Supplementary Material

Supplementary Table 1: Customized renal gene panel

Symbol	Description	OMIM ID	Synonyms
ACE	Angiotensin I converting enzyme	--	ACE1, CD143
ACTN4	Actinin, alpha 4	604638	--
AGXT	Alanine-glyoxylate aminotransferase	604285	AGXT1, PH1, AGT, SPT, AGT1
APRT	Adenine phosphoribosyltransferase	102600	--
ATP6V0A4	ATPase, H+ transporting, lysosomal V0 su	605239	RDRTA2, VPP2, RTADR, a4, Vph1, Stv1
ATP6V1B1	ATPase, H+ transporting, lysosomal 56/58	192132	VATB, RTA1B, Vma2
AVPR2	Arginine vasopressin receptor 2	300538	V2R
B9D1	B9 protein domain 1	614144	B9, EPPB9
B9D2	B9 protein domain 2	611951	MGC4093
BSND	Bartter syndrome, infantile, with sensoryneural deafness	606412	BART
C5orf42	Chromosome 5 open reading frame 42	614571	FLJ13231, JBTS17
CA2	Carbonic anhydrase II	611492	Car2, CA-II, CAII
CC2D2A	Coiled-coil and C2 domain containing 2A	612013	KIAA1345, MKS6, JBTS9
CD2AP	CD2-associated protein	604241	CMS
CDC5L	Cell division cycle 5-like	602868	PCDC5RP, hCDC5, CEF1, CDC5
CEP290	Centrosomal protein 290kDa	610142	KIAA0373, FLJ13615, 3H11Ag, rd16, NPHP6, JBTS5, SLSN6, LCA10, MKS4, BBS14, CT87, POC3
CLCN5	Chloride channel, voltage-sensitive 5	300008	DENTS, XLRH, hClC-K2, hCIC-K2, CLC5, XRN, ClC-5
CLDN16	Claudin 16	603959	PCLN1, HOMG3
COL4A3	Collagen, type IV, alpha 3	120070	--
COL4A4	Collagen, type IV, alpha 4	120131	CA44
COL4A5	Collagen, type IV, alpha 5	303630	--
COL4A6	Collagen, type IV, alpha 6	303631	--
COQ2	Coenzyme Q2 homolog	609825	CL640, FLJ26072

CTNS	Cystinosin	606272	CTNS-LSB, PQLC4
FAM58A	Family with sequence similarity 58	300708	MGC29729, FLJ21610
FRAS1	Fraser syndrome 1	607830	FLJ22031, FLJ14927, KIAA1500
FREM2	FRAS1-related extracellular matrix protein 2	608945	DKFZp686J0811
FXYD2	FXYD domain containing ion transport regulator 2	601814	MGC12372
GATA3	GATA binding protein 3	131320	HDR
GLA	Galactosidase, alpha	300644	GALA
GLIS2	GLIS family zinc finger 2	608539	NPHP7
GRHPR	Glyoxylate reductase/hydroxypyruvate red	604296	PH2
HNF1B	HNF1 homeobox B	189907	LFB3, VHNF1, HNF1beta, MODY5, TCF2
HPSE2	Heparanase 2	613469	HPA2, HPR2
INF2	inverted formin, FH2 and WH2 domain cont	610982	MGC13251
INVS	Inversin	243305	NPHP2
IQCB1	IQ motif containing B1	609237	KIAA0036, NPHP5
KCNJ1	Potassium inwardly-rectifying channel	600359	Kir1.1, ROMK1
LAMB2	Laminin, beta 2	150325	--
LMX1B	LIM homeobox transcription factor 1	602575	--
LPIN1	Lipin 1	605518	KIAA0188
MKS1	Meckel syndrome, type 1	609883	FLJ20345, POC12, BBS13
MT-TL1	Mitochondrially encoded tRNA leucine 1	--	TRNL1
NEK8	NIMA-related kinase 8	609799	NPHP9
NFIA	Nuclear factor I/A	600727	NFI-L, KIAA1439
NPHP1	Nephronophthisis 1	607100	JBTS4
NPHP3	Nephronophthisis 3	608002	NPH3, KIAA2000, FLJ30691, FLJ36696, MKS7
NPHP4	Nephronophthisis 4	607215	SLSN4, KIAA0673, POC10
NPHS1	Nephrosis 1	602716	CNF, NPHN
NPHS2	Nephrosis 2	604766	SRN1, PDCN
NR3C2	Nuclear receptor subfamily 3, group C, member 2	600983	MR
NXF5	Nuclear RNA export factor 5	300319	--
OCRL	Oculocerebrorenal syndrome of Lowe	300535	OCRL1

PAX2	Paired box 2	167409	--
PDSS2	Prenyl (decaprenyl) diphosphate synthase	610564	bA59I9.3
PKD1	Polycystic kidney disease 1	601313	PBP, Pc-1, TRPP1
PKD2	Polycystic kidney disease 2	173910	PKD4, PC2, Pc-2, TRPP2
PKHD1	Polycystic kidney and hepatic disease 1	606702	ARPKD, FCYT
PLCE1	phospholipase C, epsilon 1	608414	KIAA1516, PLCE, NPHS3
RET	Ret proto-oncogene	--	PTC, CDHF12, RET51, CDHR16
RPGRIP1L	RPGRIP1-like	610937	KIAA1005, CORS3, JBTS7, MKS5, NPHP8, FTM
SALL1	Sal-like 1	602218	Hsal1, ZNF794
SCARB2	Scavenger receptor class B, member 2	602257	HLGP85, LIMPII, SR-BII, LIMP-2
SCNN1A	Sodium channel, non-voltage-gated 1 alpha	600228	ENaCalpha
SCNN1B	Sodium channel, non-voltage-gated 1, beta	600760	ENaCbeta
SLC12A1	Solute carrier family 12	600839	NKCC2
SLC12A3	Solute carrier family 12, member 3	600968	NCCT
SLC3A1	Solute carrier family 3, member 1	104614	CSNU1, D2H, RBAT, ATR1, NBAT
SLC4A1	Solute carrier family 4,member 1	--	RTA1A, CD233, FR, SW, WR
SLC4A4	Solute carrier family 4, member 4	603345	NBC1, HNBC1, NBC2, pNBC, hhNMC
SLC5A1	Solute carrier family 5, member 1	182380	D22S675, NAGT
SLC5A2	Solute carrier family 5, member 2	182381	--
SLC7A9	solute carrier family 7, member 9	604144	--
SLC9A3R1	Solute carrier family 9, member 3, regulator 1	604990	NHERF, EBP50
SMARCAL1	SWI/SNF related, matrix associated, actin-dependent regulator of chromatin, subfamily 1-like protein 1	606622	HHARP, HARP
SOX17	SRY (sex determining region Y)-box 17	610928	--
TCTN2	Tectonic family member 2	613846	FLJ12975, TECT2, MKS8
TMEM216	Transmembrane protein 216	613277	MGC13379, HSPC244, JBTS2, MKS2

TMEM231	Transmembrane protein 231	614949	FLJ22167, ALYE870, PRO1886, JBTS20, MKS11
TMEM237	Transmembrane protein 237	614423	JBTS14
TMEM67	Transmembrane protein 67	609884	MGC26979, JBTS6, NPHP11
TRPC6	Transient receptor potential cation channel, subfamily C, member 6	603652	TRP6
UMOD	Uromodulin	191845	--
UPK3A	Uroplakin 3A	611559	--
USF2	Upstream transcription factor 2	600390	FIP, bHLHb12
WNK1	WNK lysine deficient protein kinase 1	605232	HSAN2
WNK4	WNK lysine deficient protein kinase 4	601844	--
WT1	Wilms tumor 1	607102	WAGR, WIT-2, AWT1
XDH	Xanthine dehydrogenase	607633	XOR, XO

Supplementary Table 2: Heterozygous Variants found in parental DNA samples from cohort B

FT-36

chr	zygosity	Gene	ref Sequence	variant	predicted change	SGP737	PolyPhen-2	Provean	MutationTaster	Human Splicing Finder	Present in Both Parents
chr2	het	TMEM237	NM_001044385	c.G176A:p.R59Q	missense	Novel	Benign	-0.795	Polymorphism		
chr3	het	IQCB1	NM_001023571	c.C1048G:p.H350D	missense	Novel	Probably Damaging	-6.439	Disease causing		
chr13	het	FREM2	NM_207361	c.C6977G:p.T2326S	missense	739	Benign	-0.703	Polymorphism		
chr15	het	FAN1	NM_001146094	c.C1009A:p.Q337K	missense	Novel	Benign	-0.505	Polymorphism		
chr17	het	NEK8	NM_178170	c.G1401A:p.W467X	nonsense	Novel	.	.	Disease causing		yes
chrX	het	COL4A6	NM_001847	c.G4319C:p.G1440A	missense	85	Probably Damaging	-5.221	Disease causing		
chrX	het	COL4A5	NM_000495	c.546+15A>T	splice variant	Novel	.	.		Potential alteration	
chrX	het	COL4A5	NM_000495	c.G797A:p.R266Q	missense	Novel	Benign	-0.212	Disease causing		
chrX	het	COL4A5	NM_000495	c.A5053G:p.T1685A	missense	Novel	Possibly damaging	-1.811	Disease causing		

FT-40

chr	zygosity	Gene	ref Sequence	variant	predicted change	SGP737	PolyPhen-2	Provean	MutationTaster	Human Splicing Finder	Present in Both Parents
chr1	het	NPHS2	NM_014625	c.709G>C:p.E237Q	missense	17	Possibly damaging	-2.331	Disease causing		
chr2	het	COL4A4	NM_000092	c.1246C>G:p.P416A	missense	Novel	Possibly damaging	-2.106	Disease causing		
chr6	het	CDC5L	NM_001253	c.1154C>T:p.T385I	missense	Novel	Possibly damaging	-4.763	Disease causing		
chr10	het	BICC1	NM_001080512	c.1319delC:p.P440fs	frameshift	7	.	.			
chr10	het	BICC1	NM_001080512	c.1319C>T:p.P440L	missense	7	Benign	-2.102	Disease causing		
chr10	het	PAX2	NM_000278	c.867C>G:p.N289K	missense	5	Benign	-2.695	Disease causing		
chr12	het	CEP290	NM_025114	c.3777_3778del:p.R1259fs	frameshift	Novel	.	.			yes
chr13	het	FREM2	NM_207361	c.6977C>G:p.T2326S	missense	739	Benign	-0.703	Polymorphism		
chr19	het	NPHS1	NM_001287760	c.713-8T>C	splice variant	Novel	.	.		Potential alteration	
chrX	het	COL4A6	NM_001287760	c.4155_4156insG:p.F1386fs	frameshift	154	.	.			

FT-41

chr	zygosity	Gene	ref Sequence	variant	predicted change	SGP737	PolyPhen-2	Provean	MutationTaster	Human Splicing Finder	Present in Both Parents
chr3	het	NPHP3	NM_153240	c.2694-1_-2delAG	frameshift	Novel	.	.		Acceptor site broken	yes
chr12	het	WNK1	NM_014823	c.A4880C:p.N1627T	missense	1	Benign	-1.211	Polymorphism		
chr12	het	SCNN1A	NM_001159576	c.C1658T:p.P553L	missense	5	Probably Damaging	-9.078	Disease causing		
chr16	het	SLC12A3	NM_000339	c.T1112C:p.I371T	missense	148	Probably Damaging	-4.735	Disease causing		
chr16	het	TMEM231	NM_001077416	c.G391A:p.D131N	missense	Novel	Benign	0.054	Polymorphism		
chrX	het	COL4A6	NM_001847	c.4329_4330insG:p.F1444fs	frameshift	154	.	.			

FT-42

chr	zygosity	refGene gene	ref Sequence	variant	predicted change	SGP737	PolyPhen-2	Provean	MutationTaster	Human Splicing Finder	Present in Both Parents
chr12	het	TCTN2	NM_001143850	c.252_253del:p.84_85del	deletion	Novel	.	.			yes
chr13	het	FREM2	NM_207361	c.C6977G:p.T2326S	missense	739	Benign	-0.703	Polymorphism		
chr16	het	PKD1	NM_000296	c.C6526T:p.R2176C	missense	1	Probably Damaging	-2.904	Polymorphism		
chr16	het	SLC12A3	NM_001126107	c.2880+15G>C	splice variant	Novel	.	.		Potential alteration	

FT-43

chr	zygosity	Gene	ref Sequence	variant	predicted change	SGP737	PolyPhen-2	Provean	MutationTaster	Human Splicing Finder	Present in Both Parents
chr2	het	TTC21B	NM_024753	c.T2504A:p.V835D	missense	Novel	Probably Damaging	-4.25	Disease causing		
chr3	het	LAMB2	NM_002292	c.1519-1G>-	splice variant	15	.	.			
chr5	het	C5orf42	NM_023073	c.3545delA:p.N1182fs	frameshift	17	.	.			
chr13	het	FREM2	NM_207361	c.C6977G:p.T2326S	missense	739	Benign	-0.703	Polymorphism		
chr16	het	GLIS2	NM_032575	c.415delG:p.G139fs	frameshift	22	.	.			
chr17	het	SLC4A1	NM_000342	c.695-3C>A	splice variant	Novel	.	.		Probably no impact	
chr17	het	MKS1	NM_001165927	c.C1036T:p.Q346X	Nonsense	Novel	.	.	Disease causing		yes
chr17	het	ACE	NM_001178057	c.G1411A:p.D471N	missense	1	Benign	0.141	Polymorphism		

FT-45

chr	zygosity	Gene	ref Sequence	variant	predicted change	SGP737	PolyPhen-2	Provean	MutationTaster	Human Splicing Finder	Present in Both Parents
chr5	het	C5orf42	NM_023073	c.9279_9280insA:p.H3094fs	frameshift	Novel	.	.			
chr5	het	C5orf42	NM_023073	c.566delA:p.N189fs	frameshift	286	.	.			
chr6	het	PKHD1	NM_138694	c.G3539A:p.G1180E	missense	Novel	Probably Damaging	-6.296	Disease causing		yes
chr16	het	SLC12A3	NM_000339	c.T1112C:p.I371T	missense	148	Probably Damaging	-4.735	Disease causing		
chrX	het	COL4A6	NM_001847	c.G4319C:p.G1440A	missense	85	Probably Damaging	-5.221	Disease causing		

SGP737 is an in house Saudi Arabian mutation database of 550 whole exome sequenced samples - the number indicates the frequency of the variant in this ethnically matched population. Boxes are coloured red for pathogenic, yellow for intermediate pathogenicity and green for benign based on in silico testing.

Supplementary Figure 1: Sequence chromatograms from maternal and paternal DNA from families FT-35,-36,-40,-41,-42,-43,-45 revealing identical heterozygous changes. A control (Normal) chromatogram is provided as reference.