



## CARRIER SCREEN

### What is Nephrotic Syndrome, *NPHS1*-related?

Nephrotic syndrome, *NPHS1*-related is an inherited disorder characterized by progressive kidney disease. It is caused by a defect in the production of a protein called nephrin that is essential for normal kidney function. Symptoms associated with nephrotic syndrome type 1 are attributed to the kidney's inability to maintain normal blood protein levels.<sup>1</sup> Nephrotic syndrome, *NPHS1*-related is also known as Finnish Congenital Nephrosis.

### What are the Symptoms of Nephrotic Syndrome, *NPHS1*-related and What Treatment is Available?

Nephrotic syndrome, *NPHS1*-related is usually present at birth or develops within the first three months of life (congenital); however, onset in infancy or later childhood has been reported.<sup>2</sup> Nephrotic syndrome, *NPHS1*-related type 1 is typically a progressive disorder that is resistant to steroid treatment and results in end-stage renal disease within a few years of onset. Atypical cases with milder symptoms and/or partial responsiveness to steroids have been reported.<sup>3</sup>

Nephrotic syndrome, *NPHS1*-related was originally described more than 50 years ago in the Finnish population and was called *Congenital Nephrotic Syndrome of the Finnish Type (CNF)*.<sup>4</sup> CNF was characterized by premature birth, large placenta, prenatal onset of proteinuria, and edema presenting in the newborn period.<sup>2</sup> Since this time, a better understanding of this disease has demonstrated that nephrotic syndrome type 1 can vary in severity and onset of symptoms, especially outside of Finland.<sup>3</sup>

Signs and symptoms of nephrotic syndrome, *NPHS1*-related type 1 may include:<sup>5</sup>

- Proteinuria (high protein levels in urine)
- Hypoalbuminemia (low protein levels in the blood)
- Hyperlipidemia (high fat levels in the blood)
- Edema (swelling due to excessive fluid in body cavities)
- Resistance to steroid therapy
- Progression to end-stage kidney disease

Kidney transplant is typically curative; however, recurrence of kidney disease following transplant has been reported.<sup>2</sup>

### How is Nephrotic Syndrome, *NPHS1*-related Inherited?

Nephrotic syndrome, *NPHS1*-related is an autosomal recessive disease caused by mutations in the *NPHS1* gene.<sup>3</sup> An individual who inherits one copy of an *NPHS1* gene mutation is a "carrier" and is not expected to have related health problems. An individual who inherits two mutations in this gene, one from each parent, is expected to be affected with nephrotic syndrome type 1.

If both members of a couple are carriers, the risk for an affected child is 25% in each pregnancy; therefore, it is especially important that the reproductive partner of a carrier be offered testing.

### Who is at Risk for Nephrotic Syndrome, *NPHS1*-related?

Nephrotic syndrome, *NPHS1*-related can occur in any race or ethnicity; however, it is particularly common in the Finnish and Maltese populations. In the Finnish population, it has an incidence of approximately 1/8,200 and a carrier frequency of 1/45, while in the Maltese population, the incidence is estimated at 1/1900 with a carrier frequency at 1/22.<sup>4,5</sup>





### What Does a Positive Test Result Mean?

If a gene mutation is identified, an individual should speak to a physician or genetic health professional about the implications of the result and appropriate testing for the reproductive partner and at-risk family members.

### What Does a Negative Test Result Mean?

A negative result reduces, but does not eliminate, the possibility that an individual carries a gene mutation. The likelihood of being a carrier is also influenced by family history, medical symptoms, and other relevant test results.

### References

1. Tryggvason K, et al. Hereditary Proteinuria Syndromes and Mechanisms of Proteinuria. *The New England Journal of Medicine*. 2006; 354:1387-401.
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4. Huttunen, N. Congenital Nephrotic Syndrome of Finnish Type. *Archives of Disease in Childhood*. 1976; 51:344-348.
5. Koziel A, et al. Genotype/phenotype correlations of NPHS1 and NPHS2 mutations in nephrotic syndrome advocate a functional inter-relationship in glomerular filtration. *Hum Molec Genet*. 2002; 11(4): 379-388.

