

Table S1 Biochemical analyses of infant blood and urine are conducted at TTUHSC hospital laboratories

Variables	Description
Creatinine	Always WNL (0.2–0.3 mg/dL)
Albumin	0.5 g/dL (DOL 2); was always between 1.5–2.6 g/dL despite regular albumin infusion (normal range 0–14 days old: 3.3–4.5 g/dL)
Urine protein/creatinine ratio	164 mg/mg (DOL 5) (nephrotic range Upr/Cr ratio >2 mg/mg)
Urinary protein	2,144 mg/dL (DOL 5)
Urinary creatinine	<13 mg/dL (DOL 5)
Triglyceride	173–792 mg/dL [reference range 0–9 yrs: <75 mg/dL]
TSH (thyroid stimulating hormone) and free T4 (thyroxine 4)	9.11 mIU/mL and 40.81 ng/dL respectively at DOL 54 when synthroid was started (normal levels TSH 1 week–3 months: 720–11,000 mIU/mL; free T4 31 days–12 months: 0.48–2.34 ng/dL)

Table S2 Gene Panel for Focal Segmental Glomerulosclerosis and Nephrotic Syndrome (Mayo Clinic Website)

Gene	Reference transcript	Gene	Reference transcript
<i>ACTN4</i>	NM_004924.6	<i>LMX1B</i>	NM_002316.4
<i>ALG1</i>	NM_019109.5	<i>MAGI2</i>	NM_012301.4
<i>ANLN</i>	NM_018685.5	<i>MYH9</i>	NM_002473.5
<i>APOL1</i>	NM_003661.4	<i>MYO1E</i>	NM_004998.4
<i>ARHGAP24</i>	NM_001025616.3	<i>NPHS1</i>	NM_004646.3
<i>ARHGDI1A</i>	NM_001185077.3	<i>NPHS2</i>	NM_014625.4
<i>CD2AP</i>	NM_012120.3	<i>NUP107</i>	NM_020401.4
<i>CLCN5</i>	NM_000084.5	<i>NUP133</i>	NM_018230.3
<i>COL4A3</i>	NM_000091.5	<i>NUP160</i>	NM_015231.2
<i>COL4A4</i>	NM_000092.5	<i>NUP205</i>	NM_015135.3
<i>COL4A5</i>	NM_000495.5	<i>NUP85</i>	NM_024844.5
<i>COQ2</i>	NM_015697.8	<i>NUP93</i>	NM_014669.5
<i>COQ6</i>	NM_182476.3	<i>OCRL</i>	NM_000276.4
<i>COQ8B</i>	NM_024876.4	<i>PAX2</i>	NM_003987.4
<i>CRB2</i>	NM_173689.7	<i>PDSS2</i>	NM_020381.4
<i>CUBN</i>	NM_001081.4	<i>PLCE1</i>	NM_016341.4
<i>DGKE</i>	NM_003647.3	<i>PLCG2</i>	NM_002661.5
<i>EMP2</i>	NM_001424.6	<i>PMM2</i>	NM_000303.3
<i>FAN1</i>	NM_014967.5	<i>PODXL</i>	NM_001018111.3
<i>FAT1</i>	NM_005245.4	<i>PTPRO</i>	NM_030667.3
<i>FN1</i>	NM_212482.3	<i>SCARB2</i>	NM_005506.4
<i>INF2</i>	NM_022489.4	<i>SGPL1</i>	NM_003901.4
<i>ITGA3</i>	NM_002204.4	<i>SMARCAL1</i>	NM_014140.4
<i>ITGB4</i>	NM_000213.5	<i>TBC1D8B</i>	NM_017752.3
<i>KANK2</i>	NM_001136191.3	<i>TRPC6</i>	NM_004621.6
<i>LAMA5</i>	NM_005560.6	<i>TTC21B</i>	NM_024753.5
<i>LAMB2</i>	NM_002292.4	<i>WDR73</i>	NM_032856.4

Table S3 The examination results of a panel of 54 genes (Table S2) reveal four genes and their nucleotide IDs (hg19) tested for variants through DNA sequencing in the congenital nephrotic syndrome case study

Gene name/description	NCBI gene ID	NCBI -nucleotide ID	Variant	Zygoty	Clinical significance
NPHS1: NPHS1 adhesion molecule, nephrin	4868	NM_004646.3	c.2150A>G; p.Tyr717Cys(p.Y717C); Chr19(GRCh37):g36335067T>C	Heterozygous	Variant of uncertain significance
NPHS1: NPHS1 adhesion molecule, nephrin	4868	NM_004646.3	c.3024A>G; p.Arg1008= (p.R1008=); Chr19(GRCh37):g36330224T>C	Heterozygous	Variant of uncertain significance
ALG1: ALG1 chitobiosyldiphosphodolichol beta-mannosyltransferase	56052	NM_019109.5	c.739C>T; p.Arg247Cys (p.F247C); Chr16(GRCh37):g5128017C>T	Heterozygous	Variant of uncertain significance
CRB2: Crumbs cell polarity complex component 2	286204	NM_173689.7	c.1654G>T; p.Ala552Ser (P.A552S); Chr9(GRCh37):g.126132986G>T	Heterozygous	Variant of uncertain significance
NUP160: Nucleoporin 160	23279	NM_015231.2	c.3271C>T; p.Arg1091Cys (p.1091C); Chr9(GRCh37):g.47819349G>A	Heterozygous	Variant of uncertain significance

The Mayo Clinic performed the analysis.

Table S4 Regulatory elements, CTCF, TFBS (Transcription Factor Binding Site) and CpG Islands (CGI) are identified in the enhancers and silencers located in the forward strand of the NPHS1 genomic region. The JASPAR tool identifies regulatory elements such as TFBS and CTCF motifs. CpG Islands (CGI) are identified by EMBOSS Cpplot and EMBOSS Newcpgreport

DNA Sequence	Type	Size (nt)	TFBS #	CTCF motif	CGI
LOC127891330	Enhancer	641	1926	8	2
LOC127891331	Enhancer	642	1957	10	0
LOC129664432	Silencer	253	694	1	1
LOC129664433	Silencer	176	525	4	0

nephrin precursor [Homo sapiens]

NCBI Reference Sequence: NP_004637.1

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Figure S1 The locations of the two *NPHS1* variants along the nephrin precursor are indicated by red arrows. The exon 16 variant (c.2150A>G) may alter the function of the nephrin Ig strand F due to the substitution of tyrosine with cysteine at position 717 (p.Tyr717Cys). The exon 22 variant (c.3024A>G; p.Arg1008=) does not alter nephrin because it is of a synonymous type. Data from the nephrin precursor [Homo sapiens] NCBI reference sequence NP_004637.1.

Chromosome 19 - NC_000019.10

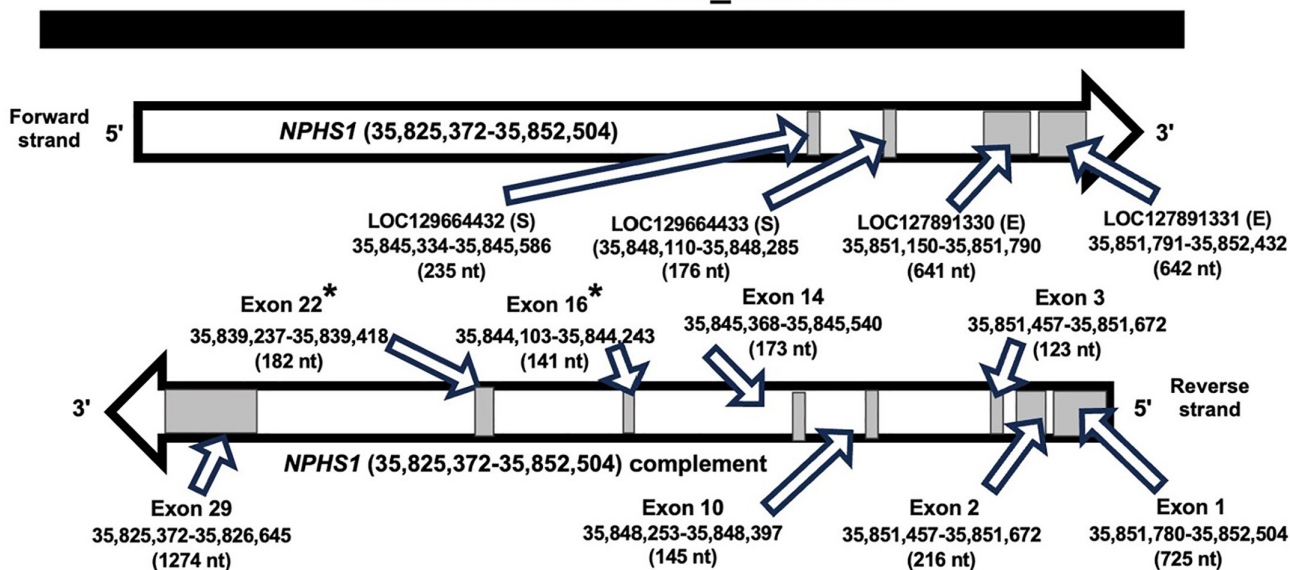


Figure S2 The genomic context of the *NPHS1* locus. Positions of *NPHS1* exons on the reverse strand, as well as enhancers and silencers on the forward strand. Variant (c.2150A>G; p.Tyr717Cys) is mapped to exon 16; variant (c.3024A>G; p.Arg1008=) is mapped to exon 22. Data are adapted from the Gene-NCBI database for human assembly GRCh38.p14 (GCF_000001405.40) updated on 23-Nov-2023. * Indicate VUS in the exon; nt, nucleotide.

A **NUP160-e27**
GTTGTGGGAATAATTGAGTCACGTGCTAGAGCTGTGGACCTTATGACTCACAATTA
CTATGAACCTTCTGTATGCCTTTCACATCTATCGCCACAATTACCGCAAGG

B **ALG1-e6**
GGCTGTGACCGTCTACGACAAGCCCGCATCTTTCTTTAAAGAGACACCTCTGGACCTGCA
GCACCGGCTCTTCATGAAGCTGGGCAGCATGCACTCTCCGTTCAGGGCCCG

C **CRB2-e7**
GGCCGACATGTGAGGAAGATGTGGATGAATGCCTGTTCGGATCCCTGCCTGCACGGCGGAA
CCTGCAGTGACACTGTGGCAGGCTATATCTGCAGGTGCCCAGAGACCTGGGGTGGGCGCG
ACTGTTCTGTGCAGCTCACTGGCTGCCAGGGCCACACCTGCCCGCTGGCTGCCACCTGCA
TCCCTATCTTCGAGTCTGGGGTCCACAGTTACGCTGTGCCACTGCCACCTGGTACCCATG
GACCGTTCTGTGGCCAGAATACCACCTTCTCTGTGATGGCTGGGAGCCCCATTCAGGCAT
CAGTGCCAGCTGGTGGCCCCCTGGGTCTGGCACTGAGGTTTCGCACCACACTGCCCGCTG
GGACCTTGCCACTCGCAATGACACCAAGGAAAGCTTGGAGCTGGCATTGGTGGCAGCCA
CACTTCAGGCCACACTCTGGAGCTACAGCACCCTGTGCTTGTCTGAGACTGCCGGACC
TGGCCCTAAACGATGGCCATGGCACCAAGGTGGAGGTTGTGCTCCATCTAGCGACCCTGG
AGCTACGGCTCTGGCATGAGGGCTGCCCTGCCCGGCTCTGTGTGGCCTCTGGTCTGTGG
CCCTGGCTTCACGGCTTCGGCAACTCCGCTGCCTGCCGGGATCTCCTCTGCCCAGCTGG
GGACCGCGACCTTTGCAGGCTGCCTCCAGGACGTGCGTGTGGATGGCCACCTCCTGCTGC
CTGAGGATCTCGGTGAGAACGTCTCCTGGGCTGTGAGCGCCGAGAGCAGTGCCGGCCTC
TGCCTTGTGTCCACGGAGGGTCTGTGTGGATCTGTGGACTCATTTCCGTTGCGACTGTG
CCCGGCCCATAGAGGTCCCACGTGCCTGATG

Figure S3 The identified ESE and CTCF motifs in NUP160 exon-27 (A), ALG1 exon-6 (B), and CRB2 exon-7 (C). The CTCF motifs are highlighted in red, ESE motifs are underlined, and the normal base of the mutated nucleotide is highlighted in blue. The CTCF motifs were identified by the JASPAR database ([/jaspar.elixir.no](http://jaspar.elixir.no)). The exonic splicing enhancer (ESE) motifs were identified by ESEfinder 3 (esefinder.ahc.umn.edu).