

Supplemental Table 1. *PRDM15* gRNA and primer sequences.

CRISPR guide RNA (gRNA) sequences	
C7	<u>CACCGCTGGCGTCCACGGTATGTGG</u>
D12	<u>CACCGGTGCTGCGCAGTTTCCGGAG</u>
A6 (scramble)	<u>CACCGGTCTTCGAGAAGACCT</u>
CRISPR PCR and sequencing primers	
F-C7	TACTTCACCACCTCCAGAGACA
R-C7	AAACAAGCAGAAAGACAGACCC
F-D12	GGACTACAAGTCCCGCCA
R-D12	AAAGAACAGTCGGCATGG
Taqman Probes (ThermoFisher catalog number)	
GAPDH	Hs02786624_g1
PRDM15	Hs00411318_m1
WT1	Hs01103751_m1
SEMA3A	Hs00173810_m1
PAX2	Hs01057416_m1
FOXC1	Hs00559473_s1

Supplemental Table 2. Clinical characteristics of four individuals from four unrelated families with GAMOS-Mildenberger type and the *PRDM15* p.Cys844Tyr mutation.

Family ID	MIC	B44	B53	B54
Ethnicity	Arab	Arab	Arab	Arab
Parental consanguinity	Yes (first cousins)	Yes (not specified)	Yes (uncle -niece)	Not known
Gender	Female	Male	Male	Male
Prenatal findings	Increased placental weight BW/PW=0.31	ND	No abnormalities recorded	Polyhydramnios, increased AFP in amniotic fluid
Birth measurements (weight, length, OFC)	2435 g	ND	2730 g, 50 cm, 34.5 cm	3450 g, 51 cm, 36 cm
Proteinuria (onset)	First week of life	Before age 2 months	First week of life	First week of life
Proteinuria (nature)	Non-selective proteinuria (age 2 weeks: 8 g/l; age 6 months: 420 mg/m ² *h), hypoproteinemia	Glomerular proteinuria (age 2 months: 4.2 g/l), hypoproteinemia	Mixed glomerular and tubular proteinuria (age 4 weeks: 55 mg/m ² *h)	Non-selective glomerular and tubular proteinuria (age 2 weeks: 5.3 g/l)
Tubular involvement	Glucosuria (age 6 months: 17 mmol/l), aminaciduria, no acidosis before onset of renal failure	Mild hyperaminoaciduria	Hyperaminoaciduria (suspected tubulopathy)	None
Renal failure (onset)	Approx. 4 months; at age 6 months creatinine 1.27 mg/dL; creatinine clearance 11 ml/min/1.73m ² ; peritoneal dialysis started at age 9 months	Approx. 12 months; at age 16 months creatinine 3.96 mg/dL, urea 100 mg/dL; on peritoneal dialysis since age of 18 months	First week of life; at age 4 weeks creatinine 1.2 mg/dL, creatinine clearance 2.5 ml/min/1.73m ² , peritoneal dialysis at age 7 months	First week of life; at age 5 weeks creatinine clearance 12.7 ml/min/1.73m ²
Kidney ultrasound	No gross morphological abnormalities	Kidneys of increased size and echogenicity, poor corticomedullary differentiation	Kidneys of increased size and echogenicity, no cystic changes	Increased echogenicity, poor corticomedullary differentiation

Kidney biopsy	Age 6 months: diffuse mesangial sclerosis, interstitial fibrosis, tubular atrophy and tubular cysts	Postmortem (28 months): diffuse glomerulosclerosis, tubular atrophy, interstitial fibrosis; EM: thickening of glomerular basement membranes	Not performed	Age 4 weeks: no gross abnormalities on light microscopy; EM: abnormal GBM, podocyte effacement
Microcephaly (secondary)	OFC of 41 cm at age 9 months (-3.1 SD)	OFC of 41 cm at age 10 months (-4.4 SD)	OFC of 39.5 cm at age 4 months (-2.1 SD)	No OFC documented after birth
Cranial abnormalities	Narrow forehead	Trigonocephaly	Narrow forehead	Trigonocephaly
Brain anomalies	Cerebellar hypoplasia / Dandy-Walker variant, gyral hypoplasia in left occipital region (Suppl. Figure 2 A-B)	Abnormal gyration mentioned (no documentation of brain MRI available)	Age 2 months: abnormal myelination, left temporal lobe hypoplasia and abnormal gyration (Figure 1B)	Dandy-Walker malformation, suspected pineal cyst, brain atrophy / simplified gyration (ultrasound only)
Ocular anomalies	Microcoria, right megalocornea, suspected buphthalmos with normal pressure, corneal clouding	Microcoria, myopia, left retinal coloboma	Large-appearing eyes, left iris coloboma, right miosis	Right microphthalmia, bilateral ectopia pupillae, left chorioretinal coloboma
Hearing	No abnormalities recorded	Sensorineural hearing loss	BERA normal	No abnormalities recorded
Cardiac anomalies	ASD II (spontaneous closure by age 4 months), septal hypertrophy	None	PFO / ASD, myocardial hypertrophy; increased QTc	ASD II
Polydactyly	Postaxial, both hands	Postaxial, both hands	Postaxial, both hands	Postaxial, both hands
Other	Rocker bottom feet, retrognathia, recurrent apnea, mild nail hypoplasia, hepatosplenomegaly from age 9 months on, severe developmental delay; cerebri media infarction at age 14 months, consecutive epilepsy	Inguinal hernia, muscular hypotonia, hypothyroidism, severe developmental delay	Pes calcaneus; mild hepatosplenomegaly, recurrent apnea, cutis laxa, developmental delay; muscle biopsy at age 2 months (suspected mitochondrial disease); non-specific abnormalities; mother: unilateral hexadactyly	Macrostomia, retrogenia, low-set and rotated ears, short neck, dysplastic vertebral body C4, bell-shaped thorax, cryptorchidism, hypospadias, pes calcaneus, hepatic siderosis (post mortem biopsy)

Death	15 months	28 months	7 months (sepsis)	6 weeks (respiratory failure due to pneumonia)
Postmortem	No autopsy	No full autopsy, postmortem kidney biopsy only	No autopsy	No full autopsy performed, postmortem liver biopsy: siderosis, kidney biopsy: non-specific on light microscopy
Publication	Mildenberger <i>Acta Paediatr</i> 87:1301, 1998	Previously unpublished	Previously unpublished	Previously unpublished

ASD, atrial septal defect; BERA, brainstem evoked response audiometry; BW/PW, birth weight / placental weight; cm, centimeter; EM, electron microscopy; GBM, glomerular basement membrane; ND, not done / not documented; OFC, occipital frontal circumference; PFO, patent foramen ovale; QTc, corrected QT interval; SD, standard deviation.

Supplemental Table 3: 51 genes that represent monogenic causes of human nephrotic syndrome, if mutated.

Gene	Protein	Reference	Mode of Inheritance
ADCK4	AarF domain containing kinase 4	Ashraf <i>J Clin Invest</i> 123:5179, 2013	AR
ALG1	ALG1, Chitobiosylidiphosphodichol Beta-Mannosyltransferase	Harshman <i>Pediatr Int</i> 58:785, 2016	AR
ARHGDI	Rho GDP dissociation inhibitor (GDI) alpha	Gee <i>J Clin Invest</i> 123:3243, 2013	AR
AVIL	Advillin	Rao <i>J Clin Invest</i> 127:4257, 2017	AR
CD2AP	CD2 associated protein	Kim <i>Science</i> 300:1298, 2003	AR
COQ2	Coenzyme Q2 4-hydroxybenzoate polyprenyltransferase	Diomed-Camassei <i>JASN</i> 18:2773, 2007	AR
COQ6	Coenzyme Q6 monooxygenase	Heeringa <i>J Clin Invest</i> 121:2013, 2011	AR
CRB2	Crumbs, Drosophila, Homolog of 2	Ebarasi <i>AJHG</i> 96: 153-161, 2015	AR
CUBN	Cubilin (intrinsic factor-cobalamin receptor)	Ovunc <i>JASN</i> 22:1815, 2011	AR
DGKE	Diacylglycerol kinase epsilon	Lemaire <i>Nat Genet</i> 45: 531, 2013	AR
EMP2	Epithelial membrane protein 2	Gee <i>AJHG</i> 94:884, 2014	AR
FAT1	Fat tumor suppressor, drosophila, homolog of, 1	Gee <i>Nat Commun</i> 7:10822, 2016	AR
ITGA3	Integrin, alpha 3 (antigen CD49C, alpha 3 subunit of VLA-3 receptor)	Yalcin <i>Hum Mol Genet</i> 24:3679, 2015	AR
ITGB4	Integrin, beta 4	Kambham <i>AJKD</i> 36:190, 2000	AR
KANK1	KN motif and ankyrin repeat domain-containing protein 1	Gee <i>J Clin Invest</i> 125:2375, 2015	AR
KANK2	KN motif and ankyrin repeat domain-containing protein 2	Gee <i>J Clin Invest</i> 125:2375, 2015	AR
KANK4	KN motif and ankyrin repeat domain-containing protein 3	Gee <i>J Clin Invest</i> 125:2375, 2015	AR
LAGE3	L antigen family member 3	Braun <i>Nat Genet</i> 49:1529, 2017	AR
LAMB2	Laminin, beta 2	Zenker <i>Hum Mol Genet</i> 12:2625, 2004	AR
LCAT	Lecithin-Cholesterol Acyltransferase	Taramelli <i>Hum Genet</i> 85:195, 1990	AR
MAGI2	Membrane-associated guanylate kinase, WW and PDZ domains-containing 2	Bierzynska <i>JASN</i> 28:1614, 2017	AR
MYO1E	Homo sapiens myosin IE (MYO1E)	Mele <i>NEJM</i> 365:295, 2011	AR
NPHS1	Nephrin	Kestila <i>Mol Cell</i> 1:575, 1998	AR
NPHS2	Podocin	Boute <i>Nat Genet</i> 24:349, 2000	AR
NUP107	Nucleoporin, 107-KD	Miyake <i>AJHG</i> 97:555, 2015	AR
NUP133	Nucleoporin 133-KD	Braun <i>Nat Genet</i> 48:457, 2016	AR
NUP205	Nucleoporin, 205-KD	Braun <i>Nat Genet</i> 48:457, 2016	AR
NUP85	Nucleoporin 85-KD	Braun <i>Nat Genet</i> 48:457, 2016	AR
NUP93	Nucleoporin, 93-KD	Braun <i>Nat Genet</i> 48:457, 2016	AR
OSGEP	O-sialoglycoprotein endopeptidase	Braun <i>Nat Genet</i> 48:457, 2016	AR
PDSS2	Prenyl (decaprenyl) diphosphate synthase, subunit 2	Lopez <i>AJHG</i> 79:1125, 2006	AR
PLCE1	Phospholipase C, epsilon 1	Hinkes <i>Nat Genet</i> 38:1397, 2006	AR
PTPRO	Protein tyrosine phosphatase, receptor type, O	Ozaltin <i>AJHG</i> 89:139, 2011	AR
SCARB2	Scavenger receptor class B, member 2	Badhwar <i>Brain</i> 127: 2173, 2004	AR
SGPL1	Sphingosine 1 phosphate lyase 1	Lovric <i>J Clin Invest</i> 127: 912, 2017	AR
SMARCAL1	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a-like 1	Boerkoel <i>Nat Genet</i> 30:215, 2002	AR
TP53RK	TP53-regulating kinase	Braun <i>Nat Genet</i> 49:1529, 2017	AR
TPRKB	TP53RK binding protein	Braun <i>Nat Genet</i> 49:1529, 2017	AR
WDR4	WD repeat-containing protein 4	Braun <i>Am J Med Genet A</i> 176:2460, 2018	AR
WDR73	WD repeat-containing protein 73	Colin <i>AJHG</i> 95:637, 2014	AR
XPO5	Exportin 5	Braun <i>Nat Genet</i> 48:457, 2016	AR
ACTN4	Actinin, alpha 4	Kaplan <i>Nat Genet</i> 24(3):251, 2000	AD
ANLN	Actin-binding protein anillin	Gbadegesin <i>JASN</i> 25:1991, 2014	AD
ARHGAP24	Rho GTPase activating protein 24	Akilesh <i>J Clin Invest</i> 121:4127, 2011	AD
INF2	Inverted formin, FH2 and WH2 domain containing	Brown <i>Nat Genet</i> 42:72, 2010	AD
LMX1B	LIM Homeobox Transcription Factor 1 Beta	Dreyer <i>Nat Genet</i> 19:47 1998	AD
MYH9	Myosin heavy chain 9, nonmuscle	Heath <i>AJHG</i> 69:1033, 2001	AD
TRPC6	Transient receptor potential cation channel, subfamily C, member 6	Winn <i>Science</i> 308:1801, 2005	AD
WT1	Wilms Tumor 1	Melo <i>J Clin Endocrinol Metab</i> 87:2500, 2002	AD
NXF5	Nuclear RNA export factor 5	Esposito <i>Hum Mol Genet</i> 22:3654, 2013	XL
APOL1	Apolipoprotein L-1	Parsa <i>NEJM</i> 369:2183, 2013	Unknown

AR, autosomal recessive; AD, autosomal dominant; XL; X-linked; Unknown, mode of inheritance not clearly characterized. .

Supplemental Table 4. Comparison of *PRDM15* expression in an immortalized human podocyte cell line with expression of other known genetic causes of Galloway-Mowat syndrome.

Ensembl	GeneID	A6 (scramble)		
		CPM (1)	CPM (2)	CPM (3)
ENSG00000141956	<i>PRDM15</i>	12.5126471	14.4832217	13.5565422
ENSG00000177082	<i>WDR73</i>	29.5201285	30.5821017	29.3222986
ENSG00000196976	<i>LAGE3</i>	8.2607767	8.13599309	9.94146426
ENSG00000092094	<i>OSGEP</i>	37.5986822	44.8922172	39.2637629
ENSG00000172315	<i>TP53RK</i>	38.7527613	39.1220093	35.2470097
ENSG00000160193	<i>WDR4</i>	23.506769	24.3502772	23.8996818
ENSG00000111581	<i>NUP107</i>	133.933916	129.541167	135.063328
ENSG00000069248	<i>NUP133</i>	85.1588892	79.6288685	90.1761102

A6, scramble CRISPR treated cells (in triplicate); CPM, counts per million (normalized)