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Nineteen novel NPHS1 mutations in a worldwide cohort of patients with congenital nephrotic syndrome (CNS).

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Source

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Abstract

BACKGROUND:

Recessive **mutations** in the **NPHS1** gene encoding nephrin account for approximately 40% of infants with **congenital nephrotic syndrome** (**CNS**). **CNS** is defined as steroid-resistant **nephrotic syndrome** (SRNS) within the first 90 days of life. Currently, more than 119 different **mutations** of **NPHS1** have been published affecting most exons.

METHODS:

We here performed mutational analysis of **NPHS1** in a **worldwide cohort** of 67 children from 62 different families with **CNS**.

RESULTS:

We found bi-allelic **mutations** in 36 of the 62 families (58%) confirming in a **worldwide cohort** that about one-half of **CNS** is caused by **NPHS1 mutations**. In 26 families, **mutations** were homozygous, and in 10,

they were compound heterozygous. In an additional nine **patients** from eight families, only one heterozygous mutation was detected. We detected 37 different **mutations**. **Nineteen** of the 37 were **novel mutations** (approximately 51.4%), including 11 missense **mutations**, 4 splice-site **mutations**, 3 nonsense **mutations** and 1 small deletion. In an additional patient with later manifestation, we discovered two further **novel mutations**, including the first one affecting a glycosylation site of nephrin.

CONCLUSIONS:

Our data hereby expand the spectrum of known **mutations** by 17.6%. Surprisingly, out of the two siblings with the homozygous **novel** mutation L587R in **NPHS1**, only one developed **nephrotic syndrome** before the age of 90 days, while the other one did not manifest until the age of 2 years. Both siblings also unexpectedly experienced an episode of partial remission upon steroid treatment.