NPHS2 gene

NPHS2 stomatin family member, podocin

Normal Function

The *NPHS2* gene provides instructions for making a protein called podocin. Podocin is primarily found in the kidneys, which are organs that filter waste products from the blood and remove them in urine. Specifically, podocin is found in cells called podocytes, which are located in specialized kidney structures called glomeruli. Podocin 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. Podocin likely helps bring other proteins that are needed for a functional slit diaphragm to the podocyte cell surface. The protein also is involved with podocyte cell signaling, helping the cell adapt to changes that occur during the filtration process.

Health Conditions Related to Genetic Changes

Congenital nephrotic syndrome

At least 170 mutations in the *NPHS2* 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. Mutations in this gene appear to be the most frequent cause of congenital nephrotic syndrome. Most *NPHS2* gene mutations change single protein building blocks (amino acids) in the podocin protein. These mutations result in a reduction or absence of functional protein, which 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 disorders

NPHS2 gene mutations can cause other forms of nephrotic syndrome that develop later in life. In one form, called infantile nephrotic syndrome, signs and symptoms of the condition appear between 4 and 12 months of age. The features of this condition are similar to congenital nephrotic syndrome (described above), but they are often less severe. It is likely that *NPHS2* gene mutations that cause infantile nephrotic syndrome

have less effect on podocin function than those that cause congenital nephrotic syndrome, accounting for the later onset of the disorder.

Other Names for This Gene

- nephrosis 2, idiopathic, steroid-resistant (podocin)
- NPHS2 podocin
- PDCN
- podocin isoform 1
- podocin isoform 2
- SRN1

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of NPHS2 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=7827[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28NPHS2%5BTIAB%5D%29+OR+%28podocin%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

- NPHS2 STOMATIN FAMILY MEMBER, PODOCIN; NPHS2 (https://omim.org/entry/604766)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/7827)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=NPHS2[gene])

References

- 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)
- Machuca E, Benoit G, Nevo F, Tete MJ, Gribouval O, Pawtowski A, Brandstrom P,

Loirat C, Niaudet P, Gubler MC, Antignac C. Genotype-phenotype correlations innon-Finnish congenital nephrotic syndrome. J Am Soc Nephrol. 2010Jul;21(7):1209-17. doi: 10.1681/ASN.2009121309. Epub 2010 May 27. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20507940) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3152225/)

- Sadowski CE, Lovric S, Ashraf S, Pabst WL, Gee HY, Kohl S, Engelmann S,Vega-Warner V, Fang H, Halbritter J, Somers MJ, Tan W, Shril S, Fessi I, LiftonRP, Bockenhauer D, El-Desoky S, Kari JA, Zenker M, Kemper MJ, Mueller D, FathyHM, Soliman NA; SRNS Study Group; Hildebrandt F. A single-gene cause in 29.5% ofcases of steroid-resistant nephrotic syndrome. J Am Soc Nephrol. 2015Jun;26(6): 1279-89. doi: 10.1681/ASN.2014050489. Epub 2014 Oct 27. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/25349199) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4446877/)
- 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 *NPHS2* gene is found on chromosome 1 (https://medlineplus.gov/genetics/chromosome/1/).

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