Supplemental Table 1. Characteristics of patients with lower than average eGFR but smaller than average kidneys (Fig 2C, Quadrant (iii))

Variable	Segment C	Segments A,B,D	P Value
Patients *(n)*	143	520	
Median Age (Q1, Q3)	36.2 (29.7, 42.4)	37.2 (28.7, 42.7)	0.974[1]
Median Age Onset HTN (Q1, Q3)	30.0 (23.0, 37.0)	30.9 (25.0, 38.0)	0.195[1]
Irazabal* Class (%)			0.1804[2]
Typical	140 (97.9%)	484 (94.9%)	
Atypical	3 (2.1%)	26 (5.1%)	
Irazabal* Typical Sub-class			<.0001[3]
A	14 (10.0%)	26 (5.4%)	
B	64 (45.7%)	76 (15.7%)	
C	58 (41.4%)	161 (33.3%)	
D	4 (2.9%)	144 (29.8%)	
E	0 (0.0%)	77 (15.9%)	
Gene			0.202[2]
NMD	11 (7.7%)	47 (9.0%)	
PKD2	29 (20.3%)	74 (14.2%)	
PKD1	103 (72.0%)	399 (76.7%)	

Q1, Q3- 1st and 3rd quartiles
*(1) Imaging classification data was available only on 653 patients
[1] Wilcoxon
[2] Chi-squared
[3] Fisher's Exact

1. Irazabal MV, Rangel LJ, Bergstralh EJ, Osborn SL, Harmon AJ, Sundsbak JL, et al. Imaging Classification of Autosomal Dominant Polycystic Kidney Disease: A Simple Model for Selecting Patients for Clinical Trials. J Am Soc Nephrol. 2015 Jun 5;26(1):160-72.

Supplemental Table 2. Details of the evaluation of *PKD1* non-truncating mutations (MSG2 and MSG3)

Mutation Type[1]	Codon Position	Exon	Mutation Designation (nt)	Mutation Designation (aa)	Domain/ Region[2]	GV/GD score[3]	Domain score[4]	Structure score[5]	Recurrent AA score[6]	Splicing score[7]	Substitution Score[8]	MSG	Frequency in study[9]
InFrame D/I	424	6	c.1270_1276del7insC	p.V424_E425del2:K426Q	C-type lectin	8	0	4	0		12	**2**	1
InFrame D/I	687	10	c.2059_2061delCTC	p.L687del	ND	8	0	2	0		10	**2**	1
Inframe D/I	910	11	c.2729_2737del9	p.D910_V912del3	PKD-II	14	2	6	0		22	**2**	1
InFrame D/I	1205	15	c.3615_3617delTGT	p.D1205E:V1206del	PKD-V	6	4	2	0		12	**2**	1
InFrame D/I	1270	15	c.3808_3810delTGC	p.C1270del	PKD-VI	0	0	2	0		2	**3**	1
InFrame D/I	1450	15	c.4349_4351delACA	p.N1450del	PKD-VIII	8	0	2	0		10	**2**	1
InFrame D/I	1967	15	c.5899_5901delGTG	p.V1967del	PKD-XIV	8	4	2	0		14	**2**	1
Inframe D/I	1993	15	c.5976_5978delCAC	p.F1992L, T1993del	PKD-XV	4	0	2	0		6	**3**	1
InFrame D/I	2133	15	c.6397_6399delTCC	p.F2133del	PKD-XVI	6	0	2	0		8	**2**	2
InFrame D/I	2412	18	c.7236_7238delCAA	p.N2412del	REJ	8	0	2	0		10	**2**	1
InFrame D/I	2514	19	c.7529_7540dup12	p.L2511_L2513dup3,insH	REJ	0	2	8	0		10	**2**	1
InFrame D/I	2524	19	c.7570_7572delGAG	p.E2524del	REJ	6	0	2	0		8	**2**	2
InFrame D/I	2609	20	c.7826_7828delTCG	p.I2609K:E2610del	REJ	8	0	2	0		10	**2**	1
InFrame D/I	2613	20	c.7836_7838delGTT	p.L2613del	REJ	8	0	2	0		10	**2**	1
InFrame D/I	2816	23	c.8447_8452del6	p.L2816_N2818del,insH	GAIN	12	0	4	0		16	**2**	1
Inframe D/I	2979	24	c.8935_8937delTTC	p.F2979del	GAIN	8	0	2	0		10	**2**	1
InFrame D/I	3035	25	c.9103_9105delGAG	p.E3035del	GPS	6	0	2	0		8	**2**	1
Inframe D/I	3168	27	c.9502_9504delTTC	p.F3168del	PLAT	8	6	2	1		17	**2**	1
Inframe D/I	3287	29	c.9859_9861delCTC	p.L3287del	TM2	8	4	2	0		14	**2**	2
InFrame D/I	3571	36	c.10710_10715del6	p.A3571_V3572del2	TM4	12	1	4	0		17	**2**	1
InFrame D/I	3777	40	c.11330_11332delGCA	p.S3777del	ExL3	0	0	2	0		2	**3**	1
InFrame D/I	3781	40	c.11340_11345del6	p.Y3781_D3782del2	ExL3	6	2	4	0		12	**2**	1
InFrame D/I	3782	40	c.11345_11347delACG	p.D3782del	ExL3	4	0	2	0		6	**3**	1
InFrame D/I	3782	40	c.11345_11347dup	p.D3782dup	ExL3	0	0	2	0		2	**3**	2
InFrame D/I	3782	40	c.11340_11345dup6	p.Y3781_D3782dup	ExL3	0	2	4	0		6	**3**	1
InFrame D/I	3832	41	c.11493_11498dup6	p.D3832_R3833dup	ExL3	0	1	4	0		5	**3**	1
Missense	14	1	c.41G>A	p.G14D	SP	-2	0	5	0		3	**3**	1
Missense	39	1	c.115T>C	p.C39R	LRR N-flank	8	6	0	0		14	**2**	1
Missense	70	1	c.208A>C	p.T70P	LRR N-flank	-2	0	5	0		3	**3**	1
Missense	71	1	c.211G>C	p.A71P	LRR N-flank	-2	0	5	0		3	**3**	1
Missense	74	2	c.221T>A	p.V74D	LRR	6	6	0	0		12	**2**	1
Missense	101	2	c.301A>G	p.N101D	LRR	2	6	0	1		9	**2**	1
Missense	101	3	c.303C>G	p.N101K	LRR	6	6	0	1		13	**2**	1
Missense	117	3	c.350T>C	p.L117S	LRR	7	6	0	0		13	**2**	1
Missense	120	3	c.359T>C	p.I120T	LRR	6	6	0	0		12	**2**	1
Missense	140	4	c.419C>A	p.A140E	LRR C-flank	-2	0	5	0		3	**3**	1
Missense	222	5	c.665C>A	p.A222E	WSC	3	3	0	0		6	**3**	1
Missense	230	5	c.688T>A	p.C230S	WSC	6	6	0	0		12	**2**	1
Missense	259	5	c.776G>A	p.C259Y	WSC	8	6	0	0		14	**2**	1
Missense	325	5	c.974A>G	p.Y325C	PKD-I	8	4	2	0		14	**2**	2
Missense	381	5	c.1141G>A	p.G381S	ND	5	0	0	1		6	**3**	4
Missense	421	6	c.1261C>T	p.R421C	C-type lectin	6	0	2	0		8	**2**	1
Missense	432	6	c.1294G>A	p.A432V	C-type lectin	5	2	0	1		8	**2**	3
Missense	432	6	c.1294G>A	p.A432T	C-type lectin	5	2	0	1		8	**2**	1
Missense	436	6	c.1307G>A	p.C436Y	C-type lectin	8	6	0	1		15	**2**	2

Mutation Type[1]	Codon Position	Exon	Mutation Designation (nt)	Mutation Designation (aa)	Domain/ Region[2]	GV/GD score[3]	Domain score[4]	Structure score[5]	Recurrent AA score[6]	Splicing score[7]	Substitution Score[8]	MSG	Frequency in study[9]
Missense	444	6	c.1331T>C	p.L444P	C-type lectin	6	4	0	0		10	**2**	1
Missense	445	6	c.1334C>A	p.A445E	C-type lectin	6	0	0	0		6	**3**	1
Missense	458	5	c.1373C>G	p.S458C	C-type lectin	3	0	2	0		5	**3**	1
Missense	459	6	c.1376G>C	p.R459P	C-type lectin	3	0	2	0		5	**3**	1
Missense	466	7	c.1397T>A	p.V466E	C-type lectin	5	0	0	0		5	**3**	1
Missense	508	7	c.1522T>C	p.C508R	C-type lectin	8	6	0	0		14	**2**	2
Missense	510	7	c.1529G>C	p.R510P	C-type lectin	-2	0	5	0		3	**3**	2
Missense	515	7	c.1543G>A	p.G515R	C-type lectin	3	4	0	1		7	**3**	1
Missense	605	9	c.1814T>G	p.L605R	ND	5	0	0	0		5	**3**	1
Missense	611	9	c.1831C>T	p.R611W	ND	6	0	0	0		6	**3**	3
Missense	690	10	c.2069T>G	p.V690G	ND	5	0	0	1		6	**3**	1
Missense	727	11	c.2180T>C	p.L727P	ND	6	0	0	2		6	**3**	10
Missense	845	11	c.2534T>C	p.L845S	ND	6	0	0	0		6	**3**	1
Missense	960	12	c.2879G>A	p.G960D	PKD-II	6	2	0	1		8	**2**	1
Missense	960	12	c.2879G>T	p.G960V	PKD-II	6	2	0	1		8	**2**	1
Missense	967	12	c.2899T>C	p.W967R	PKD-II	6	6	0	0		12	**2**	1
Missense	1181	15	c.3542A>G	p.Y1181C	PKD-III	8	4	2	0		14	**2**	1
Missense	1243	15	c.3729G>C	p.W1243C	PKD-IV	8	6	2	0		16	**2**	1
Missense	1328	15	c.3982T>C	p.W1328R	PKD-V	6	6	0	0		12	**2**	1
Missense	1329	15	c.3985A>C	p.T1329P	PKD-V	-2	0	5	0		3	**3**	1
Missense	1400	15	c.4199T>C	p.L1400P	PKD-VI	5	0	0	0		5	**3**	1
Missense	1412	15	c.4234T>G	p.Y1412D	PKD-VI	7	2	0	0		9	**2**	1
Missense	1499	15	c.4496T>TC	p.L1499P	PKD-VII	-2	0	5	0		3	**3**	1
Missense	1503	15	c.4507G>C	p.G1503R	PKD-VII	6	0	0	0		6	**3**	2
Missense	1654	15	c.4961C>A	p.A1654D	PKD-IX	6	0	0	0		6	**3**	1
Missense	1837	15	c.5509T>C	p.W1837R	PKD-XI	6	2	0	0		8	**2**	1
Missense	1839	15	c.5516G>T	p.W1839L	PKD-XI	5	6	0	1		12	**2**	1
Missense	1839	15	c.5515T>C	p.W1839R	PKD-XI	6	6	0	1		13	**2**	1
Missense	1870	15	c.5608A>C	p.N1870H	PKD-XII	5	4	0	3		12	**2**	1
Missense	1870	15	c.5609A>T	p.N1870I	PKD-XII	7	4	0	3		14	**2**	1
Missense	1992	15	c.5975T>C	p.F1992S	PKD-XIII	6	0	0	0		6	**3**	1
Missense	1999	15	c.5995G>A	p.G1999S	PKD-XIV	5	2	0	3		10	**2**	2
Missense	1999	15	c.5996G>C	p.G1999A	PKD-XIV	5	2	0	3		10	**2**	1
Missense	2051	15	c.6152G>C	p.R2051P	PKD-XV	-2	0	5	1		4	**3**	1
Missense	2053	15	c.6158T>C	p.L2053P	PKD-XV	-2	2	5	0		5	**3**	1
Missense	2114	15	c.6341A>G	p.Y2114C	PKD-XVI	8	2	2	0		12	**2**	1
Missense	2187	15	c.6559T>C	p.W2187R	REJ	6	4	0	0		10	**2**	1
Missense	2213	15	c.6638G>C	p.R2213P	REJ	6	0	2	1		8	**2**	1
Missense	2215	15	c.6643C>T	p.R2215W	REJ	3	0	0	0		3	**3**	4
Missense	2278	15	c.6832G>A	p.G2278R	REJ	3	4	0	0		7	**3**	1
Missense	2297	15	c.6890A>C	p.H2297P	REJ	4	0	0	0		4	**3**	1
Missense	2313	16	c.6937C>G	p.L2313V	REJ	2	0	0	0		2	**3**	1
Missense	2370	17	c.7108T>A	p.C2370S	REJ	6	4	0	1		11	**2**	2
Missense	2372	17	c.7115C>T	p.S2372F	REJ	7	2	0	2		11	**2**	2
Missense	2373	17	c.7118G>A	p.C2373Y	REJ	8	4	0	0		12	**2**	1
Missense	2392	17	c.7175G>C	p.R2392P	REJ	3	0	0	0		3	**3**	1
Missense	2423	18	c.7268C>T	p.S2423F	REJ	4	0	0	0		4	**3**	1
Missense	2434	18	c.7300C>T	p.R2434W	REJ	6	2	0	1		9	**2**	1
Missense	2459	18	c.7376G>A	p.G2459D	REJ	6	0	0	0		6	**3**	1
Missense	2516	19	c.7546C>T	p.R2516C	REJ	8	0	2	0		10	**2**	4

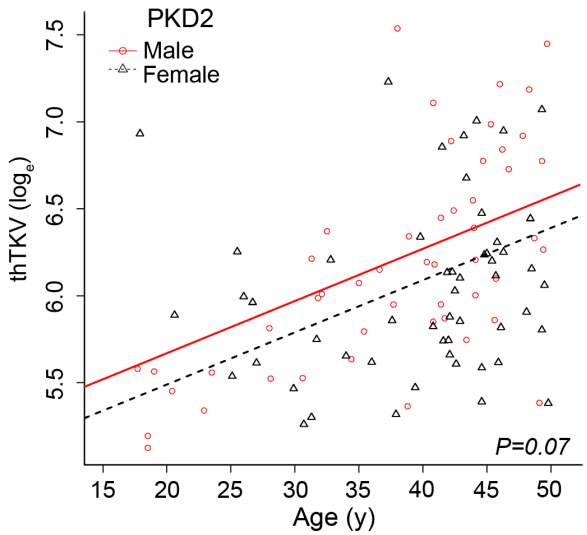
Mutation Type[1]	Codon Position	Exon	Mutation Designation (nt)	Mutation Designation (aa)	Domain/ Region[2]	GV/GD score[3]	Domain score[4]	Structure score[5]	Recurrent AA score[6]	Splicing score[7]	Substitution Score[8]	MSG	Frequency in study[9]
Missense	2643	21	c.7928G>C	p.R2643P	REJ	6	4	0	1		11	**2**	1
Missense	2660	21	c.7978 G>A	p.D2660N	REJ	2	0	0	0		2	**3**	1
Missense	2723	23	c.8168T>C	p.L2723P	REJ	6	4	0	0		10	**2**	1
Missense	2759	23	c.8276T>C	p.L2759P	REJ	6	2	0	0		8	**2**	1
Missense	2764	23	c.8291T>A	p.M2764K	REJ	6	0	0	0		6	**3**	1
Missense	2767	23	c.8299C>T	p.R2767C	REJ	8	2	2	0		12	**2**	2
Missense	2768	23	c.8302G>A	p.V2768M	GAIN	2	0	0	0		2	**3**	1
Missense	2771	23	c.8311G>A	p.E2771K	GAIN	5	0	6	0		11	**2**	9
Missense	2785	23	c.8354G>A	p.G2785D	GAIN	6	0	0	0		6	**3**	1
Missense	2786	23	c.8358G>C	p.K2786N	GAIN	6	0	0	1		7	**3**	1
Missense	2809	23	c.8426C>T	p.P2809L	GAIN	6	0	0	0		6	**3**	2
Missense	2833	23	c.8497C>T	p.P2833S	GAIN	5	0	0	0		5	**3**	2
Missense	2850	23	c.8548T>C	p.S2850P	GAIN	5	0	0	0		5	**3**	2
Missense	2866	23	c.8597T>C	p.L2866P	GAIN	6	0	0	0		6	**3**	1
Missense	3007	25	c.9019T>C	p.S3007P	GAIN	-2	0	4	0		2	**3**	1
Missense	3030	25	c.9088C>T, 9089T>G	p.L3030W	GPS	4	0	0	0		4	**3**	1
Missense	3036	25	c.9107C>T	p.T3036I	GPS	6	2	0	0		8	**2**	1
Missense	3049	25	c.9146C>T	p.T3049I	GPS	6	2	0	0		8	**2**	1
Missense	3053	25	c.9157G>A	p.A3053T	GPS	5	0	0	0		5	**3**	1
Missense	3054	25	c.9161G>T	p.S3054I	GPS	4	0	0	0		4	**3**	1
Missense	3095	26	c.9284T>C	p.L3095P	TM1	5	2	4	0		11	**2**	1
Missense	3126	26	c.9376A>C	p.T3126P	PLAT	5	4	0	1		10	**2**	1
Missense	3126	26	c.9377C>T	p.T3126I	PLAT	6	4	0	1		11	**2**	1
Missense	3127	26	c.9379G>T	p.G3127C	PLAT	7	4	0	0		11	**2**	1
Missense	3135	27	c.9404C>T	p.T3135M	PLAT	6	2	0	0		8	**2**	2
Missense	3137	27	c.9411C>G	p.H3137Q	PLAT	2	0	0	1		3	**3**	1
Missense	3138	27	c.9413T>A	p.V3138E	PLAT	6	4	0	2		12	**2**	1
Missense	3139	27	c.9416G>T	p.G3139V	PLAT	6	0	0	0		6	**3**	1
Missense	3152	27	c.9454C>G	p.R3152G	PLAT	6	0	0	0		6	**3**	1
Missense	3162	27	c.9485G>T	p.R3162L	PLAT	6	2	0	0		8	**2**	1
Missense	3168	27	c.9504C>G	p.F3168L	PLAT	2	4	0	2		6	**3**	1
Missense	3171	27	c.9511G>C	p.A3171P	PLAT	2	0	0	0		2	**3**	1
Missense	3186	27	c.9556C>T	p.H3186Y	PLAT	6	4	0	1		11	**2**	2
Missense	3194	28	c.9581C>T	p.A3194V	PLAT	-3	0	3	0		0	**3**	1
Missense	3200	28	c.9598G>T	p.V3200F	PLAT	4	2	0	0		6	**3**	1
Missense	3216	28	c.9647A>T	p.N3216I	PLAT	4	2	0	0		6	**3**	2
Missense	3263	29	c.9787T>C	p.W3263R	InL1	6	4	0	1		11	**2**	1
Missense	3264	29	c.9791T>G	p.L3264R	InL1	6	2	0	0		8	**2**	1
Missense	3283	29	c.9847T>C	p.C3283R	TM2	8	4	0	0		12	**2**	1
Missense	3326	30	c.9977G>A	p.G3326D	TM3	6	4	0	2		12	**2**	1
Missense	3469	33	c.10405G>A	p.D3469N	InL2	2	0	0	1		3	**3**	2
Missense	3469	33	c.10405G>T	p.D3469Y	InL2	7	0	0	1		8	**2**	1
Missense	3561	36	c.10682T>G	p.L3561R	TM4	-2	2	4	0		4	**3**	1
Missense	3599	36	c.10796C>T	p.S3599L	TM5	7	2	0	0		9	**2**	1
Missense	3604	35	c.10810G>C	p.E3604Q	InL3	2	0	0	1		3	**3**	1
Missense	3604	36	c.10810G>A	p.E3604K	InL3	5	0	0	1		6	**3**	1
Missense	3651	37	c.10951G>A	p.G3651S	InL3	5	0	0	1		6	**3**	3
Missense	3653	37	c.10958C>T	p.A3653V	InL3	5	0	0	0		5	**3**	1
Missense	3654	37	c.10960C>CG	p.L3654V	InL3	2	0	0	0		2	**3**	1
Missense	3657	37	c.10970C>T	p.A3657V	InL3	5	0	0	1		6	**3**	1

Mutation Type[1]	Codon Position	Exon	Mutation Designation (nt)	Mutation Designation (aa)	Domain/ Region[2]	GV/GD score[3]	Domain score[4]	Structure score[5]	Recurrent AA score[6]	Splicing score[7]	Substitution Score[8]	MSG	Frequency in study[9]
Missense	3678	38	c.11033T>G	p.M3678R	TM6	6	2	4	0		12	**2**	1
Missense	3682	38	c.11045T>A	p.L3682Q	TM6	5	2	0	0		7	**3**	1
Missense	3727	39	c.11180T>TA	p.M3727K	ExL3	5	2	0	0		7	**3**	1
Missense	3750	39	c.11249G>A	p.R3750Q	PC-A	5	6	0	1		12	**2**	1
Missense	3750	39	c.11249G>C	p.R3750P	PC-A	6	6	0	1		13	**2**	1
Missense	3753	39	c.11258G>A	p.R3753Q	PC-A	5	6	0	2		13	**2**	2
Missense	3753	39	c.11257C>T	p.R3753W	PC-A	6	6	0	2		14	**2**	1
Missense	3818	40	c.11452G>A	p.G3818S	PC-B	5	6	0	2		13	**2**	1
Missense	3818	41	c.11453G>T	p.G3818V	PC-B	6	6	0	2		14	**2**	2
Missense	3818	41	c.11452G>C	p.G3818R	PC-B	6	6	0	2		14	**2**	1
Missense	3834	41	c.11501T>G	p.L3834R	PC-B	6	2	0	0		8	**2**	1
Missense	3842	41	c.11524T>C	p.W3842R	PC-B	6	6	0	1		13	**2**	2
Missense	3885	42	c.11654T>G	p.V3885G	ExL3	6	2	0	0		8	**2**	1
Missense	3908	43	c.11723T>G	p.L3908R	TM7	5	0	0	0		5	**3**	1
Missense	4137	45	c.12410T>C	p.L4137P	GPPAS	6	0	2	0		8	**2**	1
Missense	4139	45	c.12416T>C	p.L4139P	GPPAS	5	0	2	0		7	**3**	1
Missense	4150	46	c.12448C>T	p.R4150C	GPPAS	8	2	0	0		10	**2**	2
Missense	4155	46	c.12463T>C	p.F4155L	C-tail	2	0	0	2		4	**3**	1
Missense	4155	46	c.12463T>G	p.F4155V	C-tail	5	0	0	2		7	**3**	1
Missense	4155	46	c.12464T>C	p.F4155S	C-tail	7	0	0	2		9	**2**	1
Splice	120	IVS3	c.359+3A>T	p.I120fs						7	7	**3**	1
Splice	120	IVS3	c.359+2dupT	p.I120fs						8	8	**2**	1
Splice	120	IVS3	c.359+5G>T	p.I120fs						8	8	**2**	1
Splice	177	IVS4	c.529+3G>C	p.G177fs						7	7	**3**	1
Splice	401	IVS5	c1202-9G>A	p.A401fs						8*	8	**2**	3
Splice	609	9	c.1827G>A	p.V609fs						6*	6	**3**	1
Splice	952	IVS11	c.2853+5G>A	p.R952fs						4	4	**3**	1
Splice	1054	IVS13	c.3161+5_+8del4	p.L1054fs						8*#	8	**2**	1
Splice	2306	IVS15	c.6916-10C>A	p.R2306fs						10*#	10	**2**	1
Splice	2306	IVS15	c.6916-9G>A	p.R2306fs						10*#	10	**2**	5
Splice	2404	IVS17	c.7209+4_+7delAGTG	p.R2404fs						10#	10	**2**	2
Splice	2931	IVS23	c.8791+5G>C	p.G2931fs						8	8	**2**	1
Splice	3068	IVS25	c.9202-16G>A	p.E3068fs						8*#	8	**2**	1
Splice	3389	IVS31	c.10167+25_+43del19	p.Q3390fs						8#	8	**2**	1
Splice	3540	IVS35	c.10618+19_+28del10	p.G3540fs						6	6	**3**	1
Splice	3673	IVS37	c.11017-10C>A	p.S3673fs						6#	6	**3**	4
Splice	3719	38	c.11156G>A	p.R3719fs						8	8	**2**	2
Splice	3719	IVS38	c.11156+5G>C	p.R3719fs						8	8	**2**	1
Splice	3956	43	c.11866C>T	p.L3956fs						6*	6	**3**	1
Splice	4002	IVS43	c.12003+14_+33del	p.A4002fs						6#	6	**3**	2

1. Only small inframe deletion or insertion (InFrame D/I) mutations, four amino acids or less, and only atypical splicing mutations, those not mutating the canonical di-nucleotides flanking each exon, were considered non-truncating and evaluated for these two mutation types.
2. Domain information: Signal Peptide (SP), Leucine Rich Repeat (LRR), cell-Wall integrity and Stress-response Components 1-4 (WSC), Polycystic Kidney Disease protein repeat -# (PKD-#). Receptor for Egg Jelly (REJ), G-protein-coupled receptor Proteolytic Site (GPS), G-protein-coupled receptor-Autoproteolysis INducing (GAIN), Polycystin-1, Lipoxygenase, Alpha-Toxin (PLAT), Transmembrane # (TM#), Extracellular Loop # (ExL#), Intracellular Loop # (InL#), Polycystin Motif –A, or –B (PC-A, PC-B), G-Protein Peptide Activating Sequence (GPPAS), None Defined (ND).

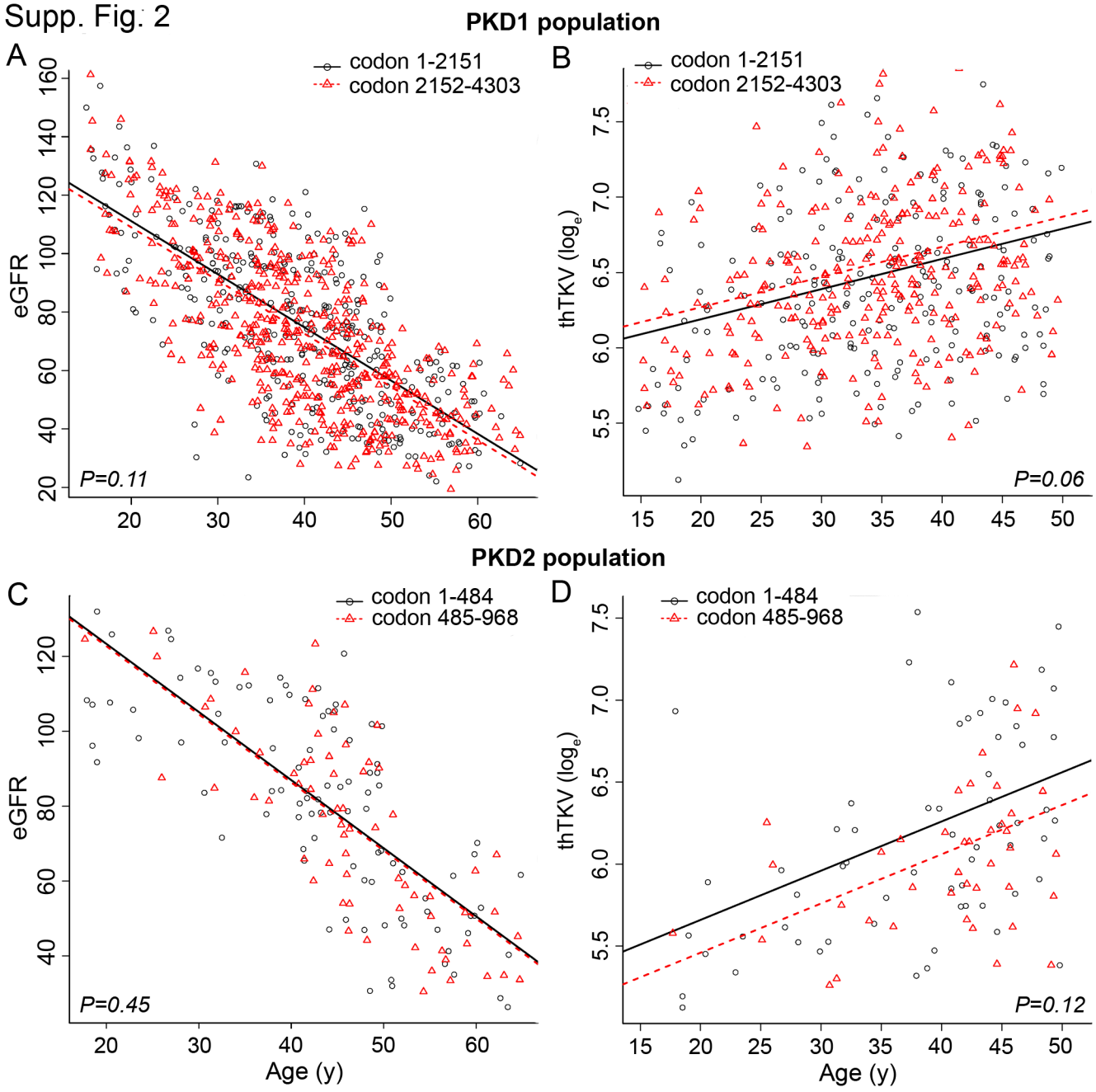
3. GV/GD Score: Score derived from Grantham Variation (GV) and Grantham Difference (GD) values (see Concise Methods for details) (scale, -8 to +8 per amino acid)
4. Domain score: Score of conservation in the defined domain (scale, 0 to 6 per amino acid) (see Concise Methods for details)
5. Structure Score: Scores reflecting disrupted structure (scale, 0 to 5 per amino acid) (see Concise Methods for details)
6. Recurrent AA Score: Number of additional different mutant disruptions of this amino acid (AA) described
7. Splicing Score: Score derived from predictions using the Berkeley Drosophila Genome Project (BDGP) browser (scale, 0 to 10). * = new cryptic splice site revealed, # = previous RT-PCR data showing altered slicing.
8. Substitution Score: Derived from summing the GV/GD, Domain, Structure, Recurrent AA and Splicing Scores
9. Frequency in Study: Number of families in the study with this mutation

Supp. Fig. 1



Supplemental Fig. 1. **Comparison of gender differences by htTKV in PKD2**
This analysis shows a non-significant trend to smaller kidneys in females (Table 2).

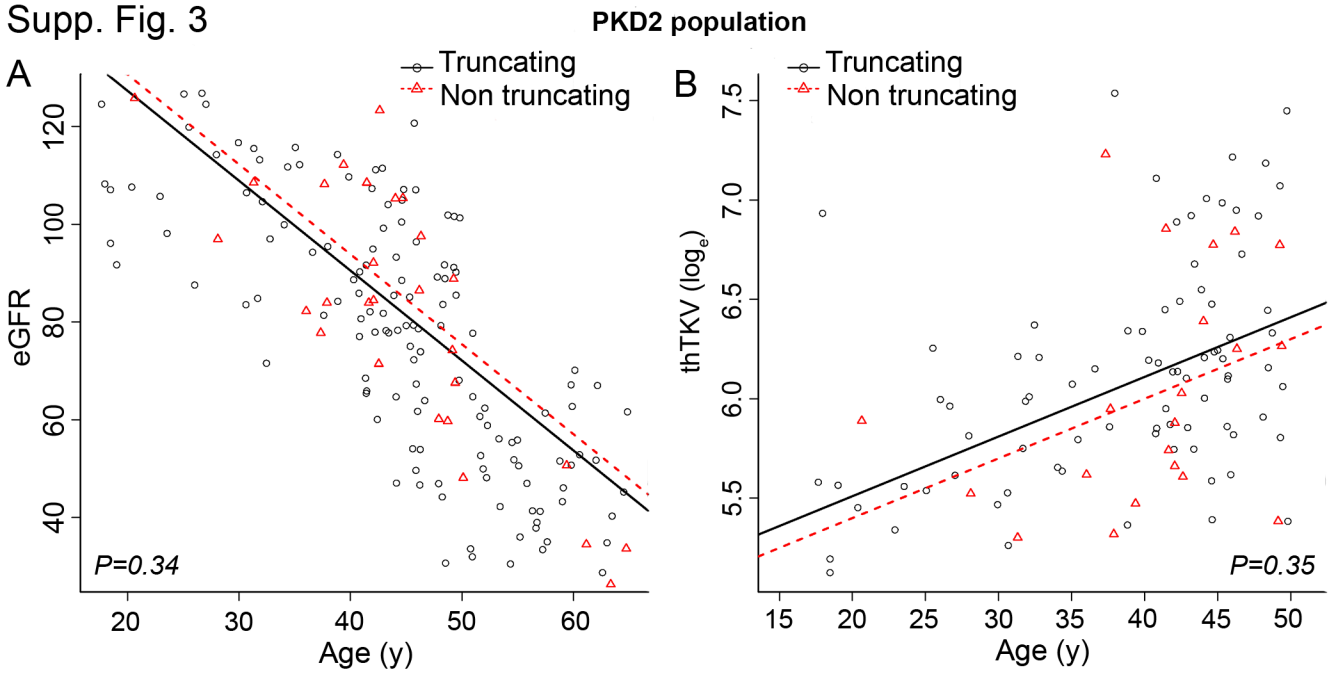
Supp. Fig. 2



Supplemental Fig. 2. **Analyses of the significance of mutation position in PKD1 and PKD2 to renal disease severity**

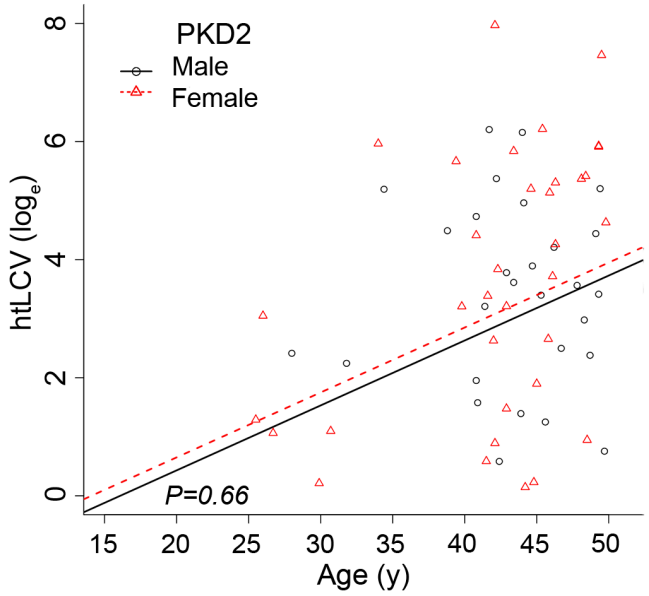
PKD1 (A, B) and PKD2 (C, D) are assayed by eGFR (A, C) and htTKV (B, D). The positions of the mutations in *PKD1* and *PKD2* were divided at the midpoint of the coding region and are illustrated here as the codon position in the corresponding protein. No significant difference was seen between mutations 3' compared to 5' of the midpoint for *PKD1* with eGFR (A) or htTKV (B) and PKD2 with eGFR (C) or htTKV (D; Table 2).

Supp. Fig. 3



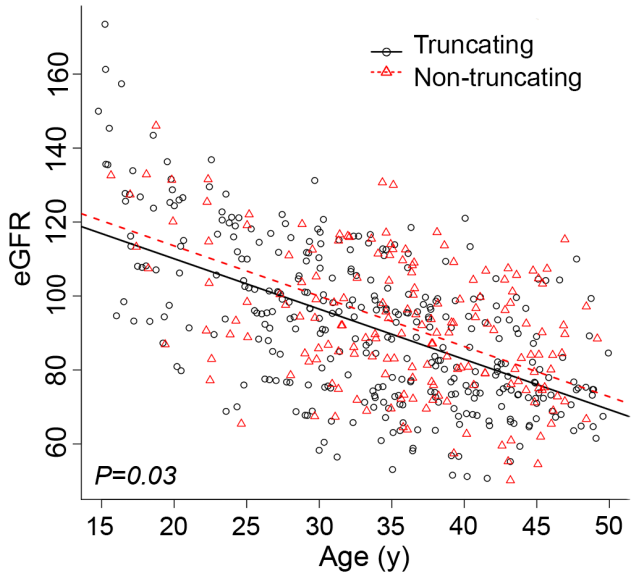
Supplemental Fig. 3. **Analyses of *PKD2* mutation type (truncating or non-truncating) and renal function** Neither by eGFR (A; non-truncating relative to truncating) or htTKV (B) was there a significant difference between the mutation types (Table 2).

Supp. Fig. 4



Supplemental Fig. 4. **Analysis of the PKD2 population shows that female htLCV is not significantly larger than males (Table 2).**

Supp. Fig. 5



Supplemental Fig. 5. **Analysis of *PKD1* mutation type (truncating or non-truncating) by eGFR in the htTKV population** There was a significant eGFR difference in this population (n=663; Table 1 and 2), although htTKV was not significant in this population (Fig. 3D).