**Genetic Etiologies for Chronic Kidney Disease Revealed through Next-Generation Renal Gene Panel**

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Table S1. **ICD-10 Codes indicating clinical diagnoses for ordering of renal genetic testing**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **ICD-10 Code\*** | **Indication** | **All Patients** | | **Positive Cases** | |
|  |  | N=933 | (%) | N=243 | (%) |
| N18.3 | Chronic kidney disease, stage 3 (moderate) | 255 | 27.33% | 55 | 22.63% |
| N18.4 | Chronic kidney disease, stage 4 (severe) | 107 | 11.47% | 33 | 13.58% |
| N18.6 | End stage renal disease | 103 | 11.04% | 35 | 14.40% |
| N18.1 | Chronic kidney disease, stage 1 | 79 | 8.47% | 23 | 9.47% |
| N18.2 | Chronic kidney disease, stage 2 (mild) | 77 | 8.25% | 23 | 9.47% |
| Q61.2 | Polycystic kidney, adult type | 50 | 5.36% | 28 | 11.52% |
| N18.9 | Chronic kidney disease, unspecified | 48 | 5.14% | 12 | 4.94% |
| N18.5 | Chronic kidney disease, stage 5 | 44 | 4.72% | 9 | 3.70% |
| Z94.0 | Kidney transplant status | 33 | 3.54% | 7 | 2.88% |
| R80.9 | Proteinuria, unspecified | 27 | 2.89% | 4 | 1.65% |
| Q61.3 | Polycystic kidney, unspecified | 18 | 1.93% | 10 | 4.12% |
| Z52.4\* | Kidney donor | 16 | 1.71% | 4 | 1.65% |
| Z84.1\* | Family history of disorders of kidney and ureter | 15 | 1.61% | 4 | 1.65% |
| N28.1 | Cyst of kidney, acquired | 12 | 1.29% |  |  |
| E87.6 | Hypokalemia | 11 | 1.18% |  |  |
| I10 | Essential (primary) hypertension | 10 | 1.07% | 2 | 0.82% |
| N20.0 | Calculus of kidney | 10 | 1.07% | 1 | 0.41% |
| Z00.5\* | Encounter for examination of potential donor of organ and tissue | 8 | 0.86% | 3 | 1.23% |
| N04.9 | Nephrotic syndrome with unspecified morphologic changes | 7 | 0.75% |  |  |
| N05.1 | Unspecified nephritic syndrome with focal and segmental glomerular lesions | 7 | 0.75% |  |  |
| E83.42 | Hypomagnesemia | 6 | 0.64% | 2 | 0.82% |
| N04.1 | Nephrotic syndrome with focal and segmental glomerular lesions | 4 | 0.43% | 1 | 0.41% |
| Q87.81 | Alport syndrome | 4 | 0.43% | 3 | 1.23% |
| D59.3 | Hemolytic-uremic syndrome | 3 | 0.32% |  |  |
| E11.9 | Type 2 diabetes mellitus without complications | 3 | 0.32% |  |  |
| E26.81 | Bartter's syndrome | 3 | 0.32% |  |  |
| E87.5 | Hyperkalemia | 3 | 0.32% |  |  |
| N02.8 | Recurrent and persistent hematuria with other morphologic changes | 3 | 0.32% |  |  |
| N25.8 | Other disorders resulting from impaired renal tubular function | 3 | 0.32% | 2 | 0.82% |
| N28.9 | Disorder resulting from impaired renal tubular function, unspecified | 3 | 0.32% | 1 | 0.41% |
| R31.0 | Gross hematuria | 3 | 0.32% |  |  |
| R31.29 | Other microscopic hematuria | 3 | 0.32% |  |  |
| Z82.71\* | Family history of polycystic kidney | 3 | 0.32% | 1 | 0.41% |
| D17.71 | Benign lipomatous neoplasm of kidney | 2 | 0.21% |  |  |
| E26.9 | Hyperaldosteronism, unspecified | 2 | 0.21% |  |  |
| E83.52 | Hypercalcemia | 2 | 0.21% |  |  |
| E83.59 | Other disorders of calcium metabolism | 2 | 0.21% |  |  |
| N05.8 | Unspecified nephritic syndrome with other morphologic change | 2 | 0.21% |  |  |
| N17.9 | Acute kidney failure, unspecified | 2 | 0.21% |  |  |
| N25.89 | Other disorders resulting from impaired renal tubular function | 2 | 0.21% |  |  |
| Q44.6 | Cystic disease of liver | 2 | 0.21% |  |  |
| Q85.1 | Tuberous sclerosis | 2 | 0.21% | 1 | 0.41% |
| Z31.69\* | Encounter for other general counseling and advice on procreation | 2 | 0.21% |  |  |
| Z87.442 | Personal history of urinary calculi | 2 | 0.21% |  |  |
| C61 | Malignant neoplasm of prostate | 1 | 0.11% |  |  |
| D59.4 | Other nonautoimmune hemolytic anemias | 1 | 0.11% | 1 | 0.41% |
| E26.0 | Primary hyperaldosteronism | 1 | 0.11% |  |  |
| E26.8 | Other hyperaldosteronism | 1 | 0.11% |  |  |
| E66.01 | Morbid (severe) obesity due to excess calories | 1 | 0.11% |  |  |
| E72.0 | Disorders of amino-acid transport | 1 | 0.11% |  |  |
| E83.51 | Hypocalcemia | 1 | 0.11% |  |  |
| E87.1 | Hypo-osmolality and hyponatremia | 1 | 0.11% |  |  |
| E87.3 | Alkalosis | 1 | 0.11% |  |  |
| I15.1 | Hypertension secondary to other renal disorders | 1 | 0.11% |  |  |
| I47.1 | Supraventricular (paroxysmal) tachycardia | 1 | 0.11% |  |  |
| M32.19 | Other organ or system involvement in systemic lupus erythematosus | 1 | 0.11% |  |  |
| M35.7\* | Hypermobility syndrome | 1 | 0.11% |  |  |
| N02.2 | Recurrent and persistent hematuria with diffuse membranous glomerulonephritis | 1 | 0.11% |  |  |
| N03.1 | Chronic nephritic syndrome with focal and segmental glomerular lesions | 1 | 0.11% |  |  |
| N03.2 | Chronic nephritic syndrome with diffuse membranous glomerulonephritis | 1 | 0.11% |  |  |
| N05.0 | Unspecified nephritic syndrome with minor glomerular abnormality | 1 | 0.11% |  |  |
| N05.2 | Unspecified nephritic syndrome with diffuse membranous glomerulonephritis | 1 | 0.11% |  |  |
| N05.5 | Unspecified nephritic syndrome with diffuse mesangiocapillary glomerulonephritis | 1 | 0.11% |  |  |
| N19 | Unspecified kidney failure | 1 | 0.11% |  |  |
| N28.89 | Other specified disorders of kidney and ureter | 1 | 0.11% |  |  |
| Q60.0 | Renal agenesis, unilateral | 1 | 0.11% | 1 | 0.41% |
| Q61.00 | Congenital renal cyst, unspecified | 1 | 0.11% |  |  |
| Q61.9 | Cystic kidney disease, unspecified | 1 | 0.11% | 1 | 0.41% |
| Q62.2 | Congenital megaureter | 1 | 0.11% | 1 | 0.41% |
| R00.0 | Tachycardia, unspecified | 1 | 0.11% |  |  |
| R31.2 | Other microscopic hematuria | 1 | 0.11% |  |  |
| R31.9 | Hematuria, unspecified. | 1 | 0.11% |  |  |
| R62.51 | failure to thrive (child) | 1 | 0.11% |  |  |
| R80.0 | Isolated proteinuria | 1 | 0.11% |  |  |
| Z02.91\* | Encounter for administrative examinations, unspecified | 1 | 0.11% |  |  |
| Z87.898 | personal history of other specified conditions | 1 | 0.11% |  |  |
| Z90.8 | Acquired absence of other organs | 1 | 0.11% |  |  |

\* indicates code considered to be unaffected

Table S2. **Genes Tested for in the Renasight panel**

*ABCC6, ABCC8, ABCG2, ACE, ACTB, ADA2, ADAMTS13, ADCY10, AGPAT2, AGT, AGTR1, AGXT, AHI1, ALG1, ALG13, ALG8, ALG9, ALMS1, ALPL, AMN, ANKS6, ANOS1, AP2S1, APOA1, APOC2, APOE, APOL1, APOPT1, APRT, AQP2, ARHGAP24, ARL6, ATP6V0A4, ATP6V1B1, ATP7B, AVP, AVPR2, B2M, BBIP1, BBS1, BBS10, BBS12, BBS2, BBS4, BBS5, BBS7, BBS9, BCS1L, BICC1, BLK, BMP4, BMP7, BMPR2, BRAF, BSCL2, BSND, C5, C8orf37, CA2, CACNA1H, CASR, CAV1, CD151, CD2AP, CDC73, CDKN1C, CEL, CEP164, CEP290, CFH, CFHR5, CFI, CHD1L, CHD7, CHRM3, CHRNA3, CISD2, CLCN2, CLCN5, CLCNKB, CLDN16, CLDN19, CNNM2, COL11A1, COL4A1, COL4A3, COL4A4, COL4A5, COQ2, COQ6, COX10, COX14, COX20, COX6B1, COX8A, CPLANE1, CPT2, CREBBP, CRKL, CTNS, CUBN, CUL3, CYP11A1, CYP11B1, CYP11B2, CYP17A1, CYP24A1, CYP27B1, CYP2R1, DCDC2, DGKE, DHCR7, DLC1, DMP1, DNASE1L3, EBP, EDNRA, EGF, EIF2AK3, ELP1, ENPP1, EYA1, FAM20A, FAN1, FANCA, FANCB, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, FANCM, FASTKD2, FGA, FGF10, FGF23, FGFR1, FGFR2, FLCN, FN1, FOXC1, FOXC2, FOXI1, FOXP3, FRAS1, FREM1, FREM2, FXYD2, G6PC, GALNT3, GANAB, GATA3, GATM, GCK, GCM2, GDNF, GLA, GLI3, GLIS2, GLIS3, GNA11, GNAS, GPC3, GREM1, GRHPR, GRIP1, GSN, HBB, HGD, HNF1A, HNF1B, HNF4A, HOGA1, HOXA13, HOXD13, HPRT1, HPS1, HPSE2, HSD11B2, HSD3B2, IFT122, IFT140, IFT172, IFT43, INF2, INS, INVS, IQCB1, ITGA3, ITGA6, ITGB4, ITSN2, JAG1, KANK1, KANSL1, KAT6B, KCNA1, KCNJ1, KCNJ10, KCNJ11, KCNJ5, KCNK3, KCTD1, KL, KLF11, KLHL3, KRAS, LAMB2, LCAT, LDHA, LMNA, LMX1B, LPIN1, LRP2, LRP4, LRP5, LYZ, LZTFL1, MAFB, MAGI2, MC4R, MEFV, MKKS, MMACHC, MNX1, MOCOS, MUT, MVK, MYCN, MYH9, MYO1E, NEDD4L, NEK8, NEUROD1, NF1, NLRP3, NOTCH2, NPHP1, NPHP3, NPHP4, NPHS1, NPHS2, NR0B1, NR3C1, NR3C2, NSD1, NSDHL, OCRL, OFD1, OPLAH, PALB2, PAX2, PAX4, PBX1, PCBD1, PDSS1, PDSS2, PDX1, PET100, PGK1, PHEX, PKD1, PKD2, PKHD1, PLCE1, PLCG2, PLG, PMM2, PPP3CA, PRKCSH, PRODH, PROKR2, PRPS1, PTH1R, PTPN11, PTPRO, RAD51C, REN, RET, RMND1, ROBO2, ROR2, RPGRIP1L, RPL11, RPL26, RPL35A, RPL5, RPS10, RPS17, RPS19, RPS24, RPS26, RPS7, RRM2B, SALL1, SALL4, SARS2, SCARB2, SCN4A, SCNN1A, SCNN1B, SCNN1G, SCO1, SDCCAG8, SEC63, SEMA3E, SI, SIX1, SIX2, SIX5, SLC12A1, SLC12A2, SLC12A3, SLC16A12, SLC22A12, SLC26A1, SLC2A2, SLC2A9, SLC34A1, SLC34A3, SLC36A2, SLC37A4, SLC3A1, SLC41A1, SLC4A1, SLC4A4, SLC5A1, SLC5A2, SLC6A19, SLC6A20, SLC7A7, SLC7A9, SLC9A3R1, SLX4, SMAD9, SMARCAL1, SMC1A, SOX17, SOX18, SRCAP, STAR, STK39, STX16, SYNPO, TACO1, TFAP2A, THBD, TMEM67, TNS2, TP53RK, TP63, TRIM32, TRPC6, TRPM6, TSC1, TSC2, TTC21B, TTC8, TTR, TXNL4A, UCP3, UMOD, UPK3A, UQCC2, VDR, VHL, WAS, WDPCP, WDR19, WDR72, WDR73, WFS1, WNK1, WNK4, WNT4, WNT5A, WT1, XDH, XPNPEP3, XRCC4*

Table S3. **List of Positive Variants identified through broad-panel NGS genetic testing**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Gene** | **Positive Variants\*** | **Variant Type** | **Molecular Consequence** | **Classification**  **(P/LP)** |
| *ABCC8* | c.1893del (p.Gln632Argfs\*15) | Deletion | Frameshift | P |
| *ADCY10* | c.2215G>T (p.Glu739\*) | SNV | Nonsense | LP |
| *ALPL* | c.1171del (p.Arg391Valfs\*12) | Deletion | Frameshift | P |
| *APOL1* | G1: c.[1024A>G;1152T>G] (p.[Ser342Gly;Ile384Met])  G2: c.1164\_1169del (p.Asn388\_Tyr389d el) | SNV Haplotype  Deletion | Missense  In-frame deletion | Risk Allele  Risk Allele |
| *ATP6V0A4* | c.52C>T (p.Gln18\*) | SNV | Nonsense | P |
| *ATP6V1B1* | c.1037C>G (p.Pro346Arg) | SNV | Missense | P |
| *AVPR2* | c.310C>T (p.Arg104Cys) | SNV | Missense | P |
| *BBS1* | c.223\_224del (p.Leu75Glyfs\*23)  c.1169T>G (p.Met390Arg) | Deletion  SNV | Frameshift  Missense | P  P |
| *CASR* | c.166G>T (p.Glu56\*) | SNV | Nonsense | P |
| *CD2AP* | c.*1742dup* (p.Asn581Lysfs\*5) | Duplication | Frameshift | LP |
| *CFI* | c.763\_772+9delinsGTATCCAC (p.(Cys255Valfs\*26))  c.355G>A (p.Gly119Arg)  c.1638G>A (p.Trp546\*) | Indel  SNV  SNV | Frameshift  Missense  Splice variant | P  P  LP |
| *COL11A1* | c.3692G>T (p.Gly1231Val)  c.4186G>T (p.Gly1396Cys) | SNV  SNV | Missense  Missense | LP  LP |
| *COL4A1* | c.1702G>T (p.Gly568Cys)  c.1820G>T (p.Gly607Val) | SNV  SNV | Missense  Missense | LP  LP |
| *COL4A3* | c.2083G>A (p.Gly695Arg)  c.656G>T (p.Gly219Val)  c.2323\_2340del (p.Leu775\_Gly780de  c.2048G>A (p.Gly683Glu)  c.1372G>C (p.Gly458Arg)  c.40\_63del (p.Leu14\_Leu21del)  c.1184G>A (p.Gly395Glu)  c.2621del (p.Gly874Aspfs\*9) | SNV  SNV  Deletion  SNV  SNV  Deletion  SNV  Deletion | Missense  Missense  In-frame deletion  Missense  Missense  In-frame deletion  Missense  In-frame deletion | LP  LP  P  LP  LP  P  LP  P |
| *COL4A4* | c.1424G>C (p.Gly475Ala)  c.3289+1G>C (p.?)  c.3973+1G>T (p.?)  c.594+1G>A (p.?)  c.2312G>A (p.Gly771Glu)  c.755G>T (p.Gly252Val)  c.1544G>T (p.Gly515Val)  c.3014G>A (p.Gly1005Glu)  c.1696+1G>T (p.?)  c.1785dup (p.Gly596Argfs\*10)  c.3451G>A (p.Gly1151Arg)  c.3882\_3883del (p.Cys1294Trpfs\*24) | SNV  Insertion  Insertion  Insertion  SNV  SNV  SNV  SNV  Insertion  Duplication  SNV  Deletion | Missense  Splice variant  Splice variant  Splice variant  Missense  Missense  Missense  Missense  Splice variant  Frameshift  Missense  Frameshift | LP  LP  LP  LP  LP  LP  LP  LP  LP  P  LP  P |
| *COL4A5* | c.3152G>T (p.Gly1051Val)  c.1226G>C (p.Gly409Ala)  c.3016+2T>C (p.?)  c.1871G>A (p.Gly624Asp)  c.4307G>A (p.Gly1436Asp)  c.4298G>A (p.Gly1433Asp)  Whole Gene Deletion  c.1877G>T (p.Gly626Val)  c.4944G>A (p.Trp1648\*)  c.3508G>A (p.Gly1170Ser)  c.91G>T (p.Gly31Trp)  c.367G>C (p.Gly123Arg)  Deletion of Exon 3 (p.?)  c.3914dup (p.Gly1306Argfs\*5) | SNV  SNV  Insertion  SNV  SNV  SNV  Deletion  SNV  SNV  SNV  SNV  SNV  Deletion  Duplication | Missense  Missense  Splice variant  Missense  Missense  Missense  CNV  Missense  Nonsense  Missense  Missense  Missense  CNV  Frameshift | LP  LP  LP  P  LP  LP  P  LP  LP  P  LP  LP  LP  P |
| *CUBN* | c.6821+2T>C (p.?) | Insertion | Splice variant | P |
| *CYP24A1* | whole gene deletion  c.1186C>T (p.Arg396Trp)  c.62del (p.Pro21Argfs\*8) | Deletion  SNV  Deletion | CNV  Missense  Frameshift | P  P  P |
| *GANAB* | c.1914\_1915del (p.Asp640Glnfs\*77) | Deletion | Frameshift | P |
| *HBB* | c.20A>T (p.Glu7Val)  c.19G>A (p.Glu7Lys) | SNV  SNV | Missense  Missense | P  P |
| *HNF1A* | c.1310-2A>G (p.?) | Deletion | Splice variant | LP |
| *HNF1B* | c.884G>A (p.Arg295His) | SNV | Missense | P |
| *HNF4A* | c.340C>T (p.Arg114Trp) | SNV | Missense | P |
| *INF2* | c.1735+1G>A (p.?)  c.550G>A (p.Glu184Lys)  c.653G>A (p.Arg218Gln) | Insertion  SNV  SNV | Splice variant  Missense  Missense | LP  P  P |
| *KCNJ11* | c.652C>T (p.Gln218\*)  c.881C>T (p.Thr294Met) | SNV  SNV | Nonsense  Missense | P  LP |
| *MC4R* | c.496G>A (p.Val166Ile) | SNV | Missense | P |
| *MEFV* | c.2230G>T (p.Ala744Ser)  c.2080A>G (p.Met694Val) | SNV  SNV | Missense  Missense | P  P |
| *NPHS2* | c.851C>T (p.Ala284Val)  c.686G>A (p.Arg229Gln) | SNV  SNV | Missense  Missense | P  LP |
| *NR3C2* | c.1951C>T (p.Arg651\*) | SNV | Nonsense | P |
| *OFD1* | c.1411+1G>A (p.?) | Insertion | Splice variant | P |
| *PAX2* | Deletion of exons 8-11 (p.?) | Deletion | CNV | P |
| *PBX1* | c.265+1G>A (p.?) | Insertion | Splice variant | LP |
| *PKD1* | c.11537+2T>A (p.?)  c.12004-2A>C (p.?)  c.9404C>T (p.Thr3135Met)  c.12124C>T (p.Gln4042\*)  c.6657\_6671del (p.Arg2220\_Pro2224del)  c.5086C>T (p.Gln1696\*)  c.165\_171del (p.Leu56Argfs\*15)  c.2054\_2055del (p.Glu685Valfs\*28)  c.11563\_11564del (p.Thr3855Alafs\*105)  c.10516del (p.Glu3506Argfs\*21)  c.659del (p.Gly220Alafs\*70)  c.9202-16G>A (p.?)  c.4387C>T (p.Gln1463\*)  c.9683dup (p.Leu3229Profs\*24)  Deletion of exons 11-34 (p.?)  c.12031C>T (p.Gln4011\*)  c.215+2\_215+3del (p.?)  c.6994\_7000del (p.Ala2332Trpfs\*7)  c.9157G>A (p.Ala3053Thr)  c.1202-1G>A (p.?)  c.4306C>T(p.Arg1436\*)  c.628\_631dup (p.Ser211Metfs\*51)  c.1141G>A (p.Gly381Ser)  c.4828\_4830del (p.Ile1610del)  c.12448C>T (p.Arg4150Cys)  c.272C>A (p.Ser91\*)  c.9924-1G>C (p.?)  c.10168C>T (p.Gln3390\*)  c.4444C>T (p.Gln1482\*)  c.11557G>T (p.Glu3853\*)  c.6424C>T (p.Gln2142\*)  c.4447C>T (p.Gln1483\*)  c.7951del (p.Val2651Cysfs\*3)  c.12010C>T (p.Gln4004\*)  c.12036G>A (p.Trp4012\*)  c.1426del (p.Val476Trpfs\*82)  c.6643C>T (p.Arg2215Trp)  c.601dup (p.His201Profs\*60)  c.8017-2\_8017-1del (p.?)  c.2152C>T (p.Gln718\*)  c.5014\_5015del (p.Arg1672Glyfs\*98)  c.10951G>A (p.Gly3651Ser)  c.8935\_8937del (p.Phe2979del)  c.9691G>T (p.Glu3231\*)  c.5923C>T (p.Gln1975\*)  c.5878C>T (p.Gln1960\*)  Deletion of exons 1-43 (p.?)  c.8311G>A (p.Glu2771Lys)  c.160\_166del (p.Arg54Cysfs\*17)  c.11338\_11345dup (p.Asp3782Glufs\*47)  c.1418\_1419del (p.Val473Alafs\*45)  c.1326del (p.Ala443Profs\*22)  c.2180T>C (p.Leu727Pro)  c.12383\_12387del (p.Glu4128Glyfs\*27)  c.4743dup (p.Trp1582Leufs\*5)  c.3490G>A (p.Gly1164Arg)  c.10527\_10528del (p.Glu3509Aspfs\*117)  c.2097+1G>A (p.?)  c.2716G>T (p.Glu906\*)  c.9829C>T (p.Arg3277Cys)  c.8263del (p.Leu2755\*) | Insertion  Deletion  SNV  SNV  Deletion  SNV  Deletion  Deletion  Deletion  Deletion  Deletion  Deletion  SNV  Duplication  Deletion  SNV  Deletion  Deletion  SNV  Deletion  SNV  Duplication  SNV  Deletion  SNV  SNV  Deletion  SNV  SNV  SNV  SNV  SNV  Deletion  SNV  SNV  Deletion  SNV  Duplication  Deletion  SNV  Deletion  SNV  Deletion  SNV  SNV  SNV  Deletion  SNV  Deletion  Duplication  Deletion  Deletion  SNV  Deletion  Duplication  SNV  Deletion  Insertion  SNV  SNV  Deletion | Splice variant  Splice variant  Missense  Nonsense  In-frame deletion  Nonsense  Frameshift  Frameshift  Frameshift  Frameshift  Frameshift  Splice variant  Nonsense  Frameshift  CNV  Nonsense  Splice variant  Frameshift  Missense  Splice variant  Nonsense  Frameshift  Missense  In-frame deletion  Missense  Nonsense  Splice variant  Nonsense  Nonsense  Nonsense  Nonsense  Nonsense  Frameshift  Nonsense  Nonsense  Frameshift  Missense  Frameshift  Splice variant  Nonsense  Frameshift  Missense  In-frame deletion  Nonsense  Nonsense  Nonsense  CNV  Missense  Frameshift  Frameshift  Frameshift  Frameshift  Missense  Frameshift  Frameshift  Missense  Frameshift  Splice variant  Nonsense  Missense  Nonsense | LP  LP  P  P  LP  P  P  P  P  P  P  LP  P  P  P  P  LP  P  LP  P  P  P  P  LP  LP  P  P  P  P  P  P  P  P  P  P  P  P  P  P  P  P  P  LP  P  P  P  P  P  P  P  P  P  P  P  P  P  P  LP  LP  P  P |
| *PKD1/TSC2* gene deletion | Large deletion including PKD1 and TSC2 (p.?) | Deletion | CNV | P |
| *PKD2* | c.958C>T (p.Arg320\*)  c.2614C>T (p.Arg872\*)  c.1609C>T (p.Gln537\*)  c.973C>T (p.Arg325\*)  c.2019+1G>A (p.?)  c.952dup (p.Val318Glyfs\*23)  c.1081C>T (p.Arg361\*)  c.2159del (p.Asn720Ilefs\*17)  c.2533C>T (p.Arg845\*)  c.2159dup (p.Asn720Lysfs\*5)  c.1094+1G>A (p.?)  c.973C>T (p.Arg325\*)  Deletion of Exon 7-9  c.1837C>T (p.Gln613\*)  c.110del (p.Gly37Alafs\*80)  c.274C>T (p.Arg92Trp) | SNV  SNV  SNV  SNV  Insertion  Duplication  SNV  Deletion  SNV  Duplication  Insertion  SNV  Deletion  SNV  Deletion  SNV | Nonsense  Nonsense  Nonsense  Nonsense  Splice variant  Frameshift  Nonsense  Frameshift  Nonsense  Frameshift  Splice variant  Nonsense  CNV  Nonsense  Frameshift  Missense | P  P  P  P  LP  P  LP  P  P  P  P  P  LP  P  P  P |
| *PKHD1* | c.1854del (p.Gly619Alafs\*3)  c.274C>T (p.Arg92Trp)  c.4870C>T (p.Arg1624Trp) | Deletion  SNV  SNV | Frameshift  Missense  Missense | P  P  P |
| *PRKCSH* | c.564\_567del (p.Glu189Profs\*42) | Deletion | Frameshift | LP |
| *PTPN11* | c.794G>A (p.Arg265Gln) | SNV | Missense | P |
| *SLC12A3* | c.1315G>A (p.Gly439Ser)  c.1925G>A (p.Arg642His)  c.2221G>A (p.Gly741Arg)  c.1670-191C>T (p.?) | SNV  SNV  SNV  Deletion | Missense  Missense  Missense  Splice variant | P  P  P  P |
| *SLC34A1* | Deletion of exons 2-5 (p.?) | Deletion | CNV | P |
| *SLC3A1* | c.1093C>T (p.Arg365Trp)  c.1500+1G>T (p.?)  Duplication of Exons 5-9 (p.?)  c.1400T>C (p.Met467Thr)  Deletion of Exons 2-3 (p.?) | SNV  Insertion  Duplication  SNV  Deletion | Missense  Splice variant  CNV  Missense  CNV | LP  P  P  P  P |
| *SLC4A1* | c.1199\_1225del (p.Ala400\_Ala408del) | Deletion | In-frame deletion | P |
| *SLC7A9* | c.1262\_1263del (p.Ser421Cysfs\*66) | Deletion | Frameshift | P |
| *SMAD9* | c.386dup (p.Tyr129\*) | Duplication | Nonsense | P |
| *TSC2* | c.2713C>T (p.Arg905Trp) | SNV | Missense | P |
| *TTR* | c.424G>A (p.Val142Ile) | SNV | Missense | P |
| *UMOD* | c.278\_289delinsCCGCCTCCT (p.Val93\_Gly97delinsAlaAlaSerCys)  c.529\_555del (p.His177\_Arg185del) | Indel  Deletion | In-frame deletion-insertion  In-frame deletion | P    P |
| *VHL* | c.464-2A>G (p.?) | Deletion | Splice variant | P |
| *WNK4* | c.1693C>G (p.Gln565Glu) | SNV | Missense | P |
| *WT1* | c.1373G>A (p.Arg458Gln) | SNV | Missense | P |

\*Variant nomenclature follows standard guidelines defined by the Human Genome Variation Society ([http://varnomen.hgvs.org/)](http://varnomen.hgvs.org/)

Table S4. **Carrier findings**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Genes** | **# of Carriers** |  | **Genes (Continued)** | **# of Carriers** |  | **Genes (Continued)** | **# of Carriers** |
| *AGXT* | 1 |  | *FAM20A* | 1 |  | *PKHD1* | 11 |
| *AHI1* | 1 |  | *FAN1* | 3 |  | *PLCE1* | 1 |
| *ABCC6* | 14 |  | *FANCA* | 3 |  | *PLG* | 10 |
| *ADA2* | 2 |  | *FANCC* | 2 |  | *PMM2* | 2 |
| *ADAMTS13* | 2 |  | *FANCD2* | 5 |  | *PRODH* | 9 |
| *AGPAT2* | 3 |  | *FANCE* | 3 |  | *PROKR2* | 2 |
| *AGTR1* | 1 |  | *FANCL* | 3 |  | *ROR2* | 1 |
| *ALG8* | 2 |  | *FASTKD2* | 1 |  | *RPGRIP1L* | 2 |
| *ALG9* | 1 |  | *FGF23* | 1 |  | *SCARB2* | 1 |
| *ALPL* | 3 |  | *FRAS1* | 3 |  | *SCNN1A* | 2 |
| *ANKS6* | 1 |  | *FREM2* | 1 |  | *SCO1* | 1 |
| *APOL1* | 111 |  | *G6PC* | 1 |  | *SDCCAG8* | 1 |
| *ATP6V0A4* | 3 |  | *GALNT3* | 2 |  | *SI* | 11 |
| *ATP7B* | 11 |  | *GRHPR* | 1 |  | *SLC12A1* | 1 |
| *BBS1* | 9 |  | *HBB* | 39 |  | *SLC12A3* | 6 |
| *BBS10* | 3 |  | *HGD* | 2 |  | *SLC22A12* | 1 |
| *BBS12* | 4 |  | *HOGA1* | 5 |  | *SLC2A9* | 1 |
| *BBS4* | 2 |  | *HPS1* | 3 |  | *SLC34A3* | 4 |
| *BBS7* | 1 |  | *HPSE2* | 1 |  | *SLC37A4* | 2 |
| *BSND* | 1 |  | *HSD3B2* | 2 |  | *SLC3A1* | 7 |
| *C5* | 5 |  | *IFT122* | 2 |  | *SLC4A1* | 1 |
| *C8orf37* | 1 |  | *IFT140* | 7 |  | *SLC5A2* | 1 |
| *CA2* | 1 |  | *IFT172* | 2 |  | *SLC6A19* | 5 |
| *CEP164* | 4 |  | *INVS* | 3 |  | *SLC7A7* | 2 |
| *CEP290* | 7 |  | *IQCB1* | 2 |  | *SLC7A9* | 4 |
| *CFH* | 1 |  | *ITGA6* | 1 |  | *SLX4* | 2 |
| *CHRNA3* | 1 |  | *ITGB4* | 1 |  | *SMARCAL1* | 1 |
| *CLCNKB* | 4 |  | *KANK1* | 1 |  | *TMEM67* | 1 |
| *CLDN19* | 1 |  | *KCNJ10* | 2 |  | *TRPM6* | 1 |
| *COL4A3* | 1 |  | *LAMB2* | 2 |  | *TTC21B* | 8 |
| *COQ2* | 4 |  | *LRP2* | 1 |  | *UCP3* | 6 |
| *COX20* | 1 |  | *LRP4* | 2 |  | *WDPCP* | 1 |
| *CPLANE1* | 5 |  | *LRP5* | 1 |  | *WDR19* | 1 |
| *CPT2* | 3 |  | *MEFV* | 13 |  | *WDR73* | 1 |
| *CTNS* | 3 |  | *MKKS* | 1 |  | *WFS1* | 6 |
| *CUBN* | 8 |  | *MMACHC* | 5 |  | *XDH* | 2 |
| *CYP11A1* | 8 |  | *MOCOS* | 5 |  | *XRCC4* | 2 |
| *CYP11B1* | 1 |  | *MUT* | 3 |  |  |  |
| *CYP11B2* | 1 |  | *MVK* | 1 |  |  |  |
| *CYP11B2\_CYP11B1* | 1 |  | *MYO1E* | 1 |  |  |  |
| *CYP17A1* | 1 |  | *NPHP1* | 3 |  |  |  |
| *DGKE* | 1 |  | *NPHP4* | 3 |  |  |  |
| *DHCR7* | 11 |  | *NPHS1* | 6 |  |  |  |
| *DMP1* | 1 |  | *NPHS2* | 51 |  |  |  |
| *EIF2AK3* | 1 |  | *OPLAH* | 2 |  |  |  |
| *ELP1* | 5 |  | *PALB2* | 1 |  |  |  |
| *ENPP1* | 1 |  | *PCBD1* | 1 |  |  |  |

Table S5. **Positive Findings Among African Americans**

|  |  |  |
| --- | --- | --- |
| ***Gene*** | **N = 59** | **(%)** |
| *APOL1* | 44 | (74.6) |
| *CASR* | 1 | (1.7) |
| *COL4A1* | 1 | (1.7) |
| *COL4A4* | 3 | (5.1) |
| *COL4A5* | 2 | (3.4) |
| *CUBN* | 1 | (1.7) |
| *HBB* | 1 | (1.7) |
| *PKD1* | 5 | (8.5) |
| *PKD2* | 1 | (1.7) |
| *PTPN* | 1 | (1.7) |
| *SLC3A1* | 1 | (1.7) |
| *TTR* | 4 | (6.8) |

Table S6: **Cases with positive findings in > 1 gene**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| ***APOL1*** | *COL4A4*  *APOL1* | *COL4A5*  *APOL1* | *TTR*  *COL4A5*  *APOL1* | *TTR*  *APOL1* | *TTR*  *APOL1* | *COL4A1*  *APOL1* | *HNF4A*  *APOL1* | *PKD1*  *APOL1* | *PKD2*  *APOL1* |
| **Non-*APOL1*** | *COL4A4*  *PKD1* | *COL4A4*  *SLC4A1* | *COL4A5*  *MC4R* | *COL4A5*  *SLC3A1* | *COL4A5*  *PRKCSH* | *PKD1*  *CFI* | *GANAB*  *ALPL* |  |  |

Table S7. **Positive findings among CKD and Organ Donor groups as indicated by ICD-10 code**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Category** | **ICD-10 codes** | **Indication** | **Total Cases (N)** | **Positives Cases (N; %)** | **Positive Findings** |
| **CKD/**  **ESRD** | N18.1 | Chronic kidney disease, stage 1 | 715 | 190 (26.6%) | *PKD1:* 26.8% (51/190)  *PKD2:* 8.4% (16/190)  *COL4A3:* 4.7% (9/190)  *COL4A4:* 5.3% (10/190)  *COL4A5:* 10.5% (20/190)  *APOL1:* 23.2% (44/190) |
| N18.2 | Chronic kidney disease, stage 2 |
| N18.3 | Chronic kidney disease, stage 3 |
| N18.4 | Chronic kidney disease, stage 4 |
| N18.5 | Chronic kidney disease, stage 5 |
| N18.6 | End stage renal disease |
| N18.9 | Chronic kidney disease, unspecified |
| **Organ Donor** | Z00.5 | Encounter for examination of potential donor of organ and tissue | 24 | 7 (29.2) | *APOL1* (4/7)  *PTPN11* (1/7)  *NPHS2 (*1/7)  *SLC3A1* (1/7) |
| Z52.4 | kidney donor |

Table S8. **Positive findings among transplant cases**

|  |  |
| --- | --- |
| **Positive Gene** | **# of cases** |
| *ABCC8* | 1 |
| *ADCY10* | 1 |
| *APOL1* | 9 |
| *CD2AP* | 1 |
| *CFI* | 1 |
| *COL4A1* | 1 |
| *COL4A3* | 1 |
| *COL4A4* | 1 |
| *COL4A5* | 2 |
| *INF2* | 1 |
| *PKD1* | 2 |
| *UMOD* | 1 |
| *HNF4A* and *APOL1* | 1 |
| *CFI* and *PKD1* | 1 |

Fig. S1: **Positive Finding among Kidney disease categories.** Genes in which positive P/LP variants were identified were assigned to kidney disease categories (Table 2). Graph represents the total number of positive findings from each gene in each disease category (gray). Positive findings in genes associated with multiple kidney disease types represent the overlap (orange) and are represented multiple times.

Chart, bar chart

Description automatically generated