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Supplementary information

Podocytopathies

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Supplementary Table 1. Genetic forms of podocytopathies.

Clinical phenotype	Pathology	Gene	Inheritence	OMIM name	OMIM ID	Ref
Podocyte genes						
SRNS	FSGS	*ACTN4*	AD	Glomerulosclerosis, focal segmental, 1	* 604638	[1]
SRNS	FSGS	*ADCK4*	AR	Nephrotic syndrome, type 9	* 615567	[2]
SRNS, proteinuria	FSGS	*ANLN*	AD	Focal segmental glomerulosclerosis 8	* 616027	[3]
SRNS	FSGS	*ARHGAP24*	AR	*Nephrotic syndrome	* 610586	[4]
SRNS	FSGS	*ARHGDIA*	AR	Nephrotic syndrome, type 8	* 601925	[5]
SRNS	FSGS	*CD2AP*	AR, AD	Glomerulosclerosis, focal segmental, 3	* 604241	[6]
CNS, SSNS, SDNS, SRNS	MCD, FSGS	*CDK20*	AR	*Nephrotic syndrome	* 610076	[7]
SRNS	FSGS	*CRB2*	AR	Focal segmental glomerulosclerosis 9	* 609720	[8]
NS	FSGS	*DGKE*	AR	Nephrotic syndrome, type 7 and HUS, atypical, susceptibility to, 7	* 601440	[9]
SSNS, SRNS	FSGS	*DLC1*	AR	*Nephrotic syndrome	* 604258	[7]
SSNS, SRNS	FSGS	*EMP2*	AR	Nephrotic syndrome, type 10	* 602334	[10]
SRNS	FSGS	*INF2*	AD	Glomerulosclerosis, focal segmental, 5	* 613237	[11]
SSNS, SRNS	MCD, FSGS	*ITSN1*	AR	*Nephrotic syndrome	* 602442	[7]
SDNS, SSNS	MCD, MPGN	*ITSN2*	AR	*Nephrotic syndrome	* 604464	[7]
CNS, SRNS	MCD	*MAGI2*	AR	Nephrotic syndrome, type 15	* 606382	[12]
SRNS	FSGS	*MYO1E*	AR	Glomerulosclerosis, focal segmental, 6	* 601479	[13]
CNS, SRNS	PTRD, PMS, FSGS, MCD	*NPHS1*	AR	Nephrotic syndrome, type 1	* 602716	[14]
CNS, SRNS, proteinuria	FSGS, MCD	*NPHS2*	AR	Nephrotic syndrome, type 2	* 604766	[15]
SRNS	FSGS	*NUP107*	AR	*Nephrotic syndrome	* 607617	[16]
SRNS	FSGS	*NUP205*	AR	*Nephrotic syndrome	* 614352	[17]
SRNS	FSGS	*NUP93*	AR	*Nephrotic syndrome	* 614351	[17]
Proteinuria	FSGS	*SYNPO*	AR	*Nephrotic syndrome	* 608155	[18]
SRNS, proteinuria	FSGS	*TRPC6*	AD	Glomerulosclerosis, focal segmental, 2	* 603652	[19]
CNS, SRNS	MCD, FSGS	*PLCE1*	AR	Nephrotic syndrome, type 3	* 608414	[20]
Proteinuria	FSGS	*PODXL*	AR	*Nephrotic syndrome	* 602632	[21]
SRNS	FSGS, MCD	*PTPRO*	AR	Nephrotic syndrome, type 6	* 600579	[22]
SDNS, SSNS	MCD, DMS, FSGS	*TNS2*	AR	*Nephrotic syndrome	* 607717	[7]

CNS, SRNS, proteinuria	DMS, SRNS	*WT1*	AD	Nephrotic syndrome, type 4	256370	
Syndromal genes						
SRNS	FSGS	*ALG1*	AR	Congenital disorder of glycosylation, type Ik	*605907	[23]
SRNS, proteinuria	MCD, FSGS	*COL4A3*	AR, AD	Alport syndrome 2, autosomal recessive, Alport syndrome 3, autosomal dominant	203780 104200	[24]
SRNS, proteinuria	FSGS	*COL4A4*	AR, AD	Alport syndrome 2, autosomal recessive	*120131	[24]
SRNS, proteinuria	FSGS	*COL4A5*	XLD	Alport syndrome 1, X-linked	*303630	[25]
SRNS	FSGS	*COQ2*	AR	Coenzyme Q10 deficiency, primary, 1	* 609825	[26]
SRNS	FSGS	*COQ6*	AR	Coenzyme Q10 deficiency, primary, 6	* 614650	[27]
SRNS, proteinuria w or w/o hematuria	MCD, FSGS	*CUBN*	AR	Megaloblastic anemia-1, Finnish type	261100	[28]
Proteinuria	MCD	*CD151*	AR	Nephropathy with pretibial epidermolysis bullosa and deafness	* 602243	[29]
SRNS, proteinuria	FSGS	*CLCN5*	XLR	Proteinuria, low molecular weight, with hypercalciuric nephrocalcinosis Dent disease	308990 300009	[25]
SRNS, proteinuria	MCD, FSGS	*CTNS*	AR	Cystinosis, atypical nephropathic	606272	[25]
Proteinuria	FSGS	*E2F3*	AD	FSGS, mental retardation (gene deletion)	*600427	[30]
SRNS, proteinuria	FSGS, tubular atrophy	*FAT1*	AR	Glomerulotubular nephropathy with CNS involvement	*600976	[31]
SRNS, proteinuria	FSGS	*GLA*	XL	Fabry disease	*301500	[25]
SRNS, proteinuria	FSGS	*INF2*	AD	Charcot-Marie-Tooth disease, dominant intermediate E	* 614455	[13]
SRNS	FSGS	*ITGA3*	AR	Interstitial lung disease, nephrotic syndrome, epidermolysis bullosa, congenital	* 605025	[32]
SRNS	FSGS	*ITGB4*	AR	Epidermolysis bullosa	* 147557	[33]
SRNS w or w/o haematuria	FSGS	*KANK1*	AR	Cerebral palsy, spastic quadriplegic, 2	* 607704	[34]
SRNS w or w/o haematuria	FSGS	*KANK2*	AR	Nephrotic syndrome, type 16 Palmoplantar keratoderma and woolly hair	* 614610	[34]
SRNS w or w/o haematuria	FSGS	*KANK4*	AR	Cerebral palsy, spastic quadriplegic, 2	* 614612	[34]
SRNS	FSGS	*LAMB2*	AR	Pierson syndrome Nephrotic syndrome, type 5, w or w/o ocular abnormalities	609049 619149	[35]
SRNS	FSGS	*LMX1B*	AR	Nail-patella syndrome	*602575	[36]
Proteinuria	MCD, FSGS	*MYH9*	AD	Macrothrombocytopenia and granulocyte inclusions with or without nephritis or sensorineural hearing loss	* 160775	[37]
Proteinuria	FSGS	*NXF5*	XLD	FSGS with progressive cardiac conduction disorder	* 300319	[38]
Proteinuria	FSGS	*OCRL1*	XLR	Dent disease 2 Lowe syndrome	300555 309000	[28]
SRNS, proteinuria	FSGS	*PAX2*	AD	Glomerulosclerosis, focal segmental, 7 Papillorenal syndrome	616002 120330	[39]
SRNS	FSGS	*PDSS2*	AR	Coenzyme Q10 deficiency, primary, 3	* 610564	[40]
CNS	CG	*PMM2*	AR	Congenital defect of glycosylation		[41]

SRNS	FSGS	*SCARB2*	AR	Epilepsy, progressive myoclonic 4, with or without renal failure	* 602257	[42]
CNS, DMS, SRNS	FSGS	*SGPL1*	AR	Nephrotic syndrome, type 14 with ichthyosis and primary adrenal insufficiency	* 603729	[43]
SRNS	FSGS	*SMARCAL1*	AR	Schimke immunoosseous dysplasia	* 606622	[44]
SRNS	FSGS	*TTC21B*	AR	Nephronophthisis 12	*612014	[45]
SRNS	MCD	*XPO5*	AR	Nephrotic syndrome with speech development delay	* 607845	[17]
SRNS	FSGS	*WDR73*	AR	Galloway-Mowat syndrome 1	*6166144	[46]
SRNS, proteinuria	FSGS, DMS	*WT1*	AD AD	Frasier syndrome Denys Drash syndrome	136680 194080	[47] [48]
Proteinuria	FSGS	*ZMPSTE24*	AR	Mandibuloacral dysplasia	*606480	[49]

CKD, chronic kidney disease; FSGS, focal segmental glomerulosclerosis; HCV, hepatitis C virus; MCD, minimal change disease; SRNS, steroid-resistant nephrotic syndrome; SSNS, steroid-sensitive nephrotic syndrome; SDNS, steroid-dependent nephrotic syndrome; FRNS, frequent-relapsing nephrotic syndrome; eGFR, estimated glomerular filtration rate; FPE, foot process effacement; ESKD, end stage kidney disease; DMS, diffuse mesangial sclerosis; w, with; w/o, without; OMIM, Online Mendelian Inheritance in Man.

References

1 Kaplan, J. M. *et al.* Mutations in ACTN4, encoding alpha-actinin-4, cause familial focal segmental glomerulosclerosis. *Nat Genet* **24**, 251-256, doi:10.1038/73456 (2000).

2 Ashraf, S. *et al.* ADCK4 mutations promote steroid-resistant nephrotic syndrome through CoQ10 biosynthesis disruption. *J Clin Invest* **123**, 5179-5189, doi:10.1172/JCI69000 (2013).

3 Gbadegesin, R. A. *et al.* Mutations in the gene that encodes the F-actin binding protein anillin cause FSGS. *J Am Soc Nephrol* **25**, 1991-2002, doi:10.1681/ASN.2013090976 (2014).

4 Akilesh, S. *et al.* Arhgap24 inactivates Rac1 in mouse podocytes, and a mutant form is associated with familial focal segmental glomerulosclerosis. *J Clin Invest* **121**, 4127-4137, doi:10.1172/JCI46458 (2011).

5 Gee, H. Y. *et al.* ARHGDIA mutations cause nephrotic syndrome via defective RHO GTPase signaling. *J Clin Invest* **123**, 3243-3253, doi:10.1172/JCI69134 (2013).

6 Kim, J. M. *et al.* CD2-associated protein haploinsufficiency is linked to glomerular disease susceptibility. *Science* **300**, 1298-1300, doi:10.1126/science.1081068 (2003).

7 Ashraf, S. *et al.* Mutations in six nephrosis genes delineate a pathogenic pathway amenable to treatment. *Nat Commun* **9**, 1960, doi:10.1038/s41467-018-04193-w (2018).

8 Ebarasi, L. *et al.* Defects of CRB2 cause steroid-resistant nephrotic syndrome. *Am J Hum Genet* **96**, 153-161, doi:10.1016/j.ajhg.2014.11.014 (2015).

9 Ozaltin, F. *et al.* DGKE variants cause a glomerular microangiopathy that mimics membranoproliferative GN. *J Am Soc Nephrol* **24**, 377-384, doi:10.1681/ASN.2012090903 (2013).

10 Gee, H. Y. *et al.* Mutations in EMP2 cause childhood-onset nephrotic syndrome. *Am J Hum Genet* **94**, 884-890, doi:10.1016/j.ajhg.2014.04.010 (2014).

11 Boyer, O. *et al.* Mutations in INF2 are a major cause of autosomal dominant focal segmental glomerulosclerosis. *J Am Soc Nephrol* **22**, 239-245, doi:10.1681/ASN.2010050518 (2011).

12 Bierzynska, A. *et al.* MAGI2 Mutations Cause Congenital Nephrotic Syndrome. *J Am Soc Nephrol* **28**, 1614-1621, doi:10.1681/ASN.2016040387 (2017).

13 Boyer, O. *et al.* INF2 mutations in Charcot-Marie-Tooth disease with glomerulopathy. *N Engl J Med* **365**, 2377-2388, doi:10.1056/NEJMoa1109122 (2011).
14 Philippe, A. *et al.* Nephrin mutations can cause childhood-onset steroid-resistant nephrotic syndrome. *J Am Soc Nephrol* **19**, 1871-1878, doi:10.1681/ASN.2008010059 (2008).
15 Boute, N. *et al.* NPHS2, encoding the glomerular protein podocin, is mutated in autosomal recessive steroid-resistant nephrotic syndrome. *Nat Genet* **24**, 349-354, doi:10.1038/74166 (2000).
16 Miyake, N. *et al.* Biallelic Mutations in Nuclear Pore Complex Subunit NUP107 Cause Early-Childhood-Onset Steroid-Resistant Nephrotic Syndrome. *Am J Hum Genet* **97**, 555-566, doi:10.1016/j.ajhg.2015.08.013 (2015).
17 Braun, D. A. *et al.* Mutations in nuclear pore genes NUP93, NUP205 and XPO5 cause steroid-resistant nephrotic syndrome. *Nat Genet* **48**, 457-465, doi:10.1038/ng.3512 (2016).
18 Dai, S. *et al.* Functional analysis of promoter mutations in the ACTN4 and SYNPO genes in focal segmental glomerulosclerosis. *Nephrol Dial Transplant* **25**, 824-835, doi:10.1093/ndt/gfp394 (2010).
19 Gigante, M. *et al.* TRPC6 mutations in children with steroid-resistant nephrotic syndrome and atypical phenotype. *Clin J Am Soc Nephrol* **6**, 1626-1634, doi:10.2215/CJN.07830910 (2011).
20 Hinkes, B. *et al.* Positional cloning uncovers mutations in PLCE1 responsible for a nephrotic syndrome variant that may be reversible. *Nat Genet* **38**, 1397-1405, doi:10.1038/ng1918 (2006).
21 Barua, M. *et al.* Exome sequencing and in vitro studies identified podocalyxin as a candidate gene for focal and segmental glomerulosclerosis. *Kidney Int* **85**, 124-133, doi:10.1038/ki.2013.354 (2014).
22 Ozaltin, F. *et al.* Disruption of PTPRO causes childhood-onset nephrotic syndrome. *Am J Hum Genet* **89**, 139-147, doi:10.1016/j.ajhg.2011.05.026 (2011).
23 Kranz, C. *et al.* Congenital disorder of glycosylation type Ik (CDG-Ik): a defect of mannosyltransferase I. *Am J Hum Genet* **74**, 545-551, doi:10.1086/382493 (2004).
24 Voskarides, K. *et al.* COL4A3/COL4A4 mutations producing focal segmental glomerulosclerosis and renal failure in thin basement membrane nephropathy. *J Am Soc Nephrol* **18**, 3004-3016, doi:10.1681/ASN.2007040444 (2007).
25 Landini, S. *et al.* Reverse Phenotyping after Whole-Exome Sequencing in Steroid-Resistant Nephrotic Syndrome. *Clin J Am Soc Nephrol*, doi:10.2215/CJN.06060519 (2019).
26 Quinzii, C. *et al.* A mutation in para-hydroxybenzoate-polyprenyl transferase (COQ2) causes primary coenzyme Q10 deficiency. *Am J Hum Genet* **78**, 345-349, doi:10.1086/500092 (2006).
27 Heeringa, S. F. *et al.* COQ6 mutations in human patients produce nephrotic syndrome with sensorineural deafness. *J Clin Invest* **121**, 2013-2024, doi:10.1172/JCI45693 (2011).
28 Kaneko, K., Hasui, M., Hata, A., Hata, D. & Nozu, K. Focal segmental glomerulosclerosis in a boy with Dent-2 disease. *Pediatr Nephrol* **25**, 781-782, doi:10.1007/s00467-009-1362-z (2010).
29 Karamatic Crew, V. *et al.* CD151, the first member of the tetraspanin (TM4) superfamily detected on erythrocytes, is essential for the correct assembly of human basement membranes in kidney and skin. *Blood* **104**, 2217-2223, doi:10.1182/blood-2004-04-1512 (2004).
30 Izu, A. *et al.* Pathogenesis of focal segmental glomerular sclerosis in a girl with the partial deletion of chromosome 6p. *Tohoku J Exp Med* **223**, 187-192, doi:10.1620/tjem.223.187 (2011).
31 Gee, H. Y. *et al.* FAT1 mutations cause a glomerulotubular nephropathy. *Nat Commun* **7**, 10822, doi:10.1038/ncomms10822 (2016).
32 Has, C. *et al.* Integrin alpha3 mutations with kidney, lung, and skin disease. *N Engl J Med* **366**, 1508-1514, doi:10.1056/NEJMoa1110813 (2012).
33 Kambham, N. *et al.* Congenital focal segmental glomerulosclerosis associated with beta4 integrin mutation and epidermolysis bullosa. *Am J Kidney Dis* **36**, 190-196, doi:10.1053/ajkd.2000.8293 (2000).
34 Gee, H. Y. *et al.* KANK deficiency leads to podocyte dysfunction and nephrotic syndrome. *J Clin Invest* **125**, 2375-2384, doi:10.1172/JCI79504 (2015).
35 Zenker, M. *et al.* Human laminin beta2 deficiency causes congenital nephrosis with mesangial sclerosis and distinct eye abnormalities. *Hum Mol Genet* **13**, 2625-2632, doi:10.1093/hmg/ddh284 (2004).
36 Lemley, K. V. Kidney disease in nail-patella syndrome. *Pediatr Nephrol* **24**, 2345-2354, doi:10.1007/s00467-008-0836-8 (2009).
37 Furlano, M. *et al.* MYH9 Associated nephropathy. *Nefrologia* **39**, 133-140, doi:10.1016/j.nefro.2018.08.008 (2019).
38 Esposito, T. *et al.* Unique X-linked familial FSGS with co-segregating heart block disorder is associated with a mutation in the NXF5 gene. *Hum Mol Genet* **22**, 3654-3666, doi:10.1093/hmg/ddt215 (2013).

39 Barua, M. *et al.* Mutations in PAX2 associate with adult-onset FSGS. *J Am Soc Nephrol* **25**, 1942-1953, doi:10.1681/ASN.2013070686 (2014).
40 Lopez, L. C. *et al.* Leigh syndrome with nephropathy and CoQ10 deficiency due to decaprenyl diphosphate synthase subunit 2 (PDSS2) mutations. *Am J Hum Genet* **79**, 1125-1129, doi:10.1086/510023 (2006).
41 van der Knaap, M. S. *et al.* Congenital nephrotic syndrome: a novel phenotype of type I carbohydrate-deficient glycoprotein syndrome. *J Inherit Metab Dis* **19**, 787-791, doi:10.1007/bf01799174 (1996).
42 Berkovic, S. F. *et al.* Array-based gene discovery with three unrelated subjects shows SCARB2/LIMP-2 deficiency causes myoclonus epilepsy and glomerulosclerosis. *Am J Hum Genet* **82**, 673-684, doi:10.1016/j.ajhg.2007.12.019 (2008).
43 Lovric, S. *et al.* Mutations in sphingosine-1-phosphate lyase cause nephrosis with ichthyosis and adrenal insufficiency. *J Clin Invest* **127**, 912-928, doi:10.1172/JCI89626 (2017).
44 Boerkoel, C. F. *et al.* Mutant chromatin remodeling protein SMARCAL1 causes Schimke immuno-osseous dysplasia. *Nat Genet* **30**, 215-220, doi:10.1038/ng821 (2002).
45 Huynh Cong, E. *et al.* A homozygous missense mutation in the ciliary gene TTC21B causes familial FSGS. *J Am Soc Nephrol* **25**, 2435-2443, doi:10.1681/ASN.2013101126 (2014).
46 Colin, E. *et al.* Loss-of-function mutations in WDR73 are responsible for microcephaly and steroid-resistant nephrotic syndrome: Galloway-Mowat syndrome. *Am J Hum Genet* **95**, 637-648, doi:10.1016/j.ajhg.2014.10.011 (2014).
47 Barbaux, S. *et al.* Donor splice-site mutations in WT1 are responsible for Frasier syndrome. *Nat Genet* **17**, 467-470, doi:10.1038/ng1297-467 (1997).
48 Pelletier, J. *et al.* Germline mutations in the Wilms' tumor suppressor gene are associated with abnormal urogenital development in Denys-Drash syndrome. *Cell* **67**, 437-447, doi:10.1016/0092-8674(91)90194-4 (1991).
49 Agarwal, A. K. *et al.* Focal segmental glomerulosclerosis in patients with mandibuloacral dysplasia owing to ZMPSTE24 deficiency. *J Investig Med* **54**, 208-213, doi:10.2310/6650.2006.05068 (2006).