Supplemental Table 1. Summary of measurements in *Pkd2*$^{-/WS25}$ mice by *Pde* genotype.

Pde genotype	Gender (n)	Body Weight (g)	Kidney Weight (% BWt)	Kidney Cyst Index (%BWt)	Kidney Fibrosis Index (%BWt)	Renal cAMP (pmol/mg protein)	Liver Weight (% BWt)	Liver Cyst Index (%BWt)	Liver Fibrosis Index (%BWt)	Serum Urea (mg/dl)
Pde$^{+/+}$	M (51)	27.1±2.5	1.68±0.31	0.36±0.33	0.04±0.05	7.29±4.51	4.99±0.46	0.26±0.18	0.05±0.06	53.6±16.3
	F (51)	20.9±1.7	1.68±0.54	0.39±0.39	0.06±0.07	8.69±6.10	4.91±0.65	0.23±0.19	0.04±0.04	52.2±18.6
	M&F (102)	24.0±3.8	1.68±0.44	0.37±0.36	0.05±0.06	7.92±5.22	4.95±0.56	0.24±0.18	0.04±0.05	52.9±17.4
Pde1a$^{-/-}$	M (13)	27.1±1.5	2.38±0.88	1.08±0.91	0.10±0.01	7.87±3.07	4.70±0.21	0.22±0.11	0.04±0.03	50.7±18.7
	F (10)	21.6±1.8	2.17±0.96	0.72±0.87	0.14±0.11	9.97±5.39	5.67±1.72	0.37±0.49	0.12±0.21	44.4±11.0
	M&F (23)	25.0±3.5	2.32±0.85	0.94±0.84	0.12±0.07	8.91±4.40	5.07±1.23	0.29±0.34	0.07±0.15	47.3±15.6
P value[1] vs +/+		0.44	<0.001	<0.001	<0.001	0.46	0.21	0.33	0.07	0.20
P value[2] vs +/+		0.19	<0.001	<0.001	<0.001	0.17	0.41	0.50	0.43	0.042
Pde1b$^{-/-}$	M (11)	27.1±2.5	1.52±0.17	0.33±0.22	0.03±0.02	8.98±0.52	5.17±0.55	0.28±0.21	0.03±0.02	52.6±17.7
	F (10)	20.4±1.3	1.48±0.14	0.28±0.18	0.03±0.01	8.42±0.78	4.88±0.46	0.25±0.11	0.04±0.02	47.1±16.0
	M&F (21)	23.9±4.0	1.50±0.16	0.30±0.20	0.03±0.01	8.71±0.70	5.03±0.52	0.26±0.17	0.03±0.02	50.0±13.4
P value[1] vs +/+		0.65	0.068	0.39	0.056	0.55	0.66	0.65	0.23	0.45
P value[2] vs +/+		0.87	0.09	0.85	0.11	0.001	0.43	0.54	0.42	0.63
Pde1c$^{-/-}$	M (9)	27.7±2.9	2.34±0.64	0.95±0.70	0.05±0.05	8.44±3.44	5.58±0.97	0.37±0.47	0.05±0.10	64.2±13.1
	F (11)	24.4±3.7	2.27±1.90	1.07±1.65	0.05±0.06	8.11±1.74	6.48±3.41	0.41±0.41	0.16±0.26	64.1±16.2
	M&F (20)	25.9±3.7	2.30±1.41	1.01±1.26	0.05±0.05	8.26±2.61	6.05±2.54	0.39±0.40	0.11±0.20	64.1±14.4
P value[1] vs +/+		<0.001	<0.001	<0.001	0.97	0.82	<0.001	0.016	0.009	0.009
P value[2] vs +/+		0.053	0.003	0.001	0.79	0.10	0.033	0.10	0.40	0.003
Pde3a$^{-/-}$	M (11)	30.3±3.8	2.14±0.14	0.80±0.62	0.12±0.13	6.26±2.28	5.80±0.52‡	0.25±0.20	0.04±0.06	48.1±15.1
	F (9)	23.5±2.4	2.31±0.78	0.83±0.74	0.13±0.08	6.45±1.94	5.31±0.40	0.28±0.34	0.03±0.03	51.3±15.3
	M&F (20)	27.3±4.7	2.26±0.64	0.85±0.64	0.12±0.06	6.62±2.08	5.65±0.55	0.26±0.26	0.03±0.05	49.5±14.8
P value[1] vs +/+		<0.001	<0.001	<0.001	<0.001	0.19	<0.001	0.69	0.39	0.45
P value[2] vs +/+		0.003	<0.001	<0.001	<0.001	0.57	<0.001	0.22	0.024	0.42
Pde3b$^{-/-}$	M (10)	28.5±5.9	1.70±0.28	0.42±0.39	0.03±0.03	5.05±2.81	5.33±0.62	0.43±0.35	0.06±0.03	56.6±12.1
	F (9)	20.1±2.5	2.04±0.55	0.56±0.31	0.05±0.04	6.13±2.70	5.01±0.38	0.40±0.35	0.04±0.03	59.5±12.8
	M&F (19)	24.5±6.2	1.86±0.45	0.48±0.34	0.04±0.03	5.56±2.74	5.18±0.53	0.42±0.34	0.05±0.03	57.7±10.3
P value[1] vs +/+		0.62	0.086	0.21	0.50	0.061	0.15	0.002	0.86	0.22
P value[2] vs +/+		0.93	0.025	0.09	0.72	0.006	0.08	0.001	0.23	0.08

[1] P values for *Pde* genotype effects from two-way ANOVA. Gender effects were statistically significant for body weight.
[2] P values for comparisons using a nonparametric t-test between groups combining male and female mice.

Supplemental Table 2. Effect of DDAVP administration on disease development in *Pkd2*$^{-/WS25}$ mice depending on *Pde* genotype.

	Gender (n)	Treatment	Body Weight (g)	Kidney Weight (% BWt)	Kidney Cyst Index (%BWt)	Kidney Fibrosis Index (%BWt)	Renal cAMP (pmol/mg protein)	Liver Weight (% BWt)	Liver Cyst Index (%BWt)	Liver Fibrosis Index (%BWt)	Serum Urea (mg/dl)
Pde+/+	M (20)	Saline	27.5±3.1	1.74±0.37	0.46±0.41	0.05±0.04	4.66±1.32	4.94±0.52	0.25±0.13	0.05±0.04	62.1±18.3
	F (20)	Saline	20.8±2.1	1.77±0.56	0.41±0.31	0.05±0.03	6.27±1.37	4.92±0.61	0.20±0.09	0.04±0.04	55.3±19.7
	M&F (40)		24.2±4.3	1.76±0.47	0.44±0.36	0.05±0.04	5.46±1.52	4.93±0.56	0.23±0.11	0.04±0.04	58.7±19.0
Pde+/+	M (20)	DDAVP	26.6±2.2	2.59±1.66	1.07±1.60	0.12±0.17	15.4±11.5	4.84±0.94	0.27±0.20	0.03±0.04	92.3±40.6
	F (23)	DDAVP	21.5±1.4	2.03±0.70	0.49±0.32	0.07±0.05	12.4±8.4	4.62±0.55	0.24±0.17	0.030±0.032	78.34±19.2
	M&F (43)		23.9±3.1	2.29±1.26	0.75±1.01	0.09±0.12	13.7±9.7	4.72±0.76	0.25±0.18	0.03±0.03	84.8±31.4
p value[1] vs +/+ saline			0.77	0.010	0.075	0.039	<0.001	0.18	0.40	0.17	<0.001
p value[2] vs +/+ saline			0.84	0.005	0.12	0.11	<0.001	0.024	0.77	0.12	<0.001
Pde3a-/-	M (10)	DDAVP	27.5±1.6	3.27±1.11	1.14±0.88	0.20±0.09	14.6±11.5	5.90±1.85	0.32±0.29	0.05±0.06	93.0±48.0
	F (9)	DDAVP	23.8±2.4	3.51±2.72	2.08±2.81	0.33±0.47	18.5±23.6	5.37±0.57	0.26±0.15	0.05±0.03	77.8±17.6
	M&F (19)		25.7±2.7	3.38±1.98	1.58±1.82	0.26±0.29	16.4±17.8	5.65±1.39	0.29±0.23	0.05±0.04	85.8±36.7
p value[1] vs +/+ saline			0.039	<0.001	<0.001	<0.001	<0.001	0.007	0.13	0.66	<0.001
p value[2] vs +/+ saline			0.08	<0.001	<0.001	<0.001	<0.001	0.025	0.29	0.54	<0.001
p value[1] vs +/+ DDAVP			0.003	0.012	0.049	0.004	0.46	0.016	0.48	0.13	0.99
p value[2] vs +/+ DDAVP			0.036	<0.001	0.004	<0.001	0.56	<0.001	0.33	0.044	0.67
Pde3b-/-	M (10)	DDAVP	31.0±2.0	2.34±0.96	0.85±0.93	0.15±0.15	15.0±33.2	5.48±0.48	0.21±0.12	0.02±0.01	82.7±28.2
	F (10)	DDAVP	23.8±1.8	2.04±0.55	0.60±0.45	0.17±0.10	10.7±9.6	4.94±0.52	0.14±0.05	0.02±0.02	91.0±7.3
	M&F (20)		27.4±4.1	2.19±0.78	0.72±0.67	0.14±0.11	12.9±23.9	5.21±0.56	0.18±0.10	0.02±0.01	86.8±20.5
p value[1] vs +/+ saline			<0.001	0.009	0.043	<0.001	0.057	0.067	0.10	0.013	<0.001
p value[2] vs +/+ saline			0.009	0.006	0.09	<0.001	0.83	0.06	0.09	0.011	<0.001
p value[1] vs +/+ DDAVP			0.001	0.69	0.85	0.06	0.81	0.013	0.09	0.14	0.84
p value[2] vs +/+ DDAVP			0.002	0.68	0.58	0.001	0.002	<0.001	0.06	0.19	0.17

[1] P values for *Pde* genotype (or DDAVP treatment) effects from two-way ANOVA. Gender effects were statistically significant for body weight.
[2] P values for comparisons using a nonparametric t-test between groups combining male and female mice.

Supplemental Table 3. PCR primers used for genotyping.

		forward	reverse	product size (bp)
Pde1a	WT	5`-GAACACACTAACGATGTCCC-3`	5`-TGGTTTGAGTAACTGCCAC-3`	777
	mutant	(digest PCR product with PvuII-HF)		792
Pde1b	WT	5`-CACACAGGCACAACCAAC-3`	5`-TTGGGTGGCTGATGTCAGCA-3`	1420
	mutant	5`-CTGCTAAAGCGCATGCTCCAGACTGCCTTG-3`	5`-ACCTTCACCCAGCAGACCCGA-3`	1183
Pde1c	WT	5`-GGCAGTTTGTAAGATGGAG-3`	5`-GTCAAGATGGCCACCTCTAC-3`	630
	mutant	5`-GCCAAAGGAGACCCATCAGG-3`	5`-GTCAAGATGGCCACCTCTAC-3`	630
Pde3a	WT	5′-TCTCACAACACAGCCGATTC-3'	5′-AGGTCAGTAGCCAAAATCGC-3′	1500
	mutant	5′-GATGGCTGGCAACTAGAAGG-3′	5′-AAGCCGGTCTTGTCAATCAG-3′	450
Pde3b	WT	5′-ACACACCCCACAAAACACACCGTTGCACAGAACA-3'	5′-CACGTTGCAGAAGCGGCAGAGGTGGAAGAAG -3′	1500
	mutant	5′-ACACACCCCACAAAACACACCGTTGCACAGAACA-3′	5′-AAAGCGCCTCCCCTACCCGGTAGAATTGACCTGCA-3′	750