SUPPLEMENTARY DATA

Supplementary Figure 1a. Temporal co-expression of 59 known human nephrotic syndrome genes in sc-mRNA expression data of human fetal kidney cells.

Supplementary Figure 1b. Intersection of 59 known human nephrotic syndrome genes with the highest expressed genes in NPCa-d according to Hochane's sc-mRNA database [6].

Supplementary Figure 2. Sc-mRNA expression data for four genes known to cause monogenic isolated CAKUT in humans (*EYA1*, *SIX1*, *SIX2*, and *ITGA8*) in 17 developmental kidney cell types based on Lindström et al.

Supplementary Table 1. 40 genes known to cause human isolated CAKUT, if mutated.

Supplementary Table 2. 100 highest expressed genes in NPCa-d according to Hochane et al.

Supplementary Table 3. 59 genes known to cause human nephrotic syndrome, if mutated.

Supplementary Table 4. Clinical features and molecular details of families with variants in genes with high expression in NPC.

SUPPLEMENTARY FIGURE LEGENDS

Supplementary Figure 1a: Temporal co-expression of 59 known human nephrotic syndrome genes in sc-mRNA expression data of human fetal kidney cells.

15 of 59 genes known to cause human nephrotic syndrome show temporal co-expression in podocytes (Pod). Each of the rows corresponds to the expression data of one gene and each column from left to right corresponds to one specific cell type in their order from early to late development of the kidney. The order of genes is arranged in a way that a maximum of genes shows consecutive co-expression in a maximum of timepoints. The importance of podocytes in the development of nephrotic syndrome is shown by the high expression of 15 genes in podocytes and 8 genes in s-shaped body podocyte precursor cells. Evaluation of sc-RNA expression data shows that the known nephrotic syndrome genes arrange in a spatial clustering in distinct cell types rather than a temporal clustering in consecutive cell types like shown for known CAKUT genes in Figure 1.

The expression data and developmental order of cell types are based on sc-mRNA sequencing data of week 16 human fetal kidney cells by Hochane et al [6].

Glossary: sc-mRNA, single cell mRNA; NPCa-d, nephron progenitor cells a-d; PTA, pretubular aggregate; RVCSBa-b, renal vesicle/comma-shaped body a-b; SSB m/d, pr, pod, S-shaped body medial/distal, proximal precursor cells, podocyte precursor cells; CnT, connecting tubule; DTLH, distal tubule/loop of Henle; ErPrT, early proximal tubule; Pod, podocyte; UBCD, ureteric bud/collecting duct; IPC, interstitial progenitor cells; ICa-b, interstitial cells a-b; Mes, mesangial cells; End, endothelial cells.

Supplementary Figure 1b: Intersection of 59 known human genes for nephrotic syndrome with the highest expressed genes in NPCa-d according to Hochane's sc-mRNA database [6].

As a negative control (NC) we intersected 59 known human genes for nephrotic syndrome with the 100 highest expressed genes in nephron progenitor cells a-d (NPCa-d). There is no intersection between the 100 highest expressed genes in NPCa-d and the 59 genes known to cause nephrotic syndrome.

Glossary: WES, whole exome sequencing; sc-mRNA, single cell mRNA; NPCa-d, nephron progenitor cell type a-d.

Supplementary Figure 2: Sc-mRNA expression data for four genes known to cause monogenic isolated CAKUT in humans (*EYA1, SIX1, SIX2,* and *ITGA8)* in 17 developmental kidney cell types based on Lindström et al.

Lindström et al. performed single-cell sequencing of the human fetal kidney with subsequent pseudotime analysis of the nephrogenic niche at gestational week 17 [19]. They provide a graphical display of gene expression in 17 developmental cell types. A) *EYA1, B) SIX1, C) SIX2*, and D) *ITGA8* show high expression in nephron progenitor cells (NPC) of the Lindström database.

Supplementary Table 1. 40 genes known to cause human isolated CAKUT, if mutated

MOI, mode of inheritance; AR, autosomal recessive; AD, autosomal dominant; XL, X-linked

Gene	Protein	MOI	Reference
ACE	Angiotensin I-converting enzyme	AR	Gribouval *Nat Genet* 37:964, 2005
AGT	Angiotensinogen	AR	Gribouval *Nat Genet* 37:964, 2005
AGTR1	Angiotensin II receptor, type 1	AR	Gribouval *Nat Genet* 37:964, 2005
CHRM3	Muscarinic acetylcholine receptor M3	AR	Weber *AJHG* 19:634, 2011
ETV4	ETS translocation variant 4, E1A enhancer binding protein	AR	Chen *IJPCH* 4:61, 2016
FRAS1	Extracellular matrix protein FRAS1	AR	Kohl *JASN* 25:1917, 2014
FREM1	FRAS1 related extracellular matrix protein 1	AR	Kohl *JASN* 25:1917, 2014
FREM2	FRAS1 related extracellular matrix protein 2	AR	Kohl *JASN* 25:1917, 2014
GRIP1	Glutamate receptor interacting protein 1	AR	Kohl *JASN* 25:1917, 2014
HPSE2	Heparanase 2 (Inactive)	AR	Bulum *Nephron* 130:54, 2015
ITGA8	Integrin α8	AR	Humbert *AJHG* 189:1260, 2014
REN	Renin	AR	Gribouval *Nat Genet* 37:964, 2005
TRAP1	Heat-shock protein 75 (also known as TNF receptor-associated protein 1)	AR	Saisawat *KI* 85:880, 2014
FGF20	Fibroblast Growth Factor 20	AR	Barak *Dev Cell* 22:1191, 2012
BMP4	Bone morphogenic protein 4	AD	Weber *JASN* 19:891, 2008
CHD1L	Chromodomain helicase DNA binding protein 1-like	AD	Brockschmidt *NDT* 27:2355, 2012
CRKL	CRK Like Proto-Oncogene, adaptor protein	AD	Lopez-Rivera *NEJM* 376:742, 2017
DSTYK	Dual serine/threonine and tyrosine protein kinase	AD	Sanna-Cherchi *NEJM* 369:621, 2013
EYA1	Eyes absent homolog 1	AD	Abdelhak *Nat Genet* 15:157, 1997
GATA3	GATA binding protein 3	AD	Pandolfi *Nat Genet* 11:40, 1995; Van Esch *Nature* 406:419, 2000
GREB1L	Growth Regulation By Estrogen In Breast Cancer 1 Like	AD	Brophy *Genetics* 207:215, 2017
HNF1B	HNF homeobox B	AD	Lindner *Hum Mol Genet* 24:263, 1999
MUC1	Mucin 1	AD	Kirby *Nat Genet* 45:299, 2013
NRIP1	Nuclear Receptor Interacting Protein 1	AD	Vivante *JASN* 28:2364, 2017
PAX2	Paired box 2	AD	Sanyanusin *Hum Mol Genet* 4:2183, 1995

RET	Proto-oncogene tyrosine-protein kinase receptor Ret	AD	Skinner *AJHG* 82:344, 2008
ROBO2	Roundabout, axon guidance receptor, homolog 2 (*Drosophila*)	AD	Hwang *Hum Genet* 134:905, 2015; Lu *AJHG* 80:616, 2007
SALL1	Sal-like protein 1 (also known as spalt-like transcription factor 1)	AD	Kohlhase *Nat Genet* 18:81, 1998
SIX1	SIX homeobox 1	AD	Ruf *Proc Nat Acad Sci* 101: 8090, 2004
SIX2	SIX homeobox 2	AD	Weber *JASN* 19:891, 2008
SIX5	SIX homeobox 5	AD	Hoskins *AJHG* 80:800, 2007
SLIT2	Slit homolog 2	AD	Hwang *Hum Genet* 134:905, 2015
SOX17	Transcription factor SIX-17	AD	Gimelli *Hum Mut* 31:1352, 2010
SRGAP1	SLIT-ROBO Rho GTPase activating protein 1	AD	Hwang *Hum Genet* 134:905, 2015
TBX18	T-Box transcription factor	AD	Vivante *AJHG* 97:291, 2015
TNXB	Tenascin XB	AD	Gbadegesin *JASN* 24:1313, 2013
UMOD	Uromodulin	AD	Hart *JMG* 39:882, 2002
UPK3A	Uroplakin 3A	AD	Jenkins *JASN* 16:2141, 2005
WNT4	Protein Wnt-4	AD	Biason-Lauber *NEJM* 351:792, 2004; Mandel *AJHG* 82:39, 2008; Vivante *JASN* 24:550, 2013
KAL1	Anosmin 1	XL	Hardelin *PNAS* 89:8190, 1992

(modified from Van der Ven et al. (5))

Supplementary Table 2. 100 highest expressed genes in Nephron Progenitor Cells a-d (NPC a-d) according to Hochane et al.

NPCa-d, nephron progenitor cells a-d; *italics*, positive control: human CAKUT genes intersecting with the 100 highest expressed genes in NPCa-d; <u>underlined</u>, novel single/multiple CAKUT candidate genes intersecting with the 100 highest expressed genes in NPCa-d; **bold**, genes that overlap within NPCa-d

	NPCa		**NPCb**		**NPCc**		**NPCd**	
	Gene	**Z-Score**	**Gene**	**Z-Score**	**Gene**	**Z-Score**	**Gene**	**Z-Score**
1	<u>KIF19</u>	4,3	CA7	3,9	MYLK2	3,7	CCNA1	4,0
2	CHRNA1	4,2	HAS1	3,9	UNC5B-AS1	2,9	RP11-977B10.2	3,9
3	BRICD5	4,1	HRK	3,6	PHKA1	2,9	TAGLN3	3,7
4	CCK	4,1	EGR4	3,6	**DNAH12**	2,8	HIST1H3G	3,7
5	ESPN	4,1	HSPA6	3,5	RP11-616M22.11	2,8	HIST1H2AI	3,7
6	OTOS	4,1	MUC12	3,5	ZNF385C	2,7	PIF1	3,6
7	NDST4	3,9	RBM24	3,4	DAPL1	2,7	LINC01572	3,5
8	PCDH15	3,8	RP11-524C21.2	3,3	**SYT14**	2,7	AURKA	3,4
9	LIM2	3,7	MATN4	3,3	**TMEM100**	2,6	ERCC6L	3,4
10	RSPO3	3,7	GBX2	3,2	**WFIKKN1**	2,6	AC131097.4	3,4
11	CHRND	3,6	TCHH	3,2	**MRAP2**	2,6	AC093702.1	3,4
12	SHD	3,6	**SHISA8**	3,1	**CITED1**	2,6	NEK2	3,4
13	MYO15A	3,5	REM2	3,0	**DCC**	2,6	SAPCD2	3,4
14	FAT3	3,5	ADRB2	3,0	SPINK8	2,6	ALG10	3,4
15	TXLNB	3,4	RCOR2	3,0	**ELAVL4**	2,6	COCH	3,4
16	**SCX**	3,4	**IL19**	2,9	MEIS1-AS2	2,6	CKAP2	3,3

17	LRRC7	3,4	**NGFR**	2,9	**TMEM190**	2,5	FAM57B	3,3
18	BMPER	3,4	LHFPL4	2,9	**ECEL1**	2,5	HIST1H1D	3,3
19	**SLC15A1**	3,2	**GPR157**	2,8	CRABP2	2,5	ZNF732	3,3
20	AKR1C1	3,2	CDO1	2,8	PCDHB5	2,5	HIST1H2AH	3,3
21	NRXN1	3,2	**DDIT4L**	2,8	**SCG5**	2,5	BORA	3,3
22	**HAMP**	3,2	GLB1L3	2,8	AC012123.1	2,5	ARHGAP33	3,3
23	**MEOX1**	3,2	DIRAS3	2,8	**FAM78B**	2,5	CDK5RAP2	3,3
24	NBL1	3,2	OPRD1	2,8	**RP11-757F18.5**	2,4	LA16c-306E5.2	3,3
25	NPY	3,1	MIPOL1	2,7	LINC00908	2,4	FCMR	3,3
26	DLEU7	3,1	**SYT14**	2,7	LRP8	2,4	TAF5	3,2
27	MAEL	3,1	NNMT	2,7	**SLC15A1**	2,4	NUSAP1	3,2
28	FAM84A	3,1	NLRP1	2,7	LINC00574	2,4	CDC25C	3,2
29	**NKAIN3**	3,0	VWCE	2,7	HOXC6	2,4	ARHGAP11A	3,2
30	CTD-2298J14.2	3,0	**SHC4**	2,7	**FGF10**	2,4	CEP295	3,2
31	**COLGALT2**	3,0	**COL9A2**	2,7	**NGFR**	2,4	FBXO43	3,2
32	**ELAVL4**	2,9	**GRIK4**	2,6	**MEOX1**	2,4	TRIM43	3,2
33	OSR1	2,9	**BRINP1**	2,6	NSG1	2,4	KIF14	3,2
34	**TMEM100**	2,9	**FAM78B**	2,6	RP4-622L5.7	2,3	PCBP3	3,2
35	RP13-884E18.2	2,9	B3GALNT2	2,6	GPHA2	2,3	RTN1	3,2
36	TRIM36	2,9	GPR3	2,6	**ABCA5**	2,3	CDC20	3,2
37	**RP11-757F18.5**	2,9	**ADGRG2**	2,6	RP11-365O16.6	2,3	RP11-345J4.5	3,2
38	**FAIM2**	2,8	AATK	2,6	***EYA1***	2,3	CENPA	3,2
39	**LY6H**	2,8	OSBPL6	2,6	RP13-766D20.4	2,2	CLGN	3,2

40	**CITED1**	2,8	**CACNG6**	2,5	**PPP1R3G**	2,2	PMEL	3,2
41	SCHLAP1	2,8	KCNN1	2,5	**OBP2A**	2,2	ATP2A1-AS1	3,2
42	**UG0898H09**	2,7	ZFAND2A	2,5	**DMRT3**	2,2	SAP30	3,1
43	MAP2	2,7	POMK	2,5	**PDZD7**	2,2	TTC29	3,1
44	**ATOH7**	2,7	**TAC1**	2,5	HOXC5	2,2	CCNF	3,1
45	DPP10	2,7	GRM7	2,5	SCN5A	2,2	CENPF	3,1
46	RSPO1	2,7	LRRN3	2,5	HAS2	2,2	MCM10	3,1
47	MMP23B	2,7	RP4-800J21.3	2,4	CORO6	2,2	CBFB	3,1
48	RP11-352M15.2	2,6	NUDT11	2,4	**LY6H**	2,2	H1FX-AS1	3,1
49	RHPN1	2,6	MAPK8IP1	2,4	SCUBE1	2,2	RP11-452L6.7	3,1
50	HMCN1	2,6	KCNF1	2,4	CDH7	2,1	RTKN2	3,1
51	LINC00475	2,6	DNAJB1	2,4	C22orf31	2,1	CTC-209H22.3	3,1
52	CTD-2147F2.1	2,6	**WFIKKN1**	2,4	**FAM107A**	2,1	FBXO48	3,1
53	LINC00923	2,6	PPP1R27	2,4	**CACNG6**	2,1	KNSTRN	3,1
54	**MRAP2**	2,5	TRIM46	2,4	HAS2-AS1	2,1	CENPQ	3,1
55	**NPTX2**	2,5	ARL4D	2,4	**UG0898H09**	2,1	FAM122B	3,1
56	**GABBR2**	2,5	ZDHHC11B	2,3	GDNF-AS1	2,1	CENPW	3,1
57	**TRDN**	2,5	TCEAL7	2,3	**SHISA8**	2,1	PHF19	3,1
58	TNNC2	2,5	NPPC	2,3	**FAIM2**	2,1	GTSE1	3,1
59	ARPP21	2,4	RFX4	2,3	AFF2	2,1	USP35	3,1
60	**DNAH12**	2,4	**TRDN**	2,3	**NKAIN3**	2,1	RACGAP1	3,1
61	**WASF3**	2,4	COL2A1	2,3	NNAT	2,1	HIST1H3C	3,1
62	AC003092.1	2,4	**LRRTM2**	2,3	CHST1	2,1	HIST1H4F	3,1

63	**PDZD7**	2,4	TRABD2B	2,3	**ATOH7**	2,1	TROAP	3,0
64	ST8SIA4	2,3	**ADPRHL1**	2,3	**TRDN**	2,1	OIP5	3,0
65	**SCG5**	2,3	PRTG	2,2	ST8SIA2	2,1	CEP97	3,0
66	RP11-1152H14.1	2,3	PLPPR3	2,2	ZFR2	2,0	HIST1H2BL	3,0
67	VSTM2B	2,3	PLEKHF1	2,2	**IL19**	2,0	ADGB	3,0
68	LBX2	2,3	RP11-20I23.6	2,2	*GREB1L*	2,0	IQGAP3	3,0
69	**ADPRHL1**	2,3	LINC01376	2,2	**ADGRG2**	2,0	ORC6	3,0
70	CNTNAP2	2,3	EGR3	2,2	HOXC8	2,0	LAG3	3,0
71	**ECEL1**	2,2	PTCHD1	2,2	*SIX2*	2,0	RP11-481J2.3	3,0
72	SHISA3	2,2	CYP51A1	2,1	CCDC3	2,0	EME1	3,0
73	RP11-74J13.8	2,2	**DCC**	2,1	RP11-357H14.17	2,0	ZNF829	3,0
74	CNTN5	2,2	**HTR1F**	2,1	**REEP2**	2,0	TRAIP	3,0
75	PCBP4	2,2	HPCA	2,1	FGF8	2,0	**GPR157**	3,0
76	SOBP	2,2	**NPTX2**	2,1	SIL1	2,0	FZR1	3,0
77	KCNH8	2,2	ZNF460	2,1	PRKAR1A	2,0	UBE2C	3,0
78	CCDC154	2,1	SIX4	2,1	*SIX1*	1,9	**CHTF18**	3,0
79	PODNL1	2,1	**DMRT3**	2,1	**C1QTNF4**	1,9	PPM1E	3,0
80	SNTG2	2,1	KLK8	2,1	KCNC2	1,9	HYLS1	3,0
81	AKR1C2	2,1	HSPA1A	2,1	PFN3	1,9	CCNB1	3,0
82	PDGFC	2,1	ENOX1	2,1	SULT1A2	1,9	RP11-469N6.1	3,0
83	**GRIK4**	2,1	**TMEM190**	2,1	LINC00887	1,9	HJURP	3,0
84	FAM213A	2,1	ARC	2,1	STAT4	1,9	MEIOB	3,0

85	**FAM107A**	2,1	SLC25A21	2,0	IGDCC3	1,9	REEP4	3,0
86	**ABCA5**	2,1	**OBP2A**	2,0	CA14	1,9	FBXO10	3,0
87	**DDIT4L**	2,1	SH3RF3-AS1	2,0	GNG3	1,9	DLGAP5	3,0
88	**PPP1R3G**	2,1	RGS2	2,0	**LRRTM2**	1,9	ARL6IP1	3,0
89	GFRA1	2,1	RP11-1102P16.1	2,0	**WASF3**	1,9	CTB-193M12.5	3,0
90	KIAA0226L	2,1	DENND5B	2,0	**COLGALT2**	1,9	CCNB2	2,9
91	**EYA1**	2,1	**GABBR2**	2,0	KCNK12	1,9	FAM24B	2,9
92	RGS17	2,0	CTD-2034I4.2	2,0	**TAC1**	1,9	HMGB2	2,9
93	DKFZP434L187	2,0	RP11-236L14.2	2,0	YY2	1,9	FAM64A	2,9
94	**REEP2**	2,0	**C1QTNF4**	2,0	**COL9A2**	1,8	POLQ	2,9
95	RGMA	2,0	FAM216A	2,0	**SCX**	1,8	CNIH2	2,9
96	MCF2L-AS1	2,0	KIF1A	2,0	AC108142.1	1,8	HIST1H4B	2,9
97	**BRINP1**	2,0	ZNRF3-AS1	1,9	ZMAT4	1,8	TTK	2,9
98	**FGF10**	2,0	LINC00683	1,9	**HTR1F**	1,8	ZNF610	2,9
99	LRFN5	2,0	TVP23A	1,9	**SHC4**	1,8	AC078941.1	2,9
100	NALCN	1,9	TNFRSF18	1,9	**HAMP**	1,8	CDCA2	2,9

Supplementary Table 3. 59 genes known to cause human nephrotic syndrome, if mutated.

MOI, mode of inheritance; AR, autosomal recessive; AD, autosomal dominant; XL, X-linked

Gene	Protein	MOI	Reference
ADCK4	AarF domain containing kinase 4	AR	Ashraf *J Clin Invest* 123:5179, 2013
ALG1	ALG1, Chitobiosyldiphosphodolichol Beta-Mannosyltransferase	AR	Harshman *Pediatr Int* 58:785, 2016
APOA1	Apolipoprotein A-1	AR	Nichols *Genomics* 8:318, 1990
ARHGDIA	Rho GDP dissociation inhibitor (GDI) alpha	AR	Gee *J Clin Invest* 123:3243, 2013
AVIL	Advillin	AR	Rao *J Clin Invest* 127:4257, 2017
CD2AP	CD2 associated protein	AR	Kim *Science* 300:1298, 2003
COQ2	Coenzyme Q2 4-hydroxybenzoate polyprenyltransferase	AR	Diomedi-Camassei *JASN* 18:2773, 2007
COQ6	Coenzyme Q6 monooxygenase	AR	Heeringa *J Clin Invest* 121:2013, 2011
CUBN	Cubilin (intrinsic factor-cobalamin receptor)	AR	Ovunc *JASN* 22:1815, 2011
CRB2	Crumbs, Drosphilia, Homolog of 2	AR	Ebarasi *AJHG* 96: 153-161, 2015
DGKE	Diacylglycerol kinase epsilon	AR	Lemaire *Nat Genet* 45: 531, 2013
EMP2	Epithelial membrane protein 2	AR	Gee *AJHG* 94:884, 2014
FAT1	Fat tumor suppressor, drosphila, homolog of, 1	AR	Gee *Nat Commun* 7:10822, 2016
ITGA3	Integrin, alpha 3 (antigen CD49C, alpha 3 subunit of VLA-3 receptor)	AR	Yalcin *Hum Mol Genet* 24:3679, 2015
ITGB4	Integrin, beta 4	AR	Kambham *AJKD* 36:190, 2000
KANK1	KN motif and ankyrin repeat domain-containing protein 1	AR	Gee *J Clin Invest* 125:2375, 2015
KANK2	KN motif and ankyrin repeat domain-containing protein 2	AR	Gee *J Clin Invest* 125:2375, 2015
KANK4	KN motif and ankyrin repeat domain-containing protein 3	AR	Gee *J Clin Invest* 125:2375, 2015
LAGE3	L antigen family member 3	AR	Braun N*at Genet* 49:1529, 2017
LAMB2	Laminin, beta 2	AR	Zenker *Hum Mol Genet* 12:2625, 2004
LCAT	Lecithin-Cholesterol Acyltransferase	AR	Taramelli *Hum Genet* 85:195, 1990

MAGI2	Membrane-associated guanylate kinase, WW and PDZ domains-containing 2	AR	Bierzynska *JASN* 28:1614, 2017
MYO1E	Homo sapiens myosin IE (MYO1E)	AR	Mele *NEJM* 365:295, 2011
NEU1	Neuraminidase 1	AR	Mütze *Genet Metab Rep* 10:1-4, 2016
NPHS1	Nephrin	AR	Kestila *Mol Cell* 1:575, 1998
NPHS2	Podocin	AR	Boute *Nat Genet* 24:349, 2000
NUP107	Nucleoporin, 107-KD	AR	Miyake *AJHG* 97:555, 2015
NUP133	Nucleoporin 133-KD	AR	Braun Nat Gene 48:457, 2016
NUP205	Nucleoporin, 205-KD	AR	Braun Nat Genet 48:457, 2016
NUP85	Nucleoporin 85-KD	AR	Braun Nat Gene 48:457, 2016
NUP93	Nucleoporin, 93-KD	AR	Braun Nat Genet 48:457, 2016
OSGEP	O-sialoglycoprotein endopeptidase	AR	Braun N*at Genet* 49:1529, 2017
PDSS2	Prenyl (decaprenyl) diphosphate synthase, subunit 2	AR	Lopez *AJHG* 79:1125, 2006
PLCE1	Phospholipase C, epsilon 1	AR	Hinkes Nat Genet 38:1397, 2006
PTPRO	Protein tyrosine phosphatase, receptor type, O	AR	Ozaltin *AJHG* 89:139, 2011
SCARB2	Scavenger receptor class B, member 2	AR	Badhwar *Brain* 127: 2173, 2004
SGPL1	Sphingosine 1 phosphate lyase 1	AR	Lovric *J Clin Invest* 127: 912, 2017
SMARCAL1	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a-like 1	AR	Boerkoel *Nat Genet* 30:215, 2002
TP53RK	TP53-regulating kinase	AR	Braun *Nat Genet* 49:1529, 2017
TPRKB	TP53RK binding protein	AR	Braun *Nat Genet* 49:1529, 2017
TTR	Transthyretin	AR	Ando *Biochem Biophys Res Commun 211:354, 1995*
VPS33B	VPS33B, Late Endosome And Lysosome Associated	AR	Bull *J Pediatr* 148:269, 2006
WDR73	WD repeat-containing protein 73	AR	Colin *AJHG* 95:637, 2014
XPO5	Exportin 5	AR	Braun *Nat Genet* 48:457, 2016
ACTN4	Actinin, alpha 4	AD	Kaplan *Nat Genet* 24(3):251, 2000
ANLN	Actin-binding protein anillin	AD	Gbadegesin *JASN* 25:1991, 2014
ARHGAP24	Rho GTPase activating protein 24	AD	Akilesh *J Clin Invest* 121:4127, 2011
****INF2***	Inverted formin, FH2 and WH2 domain containing	AD	Brown *Nat Genet* 42:72, 2010
LMX1B	LIM Homeobox Transcription Factor 1 Beta	AD	Dreyer *Nat Genet* 19:47 1998

MYH9	Myoson heavy chain 9, nonmuscle	AD	Heath *AJHG* 69:1033, 2001
PODXL	Podocalyxin	AD	Barua Kidney Int 85:124, 2014
TRPC6	Transient receptor potential cation channel, subfamily C, member 6	AD	Winn *Science* 308:1801, 2005
WT1	Wilms Tumor 1	AD	Melo *J Clin Endocrinol Metab* 87:2500, 2002
IKBKAP	Inhibitor of kappa light polypeptide gene enhancer in B cells, kinase complex associated protein	AR/AD	Anderson *AJHG* 68:753, 2001
NXF5	Nuclear RNA export factor 5	XL	Esposito *Hum Mol Genet* 22:3654, 2013
APOE	Apolipoprotein E	XL	Oikawa *JASN* 8:820, 1997
APOL1	Apolipoprotein L-1	Unknown	Parsa *NEJM* 369:2183, 2013
GPC5	Glypican 5	Unknown	Okamoto *Nat Genet* 43:459, 2011
SYNPO	Synaptopodin	Unknown	Bierzynska *Kidney Int* 91:937, 2017

(modified from Connaughton et al. (8))

Supplementary Table 4. Clinical features and molecular details of CAKUT families with variants in genes with high expression in Nephron Progenitor Cells (NPC).

A) Homozygous mutation in *KIF19* in individual (B2730-21) with CAKUT

B) Homozygous mutation in *TRIM36* in individual (A3761-21) with CAKUT

C) Compound heterozygous mutation in *USP35* in individual (A4671-21) with CAKUT

D) Homozygous mutation in *CHTF18* in individual (A1808-21) with CAKUT

Polyphen 2: Polymorphism phenotyping v2 (http://genetics.bwh.harvard.edu/pph2/);

SIFT: Sorting Intolerant from Tolerant algorithm (https://sift.bii.a-star.edu.sg/); EVS:

Exome Variant Server (https://evs.gs.washington.edu/EVS/)

A) Homozygous mutation in *KIF19* in individual (B2730-21) with CAKUT

Family-Individual		**B2730-21**
Ethnic Origin		Saudi-Arab
Sex		Female
CAKUT phenotype		bilateral VUR
Gene		*KIF19*
Nucleotide Change		c.664G>A
Amino Acid Change		p.Ala222Thr
Conservation		Partially conserved to *Danio rerio*
Zygosity		Homozygous
Population Frequency	gnomAD allele frequency	0.002395
	EVS	Not reported
Prediction Scores	Polyphen 2	Deleterious (0.99)
	Mutation Taster	Deleterious
	SIFT Score	Disease Causing
	CADD Score	29.2

B) Homozygous mutation in *TRIM36* in individual (A3761-21) with CAKUT

Family-Individual		**A3761-21**
Ethnic Origin		Indian Subcontinent
Sex		Male
CAKUT phenotype		Right: dysplastic kidney with VUR, Left: kidney rotational anomaly
Gene		*TRIM36*
Nucleotide Change		c.361G>C
Amino Acid Change		p.Asp121His
Conservation		Conserved to *Danio rerio*
Zygosity		Homozygous
Population Frequency	gnomAD allele frequency	0.00002392
	EVS	Not reported
Prediction Scores	Polyphen 2	Benign (0.69)
	Mutation Taster	Tolerated
	SIFT Score	Disease Causing
	CADD Score	23.0

C) Compound heterozygous mutation in *USP35* in individual (A4671-21) with CAKUT

Family-Individual		**A4671-21**
Ethnic Origin		Albanian
Sex		Male
CAKUT phenotype		Right: cystic dysplastic kidney, urachus remnant
Gene		*USP35*
Nucleotide Change		c.103C>T; c.1711G>T
Amino Acid Change		p.Arg35Cys; p.Gly571*
Conservation		Conserved to *Mus musculus;* conserved to *Danio rerio*
Zygosity		compound heterozygous
Population Frequency	gnomAD allele frequency	Not reported; 0.00004009
	EVS	Not reported; not reported
Prediction Scores	Polyphen 2	Benign (0.45); stop gain
	Mutation Taster	Deleterious; stop gain
	SIFT Score	Disease Causing; stop gain
	CADD Score	26.0; 54.0

D) Homozygous mutation in *CHTF18* in individual (A1808-21) with CAKUT

Family-Individual		**A1808-21**
Ethnic Origin		Arabic
Sex		Male
CAKUT phenotype		Left: renal agenesis
Gene		*CHTF18*
Nucleotide Change		c.2564G>A
Amino Acid Change		p.Arg855Gln
Conservation		Conserved to *Ciona intestinalis*
Zygosity		Homozygous
Population Frequency	gnomAD allele frequency	0.0002028
	EVS	0/7/4112
Prediction Scores	Polyphen 2	Deleterious (0.91)
	Mutation Taster	Tolerated
	SIFT Score	Disease Causing
	CADD Score	33.0