Supplement Table 1: Detailed genetic description of children with genetic work up and Interpretation of variant as per ACMG guidelines

Pt ID	Details of genetic work up in the index child	Status of sequence variation	Population frequency (gnomAD)	Classification of sequence variation	Position in protein domain	Method used for molecular genetic testing	Carrier status of the parents	(i) F hx of sibling or fetal death (ii) Hx of Consanguinity in family	Evidence of pathogenicity	ACMG Classification
E1a	Homozygous c.1099C>T; p.Arg367Cys in the in exon 9 of *NPHS1* gene Mutation details published previously***	Reported in ClinVar as likely pathogenic	0.0000397842104425595	Missense (Mild)	Extracellular	NGS for 27 genes	Heterozygous	(i) +ve (ii) +ve	PS1, PM2, PM3, PP2, PP3, PP4, PP5	Pathogenic
E1b	Compound heterozygous c.1219C>T; p.Arg407Trp in exon 10 and c.2422delC; p.Leu808Trpfs*39 in exon 16 of *NPHS1*. Mutation details published previously***	Reported in ClinVar as likely pathogenic	0.0000212189584320604 0 (Not reported)	Missense (Mild) and Frameshift truncating (Severe)	Extracellular Extracellular	NGS for 27 genes	Heterozygous	(i) +ve (ii) +ve	PS1, PM2, PM3, PP2, PP3, PP4, PP5 PVS1, PM2, PM3, PP2, PP3, PP4, PP5	Pathogenic Pathogenic
E1c	Polymorphism: Homozygous c.1223G>A; p. Arg408Gln in exon 10 of *NPHS1* gene.	Benign		Polymorphism	Extracellular	NGS for 27 genes	Heterozygous	(i) –ve (ii) -ve		Benign
E1g	WT1 mutation c.633T>G; p. Cys211Trp	NA	0 (Not reported)	NA		SS Mutation looked into only NPHS1, NPHS2 and WT1	Neither parents showed a similar mutation	(i) –ve (ii) -ve	PS2, PM2, PP2,PP3,PP4	Likely pathogenic

E1k	Compound heterozygous: c.3325C>T ; p.Arg1109Ter in exon 26 and and c.1219C>T; p.Arg407Trp in exon 10 of NPHS1	Reported in ClinVar as pathogenic and Reported in ClinVar as pathogenic	0.000155096716721812	Truncating (Severe) and Missense (Mild)	Cytosolic Extracellular	NGS for 27 genes	Parental testing not done	(i) –ve (ii) -ve	PVS1, PM2, PM3, PP2, PP3, PP4, PP5 PS1, PM2, PM3, PP2, PP3, PP4, PP5	Pathogenic Pathogenic
E3a	Compound heterozygous c.3325C>T ; p.Arg1109Ter in exons 26 and c.1219C>T; p.Arg407Trpin exon 10 of *NPHS1*.	Reported in ClinVar as pathogenic Reported in ClinVar as pathogenic		Truncating (Severe) and Missense (Mild)	Cytosolic Extracellular	NGS for 27 genes	Parental testing not done	(i) +ve (ii) -ve	PVS1, PM2, PM3, PP2, PP3, PP4, PP5 PS1, PM2, PM3, PP2, PP3, PP4, PP5	Pathogenic Pathogenic
N1a	Compound heterozygous: c.1099C>T ; p.Arg367Cys in exon 9 and c.2758T>C; p.Cys920Arg in exon 20 of NPHS1	Reported in ClinVar as pathogenic NOVEL	0 (Not reported)	Missense (Mild) and Missense (Mild)	Extracellular Extracellular	NGS for 27 genes	Heterozygous	(i) –ve (ii) -ve	PS1, PM2, PM3, PP2, PP3, PP4, PP5 PM2, PM3, PP2, PP3, PP4, PP5	Pathogenic Likely pathogenic
N1b	PLCE1 mutations+ Homozygous nonsense mutation c.2290G>T; p.Glu764Ter	Reported in ClinVar as pathogenic	0 (Not found)	Truncating (Severe)		SS Mutation looked only	Heterozygous.	(i) + ve (ii) -ve	PVS1, PM2, PM3, PP2, PP3, PP4, PP5	Pathogenic

	located in exon 7of the PLCE1 gene. Mutation details published previously***					for NPHS1, WT1 and PLCE1				
N1c	Compound heterozygous: c.1099C>T; p.Arg367Cys in exon 9 of NPHS1 and c.2758T>C ; p.Cys920Arg in exon 20 of NPHS1	Reported in ClinVar as pathogenic and Reported in our series		Missense (Mild) and Missense (Mild)	Extracellular Extracellular	NGS for 27 genes	Hetrozygous	(i) - ve (ii) -ve	PS1, PM2, PM3, PP2, PP3, PP4, PP5 PM2, PM3, PP2, PP3, PP4, PP5	Pathogenic Likely pathogenic
W 1a	Homozygous mutation in NPHS1 Details not available	----------		----------		NGS for 27 genes	Details not available	(i) + ve (ii) +ve		
S1k	Homozygous mutation in exon 9 of NPHS1 c.1099C>T; p.Arg367Cys	Reported in ClinVar as likely pathogenic		Missense (Mild)	Extracellular	NGS for 27 genes	Parents not tested	Details not available	PS1, PM2, PM3, PP2, PP3, PP4, PP5	Pathogenic

ACMG: American Council of medical Genetics; CKD: Chronic kidney Disease, CAPD: Continuous ambulatory peritoneal dialysis, ESRD: End Stage Renal Disease, F: Female, F Hx: Family history, Hx: History, M: Male, NGS: Next generation sequencing, SS; sanger sequencing.

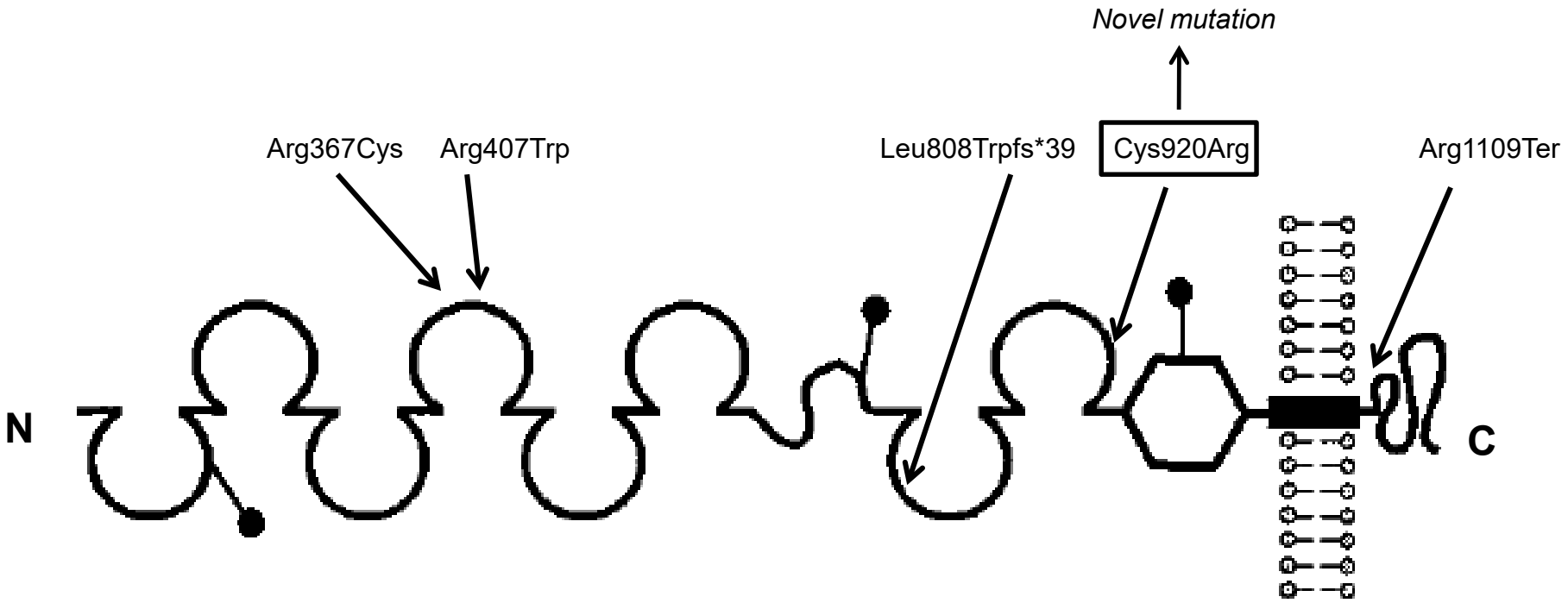
***Cases whose mutation details were published previously: **E1a** - Lovric S, Fang H, Vega-Warner V, Sadowski CE, Gee HY, Halbritter J et al. Rapid detection of monogenic causes of childhood-onset steroid-resistant nephrotic syndrome. Clin J Am Soc Nephrol. 2014 Jun 6;9(6):1109-16. **E1b-** Sadowski CE[1], Lovric S[1], Ashraf S[1], Pabst WL[1], Gee HY[1], Kohl S et al. A single-gene cause in 29.5% of cases of steroid-resistant nephrotic syndrome. J Am Soc Nephrol. 2015 Jun;26(6):1279-89. **N1b-** Sethi SK, Wadhwani N, Jha P , Duggal R, Vega-Warner V, Raina R et al. A Familial Infantile Renal Failure. Kidney Int Rep. 2016 Sep 1;2(2):130-133

Supplement Table 2: List of genes and their transcript IDs used for variant analysis

Gene	**ID**
ACTN4	NM_004924
ADCK4	NM_024876
ANLN	NM_018685
APOL1	NM_145343
ARHGAP24	NM_001025616
ARHGDIA	NM_004309
CD2AP	NM_012120
CFH	NM_000186
COQ2	NM_015697
COQ6	NM_182476
CRB2	NM_173689
CUBN	NM_001081
DGKE	NM_003647
EMP2	NM_001424
INF2	NM_022489
ITGA3	NM_002204
ITGB4	NM_000213
LAMB2	NM_002292
LMX1B	NM_001174146
MEFV	NM_000243
MYO1E	NM_004998
NEIL1	NM_024608
NPHS1	NM_004646
NPHS2	NM_014625

NUP107	NM_020401
PAX2	NM_003990
PDSS2	NM_020381
PLCE1	NM_016341
PTPRO	NM_030667
SCARB2	NM_005506
SMARCAL1	NM_014140
TRPC6	NM_004621
WT1	NM_001198551

Supplement Figure 1



Supplement Figure 1: Nephrin protein domain structure (Adapted from Kestila M et al; 1998). The amino acid sequence of nephrin is 1,241 residues. The N-terminal signal sequence is 22 residues. The extracellular part of the protein contains eight Ig-like modules, and one fibronectin type III–like module. Dots indicate Cysteine residues. The transmembrane domain contains residues 1059 to1086. Apparent positions of the different mutations in our series are shown with arrow. All are extracellular except one, which is cytosolic.