J Kidney Dis. 2015Sep;66(3):

e11-2. doi: 10.1053/j.ajkd.2015.07.008. No abstract available. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/26300201)

- Grahammer F, Schell C, Huber TB. The podocyte slit diaphragm--from a thin greyline to a complex signalling hub. Nat Rev Nephrol. 2013 Oct;9(10):587-98. doi: 10.1038/nrneph.2013.169. Epub 2013 Sep 3. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/23999399)
- Ovunc B, Ashraf S, Vega-Warner V, Bockenhauer D, Elshakhs NA, Joseph M, Hildebrandt F; Gesellschaft fur Padiatrische Nephrologie (GPN) Study Group. Mutation analysis of NPHS1 in a worldwide cohort of congenital nephrotic syndromepatients. Nephron Clin Pract. 2012;120(3):c139-46. doi: 10.1159/000337379. Epub2012 May 11. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/22584503)
- Schoeb DS, Chernin G, Heeringa SF, Matejas V, Held S, Vega-Warner V, Bockenhauer D, Vlangos CN, Moorani KN, Neuhaus TJ, Kari JA, MacDonald J, SaisawatP, Ashraf S, Ovunc B, Zenker M, Hildebrandt F; Gesselschaft fur PaediatrischeNephrologie (GPN) Study Group. Nineteen novel NPHS1 mutations in a worldwidecohort of patients with congenital nephrotic syndrome (CNS). Nephrol DialTransplant. 2010 Sep;25(9):2970-6. doi: 10.1093/ndt/gfq088. Epub 2010 Feb 18. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20172850) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2948833/)
- Wang JJ, Mao JH. The etiology of congenital nephrotic syndrome: current statusand challenges. World J Pediatr. 2016 May;12(2):149-58. doi:10.1007/s12519-016-0009-y. Epub 2016 Mar 9. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/26961288)

Genomic Location

The *NPHS1* gene is found on chromosome 19 (https://medlineplus.gov/genetics/chromosome/19/).

Last updated July 1, 2016