

**Supplemental Figure 1:** Conditional inactivation of *Pkd1*. **A**, The wild type genomic locus. **B**, After homologous recombination to form *Pkd1<sup>fllox(neo)</sup>* (targeting construct in red). **C**, Removal of the intronic *neo* cassette by FLP recombinase to form the *Pkd1<sup>fllox</sup>* allele. **D**, Deletion of exons 2-4 by Cre. H, *HindIII*; N, *NsiI*; Nh, *NheI*; blue arrowhead, *loxP*; yellow arrowhead, FRT; black boxes, numbered exons. **E**, Extensive cystic changes are revealed on the cut surface of a P14 *Pkd1<sup>fllox/-</sup>:Ksp-Cre* kidney. Scale bar, 2 mm.

**Supplemental Figure 2:** Ksp-Cre is active in type A, but not type B, intercalated cells. RA/EGFP Cre reporter mice were crossed with Ksp-Cre and kidney sections labeled with AE1 (red) to mark type A intercalated cells (top) and pendrin (red) to mark type B intercalated cells (bottom). EGFP activity co-localized with AE1, but not pendrin, indicating Ksp-Cre activity in type A, but not type B, intercalated cells.

**Supplemental Figure 3:** Phospho-ERK1/2 (pERK) expression in the kidneys of 3 month old wild type mice. Size bar, 50  $\mu$ m.

**Supplemental Figure 4:** Phospho-ERK1/2 expression in the kidneys of P14 *Pkd1<sup>fllox/-</sup>:Ksp-Cre* mice treated with vehicle only (**A**) or 32 mg/kg U0126 (**B**) on P4, P7, P10 and P13. Treatment with U0126 inhibited increased ERK1/2 activation cyst lining cells. Size bar, 50  $\mu$ m.

**Supplemental Table 1: Serum studies in mice with kidney selective inactivation of *Pkd1***

		<b>P7</b> [n=10 (±SD)]	<b>P value</b>	<b>P14</b> [n=10 (±SD)]	<b>P value</b>
<b>Glucose (mg/dL)</b>	cy	131 (±78)	0.16	<b>137 (±44)</b>	<b>3.1x10<sup>-5</sup></b>
	nc	173 (±45)		<b>262 (±53)</b>	
<b>Cholesterol (mg/dL)</b>	cy	124 (±27)	0.61	<b>285 (±50)</b>	<b>1.9x10<sup>-5</sup></b>
	nc	119 (±9.5)		<b>166 (±38)</b>	
<b>Triglycerides (mg/dL)</b>	cy	125 (±46.5)	0.72	126 (±99)	0.081
	nc	116 (±53)		64 (±37)	
<b>Total protein (g/dL)</b>	cy	3.65 (±0.68)	0.47	4.8 (±0.7)	0.77
	nc	3.82 (±0.26)		4.9 (±0.9)	
<b>Albumin (g/dL)</b>	cy	1.76 (±0.36)	1.0	2.37 (±0.4)	0.14
	nc	1.76 (±0.18)		2.68 (±0.48)	
<b>Globulin (g/dL)</b>	cy	1.89 (±0.33)	0.15	2.46 (±0.35)	0.27
	nc	2.06 (±0.14)		2.25 (±0.42)	
<b>BUN (mg/dL)</b>	cy	<b>65.9 (±21.2)</b>	<b>7.5x10<sup>-6</sup></b>	<b>168 (±90)</b>	<b>5.6x10<sup>-5</sup></b>
	nc	<b>21.8 (±3.8)</b>		<b>17 (±6.4)</b>	
<b>Calcium (mg/dL)</b>	cy	8.7 (±1.3)	0.13	9.8 (±2.0)	0.21
	nc	9.6 (±1.2)		10.8(±1.2)	
<b>Phosphorus (mg/dL)</b>	cy	11.5 (±1.1)	0.08	<b>15.5 (±2.9)</b>	<b>4.6x10<sup>-4</sup></b>
	nc	10.5 (±1.2)		<b>11.1 (±1.3)</b>	
<b>AST (U/L)</b>	cy	129.5 (±51.4)	0.06	101.8 (±40.1)	0.54

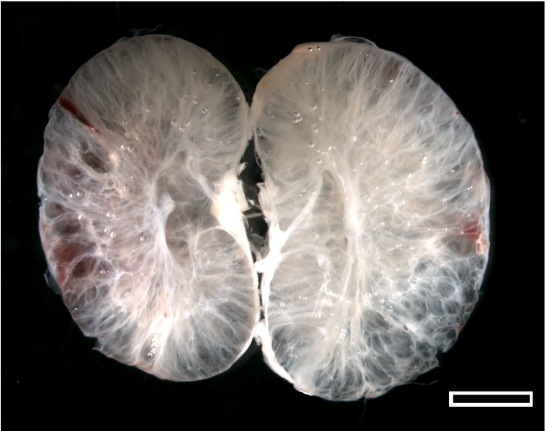
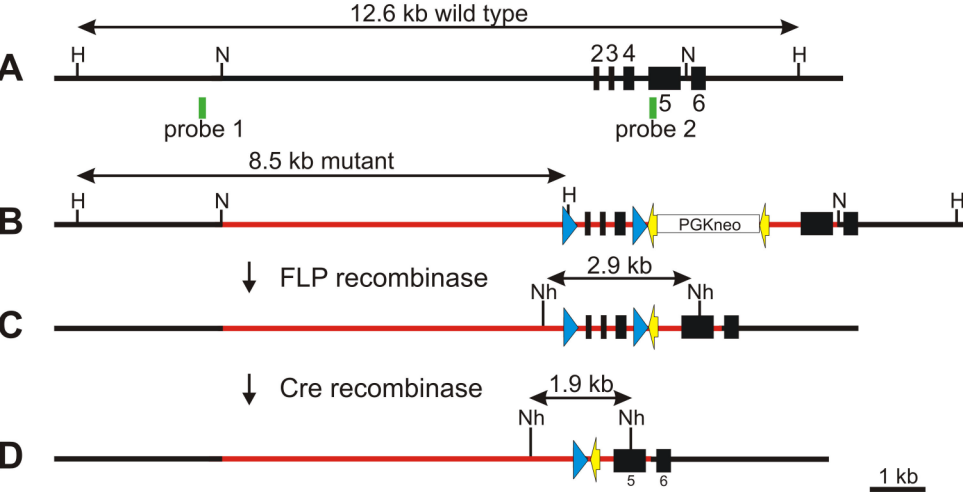
	nc	92.4 ( $\pm$ 28.2)		92.6 ( $\pm$ 21.6)	
<b>ALT (U/L)</b>	cy	18.5 ( $\pm$ 4.8)	0.79	25.0 ( $\pm$ 5.0)	0.97
	nc	19.1 ( $\pm$ 5.3)		24.9 ( $\pm$ 4.9)	
<b>Total bilirubin (mg/dL)</b>	cy	0.45 ( $\pm$ 0.25)	0.09	0.26 ( $\pm$ 0.09)	0.49
	nc	0.3 ( $\pm$ 0.07)		0.23 ( $\pm$ 0.07)	
<b>Alkaline phosphatase (U/L)</b>	cy	529 ( $\pm$ 113)	0.09	772 ( $\pm$ 288)	0.086
	nc	457 ( $\pm$ 57)		595 ( $\pm$ 108)	
<b>Amylase (U/L)</b>	cy	246 ( $\pm$ 54)	0.08	666 ( $\pm$ 232)	0.18
	nc	282 ( $\pm$ 29)		822 ( $\pm$ 278)	

cy: polycystic mice with *Pkd1*<sup>fllox/-</sup>:*Ksp-Cre*

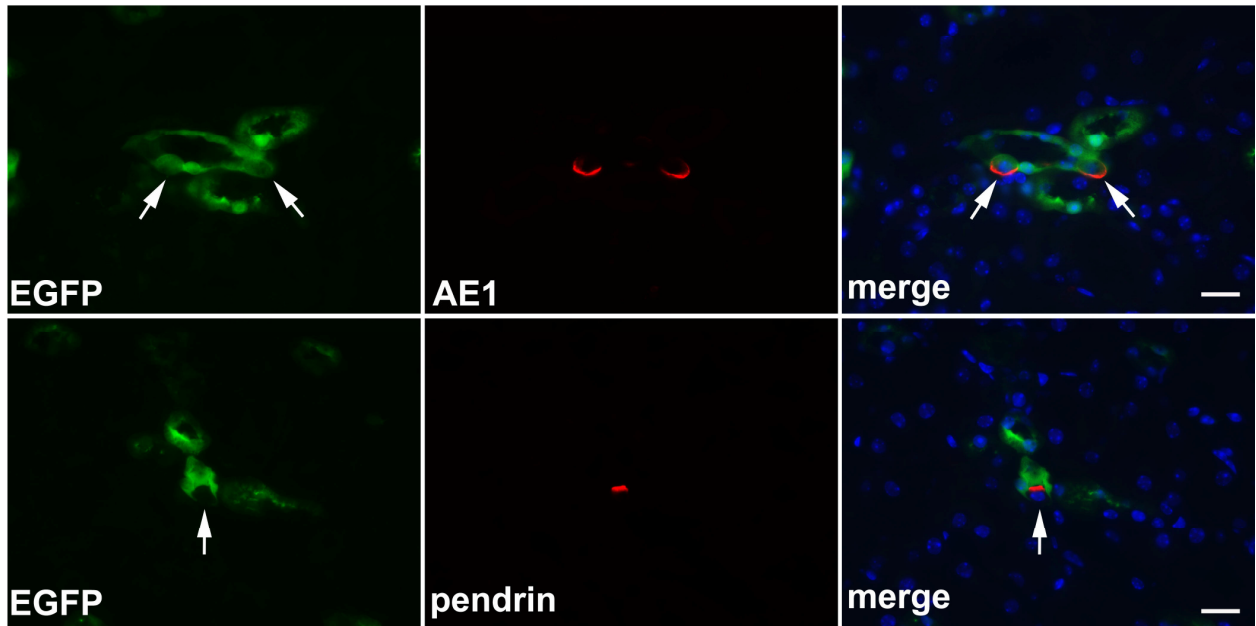
nc: non-cystic controls

**bold** indicates statistically significant differences between cystic and control mice

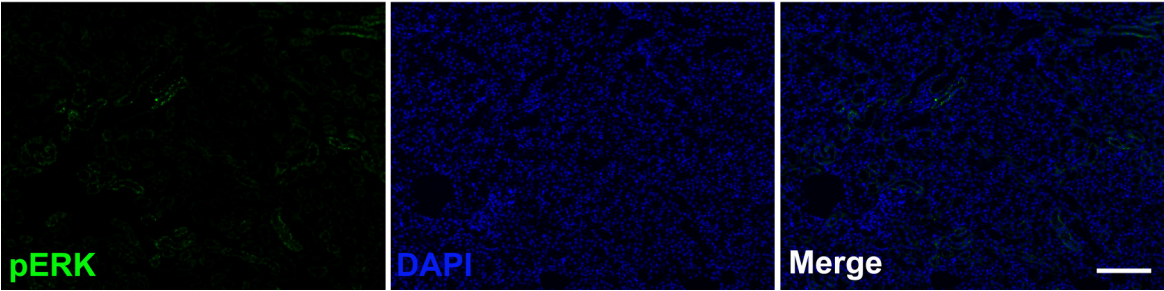
# Supplementary Fig. 1



Supplementary Fig. 2



Supplementary Fig. 3



Supplementary Fig. 4

