Table S1. Results of *PKD1* missense mutations analysis using NNSplice, ESEfinder and Rescue-ESE web sources.

		NNSplice[1]					*Mutation effects on splice sites*[3]		*Number of disrupted ESE*	
Mutation	Exon	Acceptor (3´ss)	Donor (5´ss)	Exon length (bp)	Position from exon ending (5´/3´)	Clinical Significance[2]	Functional splice sites	Activation / Creation of new splice sites	ESEfinder	Rescue-ESE
p.R80W	1		0,91	72	23 (5´)	Indeterminate	-	-	1	0
p.R80Q	1		0,91	72	24 (5´)	Likely neutral	-	-	1	0
p.N101D	3	0,88	0,97	72	14 (5´)	Highly likely pathogenic	A (0,84)	-	0	2
p.N125D	4	0,84	0,95	170	14 (5´)	Highly likely pathogenic	A (0,83)	-	0	0
p.C155Y	4	0,84	0,95	170	66 (3´)	Highly likely pathogenic	-	-	0	0
p.G168A	4	0,84	0,95	170	27 (3´)	Likely neutral	-	-	1	0
p.A401V	6	0,43	0,37	187	1 (5´)	Likely neutral	-	-	0	0
p.P404R	6	0,43	0,37	187	10 (5´)	Likely neutral	-	-	1	0
p.R454C	6	0,43	0,37	187	26 (3´)	Indeterminate	-	-	1	0
p.R454P	6	0,43	0,37	187	25 (3´)	Indeterminate	-	-	1	0
p.V460D	6	0,43	0,37	187	7 (3´)	Likey pathogenic	A (0,32)	-	0	0
p.V460A	6	0,43	0,37	187	7 (3´)	Likely pathogenic	-	-	0	0
p.V466L	7	0,65	0,56	218	11 (5´)	Indeterminate	A (0,6)	-	0	0
p.V466M	7	0,65	0,56	218	11 (5´)	Indeterminate	-	-	1	0
p.S471L	7	0,65	0,56	218	27 (5´)	Indeterminate	-	-	1	0
p.L532V	7	0,65	0,56	218	13 (3´)	Likely neutral	-	-	0	0
p.L656Q	10	0,98	0,72	127	118 (5´)	Likely pathogenic	-	(c) A (0,86)	0	0
p.V690D	10	0,98	0,72	248	29 (3´)	Highly likely pathogenic	-	-	1	0
p.Y698D	10	0,98	0,72	248	6 (3´)	Likely neutral	D (0,48)	-	0	0
p.V715F	11	1	0,99	756	46 (5´)	Likely neutral	-	(+) A (0,82)	0	0
p.S903G	11	1	0,99	756	147 (3´)	Likely neutral	-	(+) D (0,87)	0	0
p.A990L	12	0,73	0,001	132	18-17 (3´)	Likely neutral	-	-	2	0
p.L1054P	13	0,8	0,85	132	1 (3´)	Indeterminate	-	-	0	0
p.G2310R	16	0,95	0,71	150	13 (5´)	Likely neutral	-	(+) D (0,65)	0	0
p.Q2354R	16	0,95	0,71	150	5 (3´)	Likely Pathogenic	D (0,48)	-	1	1
p.A2375V	17	0,72	0,95	144	85 (3´)	Likely Pathogenic	-	(c) D (0,9)	0	1
p.R2404W	18	0,83	0,99	280	1 (5´)	Likely neutral	-	-	1	0
p.W2405R	18	0,83	0,99	280	4 (5´)	Highly Likely Pathogenic	-	-	0	0
p.R2408C	18	0,83	0,99	280	13 (5´)	Likely pathogenic	-	-	2	0
p.V2628M	21	0,67	0,31	153	9 (5´)	Likely neutral	-	-	2	0
p.A2704V	22	0,57	0,69	145	51 (3´)	Likely neutral	-	(+) A (0,63)	0	0
p.G2814R	23	0,57	0,95	630	278 (5´)	Likely neutral	-	(c) A (0,81)	0	0
p.S2935F	24	0,83	0,91	157	13 (5´)	Indeterminate	-	-	1	0
p.F2978T	24	0,83	0,91	157	17-16 (3´)	Likely Pathogenic	-	-	0	1
p.F2978C	24	0,83	0,91	157	16 (3´)	Likely Pathogenic	-	-	0	1
p.F2978S	24	0,83	0,91	157	16 (3´)	Likely Pathogenic	-	-	0	1
p.M3023K	25	0,97	0,82	253	120 (5´)	Likely neutral	-	(+) D (0,71)	0	0
p.E3068Q	26	0,84	0,96	196	1 (5´)	Likely neutral	A (0,23)	-	0	0
p.E3068D	26	0,84	0,96	196	3 (5´)	Indeterminate	-	-	0	0
p.P3069L	26	0,84	0,96	196	5 (5´)	Indeterminate	-	-	1	0

p.N3074K	26	0,84	0,96	196	21 (5´)	Likely Pathogenic	-	-	0	3
p.C3112F	26	0,84	0,96	196	63 (3´)	Highly Likely Pathogenic	-	-	0	0
p.R3117H	26	0,84	0,96	196	48 (3´)	Likely neutral	-	-	0	0
p.R3130W	26	0,84	0,96	196	10 (3´)	Likely pathogenic	-	-	2	0
p.S3132L	26	0,84	0,96	196	3 (3´)	Likely pathogenic	-	-	0	0
p.T3135M	27	1	0,87	171	7 (5´)	Likely pathogenic	-	-	2	0
p.H3137Y	27	1	0,87	171	12 (5´)	Likely pathogenic	-	-	0	0
p.G3139V	27	1	0,87	171	18 (5´)	Indeterminate	-	-	0	0
p.R3169Q	27	1	0,87	171	63 (3´)	Likely neutral	-	-	0	0
p.N3188I	27	1	0,87	171	6 (3´)	Likely Pathogenic	-	-	1	0
p.P3193A	28	0,98	0,56	144	9 (5´)	Indeterminate	-	-	1	0
p.P3193S	28	0,98	0,56	144	9 (5´)	Likely Pathogenic	-	-	1	0
p.K3232E	28	0,98	0,56	144	19 (3´)	Indeterminate	-	-	0	1
p.E3233V	28	0,98	0,56	144	15 (3´)	Likely pathogenic	-	-	0	1
p.A3240T	29	0,95	0,92	211	6 (5´)	Likely neutral	-	-	1	0
p.R3244C	29	0,95	0,92	211	18 (5´)	Indeterminate	-	-	0	0
p.R3244H	29	0,95	0,92	211	19 (5´)	Likely neutral	-	-	1	0
p.T3309M	30	0,9	0,63	127	3 (5´)	Likely Pathogenic	A (0,82)	-	1	0
p.D3469N	33	0,87	0,99	185	1 (3´)	Likely Pathogenic	D (0,68)	-	0	1
p.D3469Y	33	0,87	0,99	185	1 (3´)	Highly Likely Pathogenic	D (0,60)	-	0	1
p.G3540R	35	0,75	0,68	119	1 (3´)	Likely Pathogenic	D (0,07)	-	0	0
p.G3540A	36	0,95	0,98	119	1 (5´)	Likely neutral	A (0,84)	-	1	0
p.L3610P	37	0,91	0,67	195	8 (5´)	Indeterminate	-	-	1	1
p.L3654V	37	0,91	0,67	195	57 (3´)	Likely Pathogenic	-	-	0	0
p.R3672P	37	0,91	0,67	195	2 (3´)	Likely Pathogenic	-	-	0	0
p.R3672Q	37	0,91	0,67	195	2 (3´)	Likely neutral	-	-	0	0
p.L3682Q	38	0,34	0,97	140	29 (5´)	Highly likely pathogenic	-	-	0	0
p.W3726R	39	0,29	0,88	113	20 (5´)	Highly likely pathogenic	-	-	0	1
p.W3726S	39	0,29	0,88	113	21 (5´)	Highly likely pathogenic	-	-	0	1
p.R3750Q	39	0,29	0,88	113	21-20 (3´)	Highly likely pathogenic	-	(+) D (0,76)	1	0
p.R3753L	39	0,29	0,88	113	12 (3´)	Highly likely pathogenic	-	-	1	0
p.P3762L	40	0,34	0,82	142	16 (5´)	Indeterminate	A (0,23)	-	2	0
p.E3853K	42	0,51	0,99	175	20 (5´)	Likely Pathogenic	A (0,43)	-	1	0
p.S3904L	42	0,51	0,99	175	2 (3´)	Indeterminate	-	-	0	0
p.S3904W	42	0,51	0,99	175	2 (3´)	Indeterminate	-	-	0	0
p.C3906F	43	0,66	0,99	175	5 (5´)	Likely neutral	A (0,59)	-	0	0
p.S3976I	43	0,66	0,99	291	77 (3´)	Likely Pathogenic	-	(+) A (0,63)	0	0
p.A3987G	43	0,66	0,99	291	44 (3´)	Likely neutral	-	-	0	0
p.R4007C	44	0,85	0,82	135	16 (5´)	Highly likely pathogenic	-	-	0	0
p.I4045V	44	0,85	0,82	135	6 (3´)	Likely neutral	D (0,75)	(+) A (0,81)	0	0
p.L4137P	45	0,95	0,91	306	35 (3´)	Highly Likely Pathogenic	-	-	2	0
p.L4139P	45	0,95	0,91	306	29 (3´)	Highly likely pathogenic	-	-	1	0
p.S4144T	45	0,95	0,91	306	14 (3´)	Indeterminate	-	-	1	0
p.F4149F	46	0,56		1485	3 (5´)	Likely neutral	A (0,44)	-	0	0
p.R4150C	46	0,56		1485	4 (5´)	Highly Likely Pathogenic	-	-	0	0
p.R4150H	46	0,56		1485	5 (5´)	Indeterminate	A (0,5)	-	0	0
p.K4152T	46	0,56		1485	11 (5´)	Indeterminate	A (0,52)	-	1	1
p.V4153V	46	0,56		1485	15 (5´)	Likely neutral	-	-	1	0
p.R4154C	46	0,56		1485	16 (5´)	Likely pathogenic	A (0,4)	-	0	0
p.S4190F	46	0,56		1486	125 (5´)	Likely neutral	-	(+) A (0,72)	0	0

[(1)] NNSplice scores of functional splice sites.

[(2)] According to ADPKD Mutation Database classification

[(3)] Splice sites scores obtained from NNSplice are indicated (in brackets)

(+): Activation of new splice site

(c): Creation of new splice site

- : No changes /no significant changes in functional splice site scores (based on NNSplice analysis)

A: Acceptor (3´ss)

D: Donor (5´ss)

Table S2. Results of *PKD1* synonymous mutations analysis using NNSplice, ESEfinder and Rescue-ESE web sources.

		NNSplice[(1)]					*Mutation effects on splice sites*[(3)]		*Number of disrupted ESE*	
Mutation	Exon	Acceptor (3´ss)	Donor (5´ss)	Exon length (bp)	Position from exon ending (5´/3´)	Clinical Significance[(2)]	Functional splice sites	Activation / Creation of new splice sites	ESEfinder	Rescue-ESE
c.214C>T	1		0,86	423	2 (3´)	Likely neutral	D (0,76)	-	0	0
c.288G>A	3	0,88	0,97	72	1 (5´)	Likely neutral	A (0,82)	-	0	0
c.423G>A	4	0,84	0,95	170	63 (5´)	Likely neutral	-	-	1	0
c.570C>T	5	0,94	1	672	41 (5´)	Likely neutral	-	(+) D (0,85)	0	0
c.588C>T	5	0,94	1	672	51 (5´)	Likely neutral	-	-	0	0
c.759A>G	5	0,94	1	672	230 (5´)	Likely neutral	-	-	0	0
c.789C>T	5	0,94	1	672	260 (5´)	Likely neutral	-	-	0	0
c.837G>A	5	0,94	1	672	365 (3´)	Likely neutral	-	-	0	0
c.1185C>T	5	0,94	1	672	17 (3´)	Likely neutral	-	(c) D (0,77)	0	0
c.1209C>T	6	0,43	0,37	187	8 (5´)	Likely neutral	A (0,29)	-	1	0
c.1248C>T	6	0,43	0,37	187	3 (3´)	Likely neutral	-	-	1	0
c.1602C>T	7	0,65	0,56	218	5 (3´)	Likely neutral	D (0,55)	-	0	0
c.1710C>T	8	0,77	0,56	116	13 (3´)	Likely neutral	-	-	1	0
c.1737G>A	9	0,44	0,62	127	15 (5´)	Likely neutral	A (0,4)	-	0	0
c.2082C>T	10	0,98	0,72	248	16 (3´)	Likely neutral	-	-	1	0
c.2439C>T	11	1	0,99	756	342 (5´)	Likely neutral	-	-	0	0
c.2109C>T	11	1	0,99	756	12 (5´)	Likely neutral	-	-	2	0
c.2829C>G	11	1	0,99	756	15 (3´)	Likely neutral	-	-	1	0
c.6927C>T	16	0,95	0,71	150	12 (5´)	Likely neutral	-	-	0	0
c.7077G>C	17	0,72	0,95	144	12 (5´)	Likely neutral	A (0,7)	-	0	0
c.7485C>T	18	0,83	0,99	280	5 (3´)	Likely neutral	-	-	1	0
c.7491C>T	19	0,51	1	214	2 (5´)	Likely neutral	-	-	0	0
c.7500C>T	19	0,51	1	214	11 (5´)	Likely neutral	A (0,48)	-	0	0
c.7503G>A	19	0,51	1	214	14 (5´)	Likely neutral	A (0,49)	-	0	0
c.7623G>A	19	0,51	1	214	81 (3´)	Likely neutral	-	(+) A (0,65)	0	0
c.7866C>T	21	0,67	0,31	153	3 (5´)	Likely neutral	A (0,52)	-	0	0
c.8334C>T	23	0,57	0,95	630	173 (5´)	Likely neutral	-	(c) D (0,81)	0	0
c-8559C>T	23	0,57	0,95	630	233 (3´)	Likely neutral	-	(+) A (0,46)	0	0
c.8949G>A	25	0,97	0,82	253	1 (5´)	Likely neutral	A (0,93)	-	0	0
c.8964G>A	25	0,97	0,82	253	16 (5´)	Likely neutral	-	-	1	0
c.9186C>A	25	0,97	0,82	253	16 (3´)	Likely neutral	-	(+) D (0,66)	1	0
c.9213G>A	26	0,84	0,96	196	12 (5´)	Likely neutral	A (0,77)	-	1	0
c.9573C>G	28	0,98	0,56	144	5 (5´)	Likely neutral	-	-	1	0
c.9714C>T	29	0,95	0,92	211	2 (5´)	Likely neutral	-	-	0	0
c.9888C>T	29	0,95	0,92	211	36 (3´)	Likely neutral	-	-	0	0
c.10159C>G	31	0,97	0,99	117	9 (3´)	Likely neutral	-	-	1	0
c.10163C>T	31	0,97	0,99	117	5 (3´)	Likely neutral	-	(+) A (0,88)	0	0
c.10290G>A	33	0,87	0,99	185	70 (5´)	Likely Neutral	-	(c) A (0,79)	0	0

c.11007C>T	37	0,91	0,67	195	10 (3´)	Likely Neutral	-	(c) D (0,74)	0	0
c.11143C>T	38	0,34	0,97	140	14 (3´)	Likely Neutral	-	-	1	0
c.11313G>A	40	0,34	0,82	142	44 (5´)	Likely neutral	-	(+) A (0,41)	0	0
c.11523C>T	41	0,76	0,89	126	15 (3´)	Likely neutral	-	-	1	2
c.11700T>C	42	0,51	0,99	175	13 (3´)	Likely neutral	-	-	2	0
c.11733C>A	43	0,66	0,99	291	21 (5´)	Likely neutral	-	(c) A (0,67)	0	0
c.12153T>C	45	0,95	0,91	306	15 (5´)	Likely neutral	-	-	1	0
c.12264G>A	45	0,95	0,91	306	126 (5´)	Likely neutral	-	(c) A (0,85)	1	0
c.12402G>A	45	0,95	0,91	306	43 (3´)	Likely neutral	-	-	0	0
c.12409C>T	45	0,95	0,91	306	36 (3´)	Likely neutral	-	(+) A (0,81)	1	0
c.12570C>T	46	0,56		1485	125 (5´)	Likely neutral	-	(+) A (0,82)	0	0

[(1)] NNSplice scores of functional splice sites.

[(2)] According to ADPKD Mutation Database classification

[(3)] Splice sites scores obtained from NNSplice are indicated (in brackets)

(+): Activation of new splice site

(c): Creation of new splice site

- : No changes /no significant changes in functional splice site scores (based on NNSplice analysis)

A: Acceptor (3´ss)

D: Donor (5´ss)

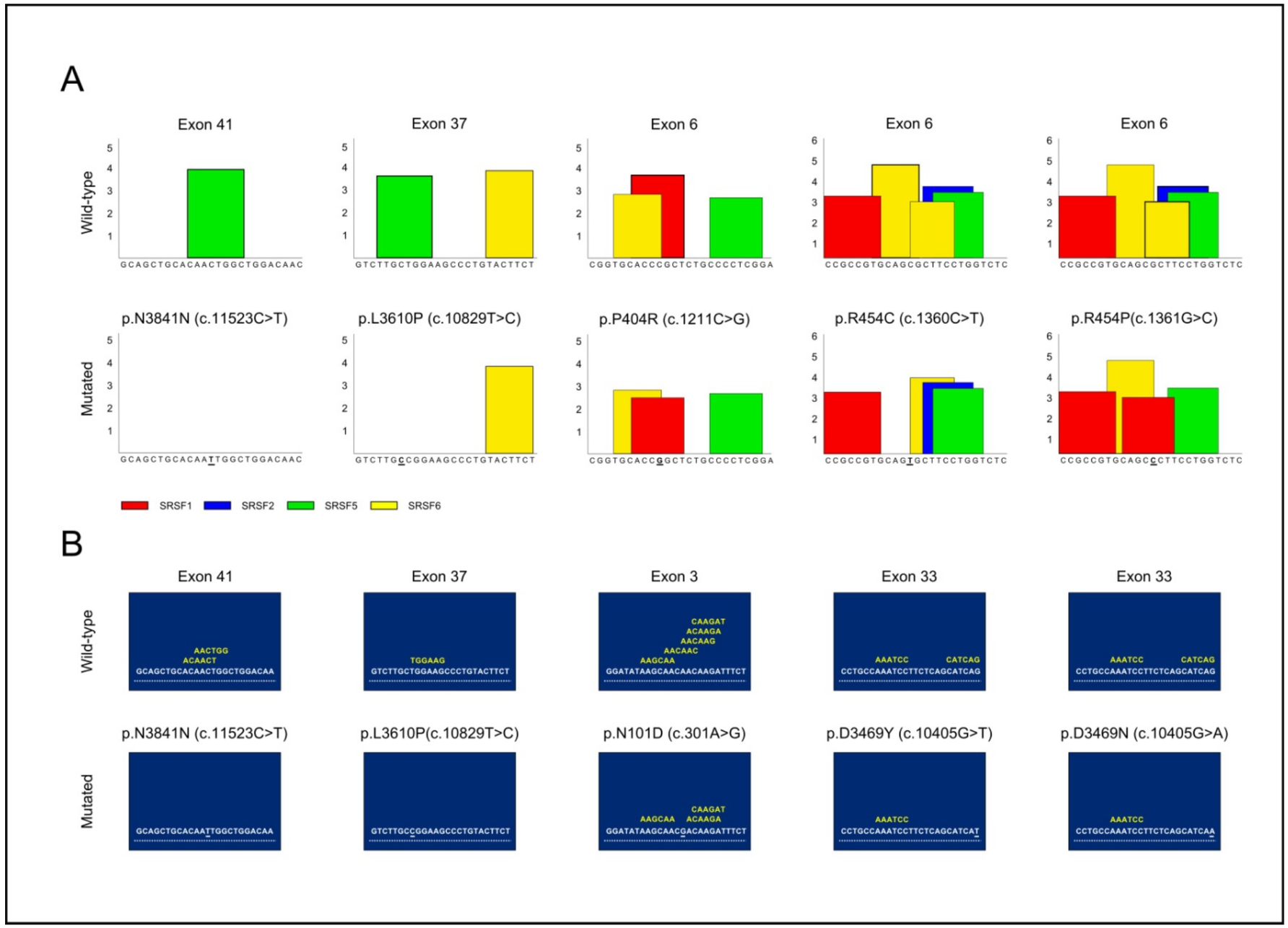

Figure S1. Effects of missense and synonymous *PKD1* mutations on ESEs according to prediction tools. The analysis of several previously reported mutations and their respective controls is shown. Potential ESE sequences were detected using ESEfinder (A) and Rescue-ESE (B) bioinformatics tools, respectively. The nucleotide changed by each mutation is underlined. In panel A, the high of the colored bars represents the motif score, and the width of the bars show the length of the motif (in nucleotides). Boxes in red, green, blue and yellow indicate potential binding sites for SR proteins SRSF1, SRSF5, SRSF2 and SRSF6, respectively.