Expanded View Figures

Figure EV1. Characterization of kidneys from *Lkb1*$^{\Delta Tub}$ mice.

A, B   Western blot (A) and quantification (B) of LKB1 expression in kidney medulla lysates from control and *Lkb1*$^{\Delta Tub}$ mice at 5 weeks. The remaining LKB1 protein derives from proximal tubule segments and glomeruli that are not targeted by *Ksp-Cre*.

C   Representative confocal microscopy images of descending thin limb of Henle (AQP1 expressing) and thick ascending limb of Henle (Tamm-Horsfall expressing, THP) from 5-week-old control ($n = 4$) and *Lkb1*$^{\Delta Tub}$ ($n = 5$) animals. LKB1 is present in cilia (Ac-Tub) from AQP1-expressing tubules (upper panel: control mice; lower panel *Lkb1*$^{\Delta Tub}$ mice) and THP-positive tubules of control animals, but not in cilia from THP-positive tubules of *Lkb1*$^{\Delta Tub}$ mice, where *Ksp-Cre* is active. Scale bars: 2 μm.

D, E   Staining (D) and quantification (E) of primary cilia (Ac-Tub) in collecting duct (CD) (Dolichos Biflorus Agglutinin expressing, DBA) at 5 weeks. Representative images of 5 mice/group. Blinded quantification of ten fields of view per biological sample. Scale bar: 50 μm.

F   Scanning electron micrographs of CD at 5 weeks. Representative images of 5 mice/group. Scale bar: 20 μm, high magnification (right): 1 μm.

G   Spot urine from 5-week-old animals.

H, I   Urinary flow rate (H) and urine osmolality (I) at 5, 14, and 23 weeks.

J   Representative kidneys from control and *Lkb1*$^{\Delta Tub}$ mice at 23 weeks. Scales in cm.

K   Kidney weight (KW)-to-body weight (BW) ratio at 5, 14, and 23 weeks.

L   Renal collagen mRNA content evaluated by qRT–PCR at 5 and 23 weeks.

Data information: In (B, E, H, I, K, L), filled circles: control mice; and open circles: *Lkb1*$^{\Delta Tub}$ mice. Each circle represents one individual mouse. Bars indicate mean. Mann–Whitney, *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$, *ns*: not statistically different. w: weeks.

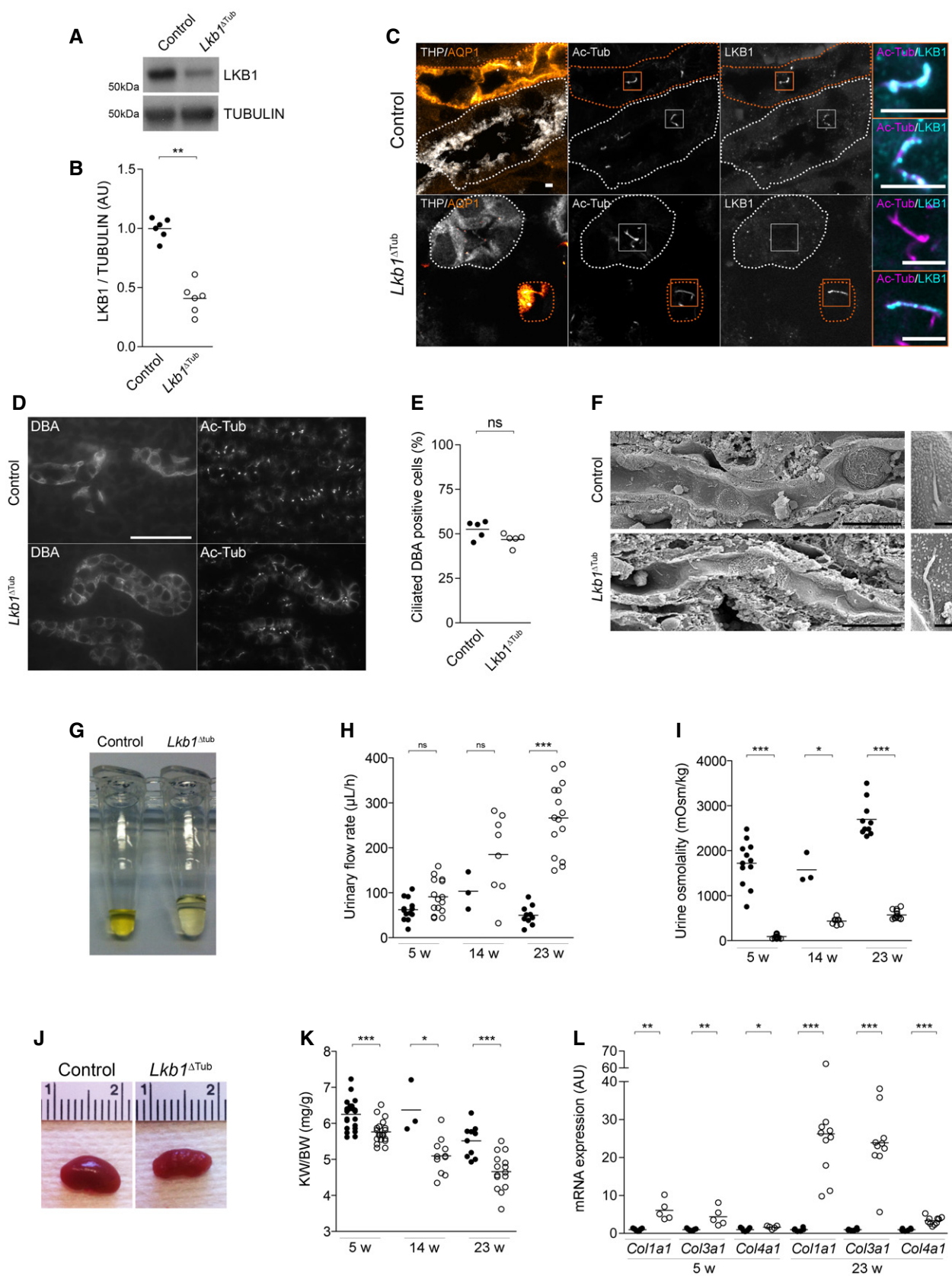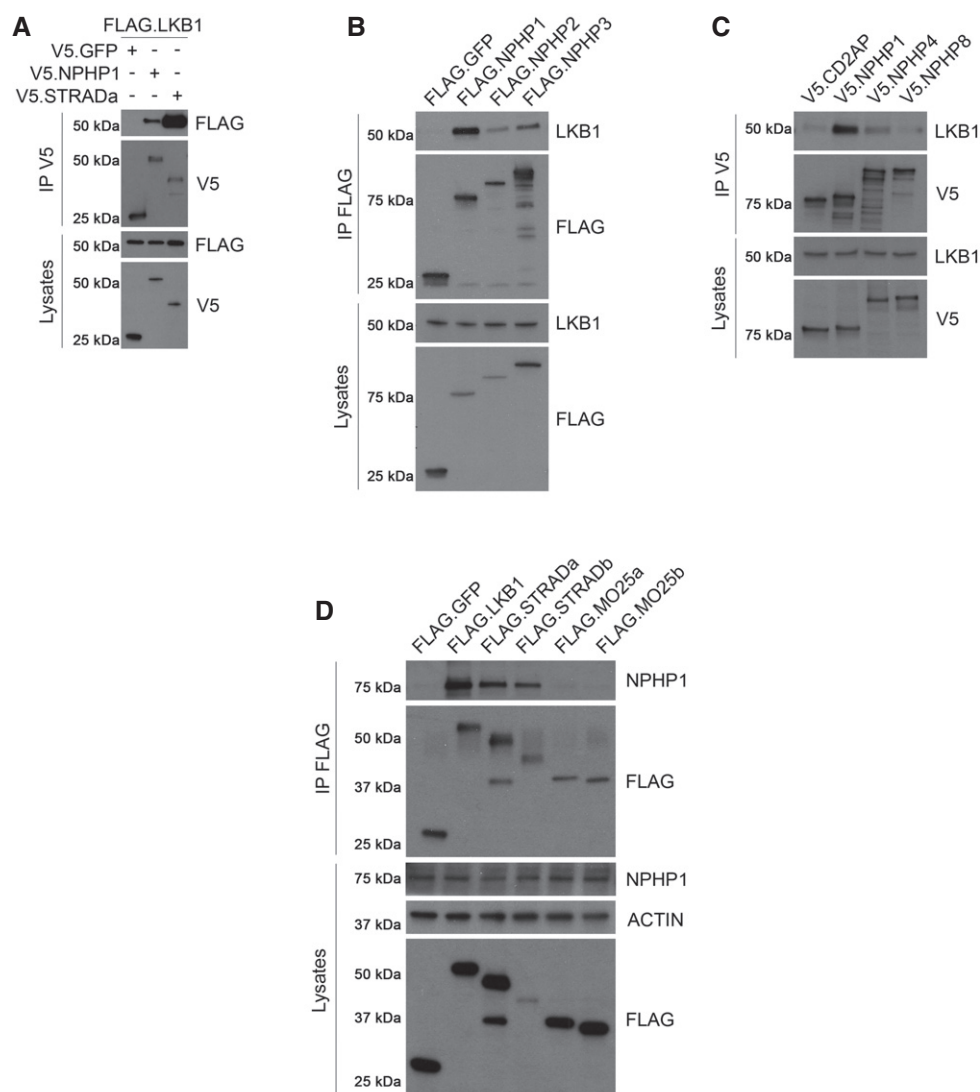Source data are available online for this figure.

Figure EV1.

Figure EV2.   Immunoprecipitation experiments (IP) from HEK 293T cells.

A   FLAG.LKB1 is enriched in the precipitates of V5.NPHP1 and V5.STRADa, but not V5.GFP.

B, C   Endogenous LKB1 is enriched in the precipitates of FLAG (B)- or V5-tagged (C) NPHP1 but interacts weakly with NPHP2, NPHP3, NPHP4, and NPHP8.

D   Endogenous NPHP1 is enriched in the precipitates of FLAG.LKB1 and FLAG.STRADs but not FLAG.MO25s or FLAG.GFP.

Data information: Representative Western blot of at least three independent experiments.
Source data are available online for this figure.

Figure EV3. Transcriptional screens identify LKB1 as a regulator of CCL2.

A   Principal component analysis (PCA) of RNAseq expression levels from MDCK cells with inducible knockdown of Lkb1 (Lkb1-i) after tetracycline incubation (PC1: −Tet vs. +Tet). *n* = 2 biological replicates (PC2).

B   PCA of microarray expression data from littermate control and *Lkb1*$^{\Delta Tub}$ kidneys at 5 weeks (PC1). *n* = 5 mice each (PC2). Replicates are enclosed in convex hulls to guide the eye.

C   Network representation of significantly enriched Biological Processes GO terms (commonly upregulated genes) derived from a hypergeometric test (*P* < 0.05). Nodes are connected if they have a semantic similarity > 0.6, and clusters are named according to the most representative GO terms. See also Dataset EV4.

D–H   *Ccl2* mRNA expression evaluated by qRT−PCR in MDCK cells expressing inducible shRNA after tetracycline induction (Tet) against Lkb1-i2 (D, *n* = 4), Lkb1-i1 (E, *n* = 3) after 5 h of 1 mM AICAR treatment, Anks3-i2 (F, *n* = 5), Nek7-i2 (G, *n* = 5), PKD1 KO1 Lkb1-i1, and PKD1 KO2 Lkb1-i1 (H, *n* = 3). See also Appendix Fig S3B, F, G and S.

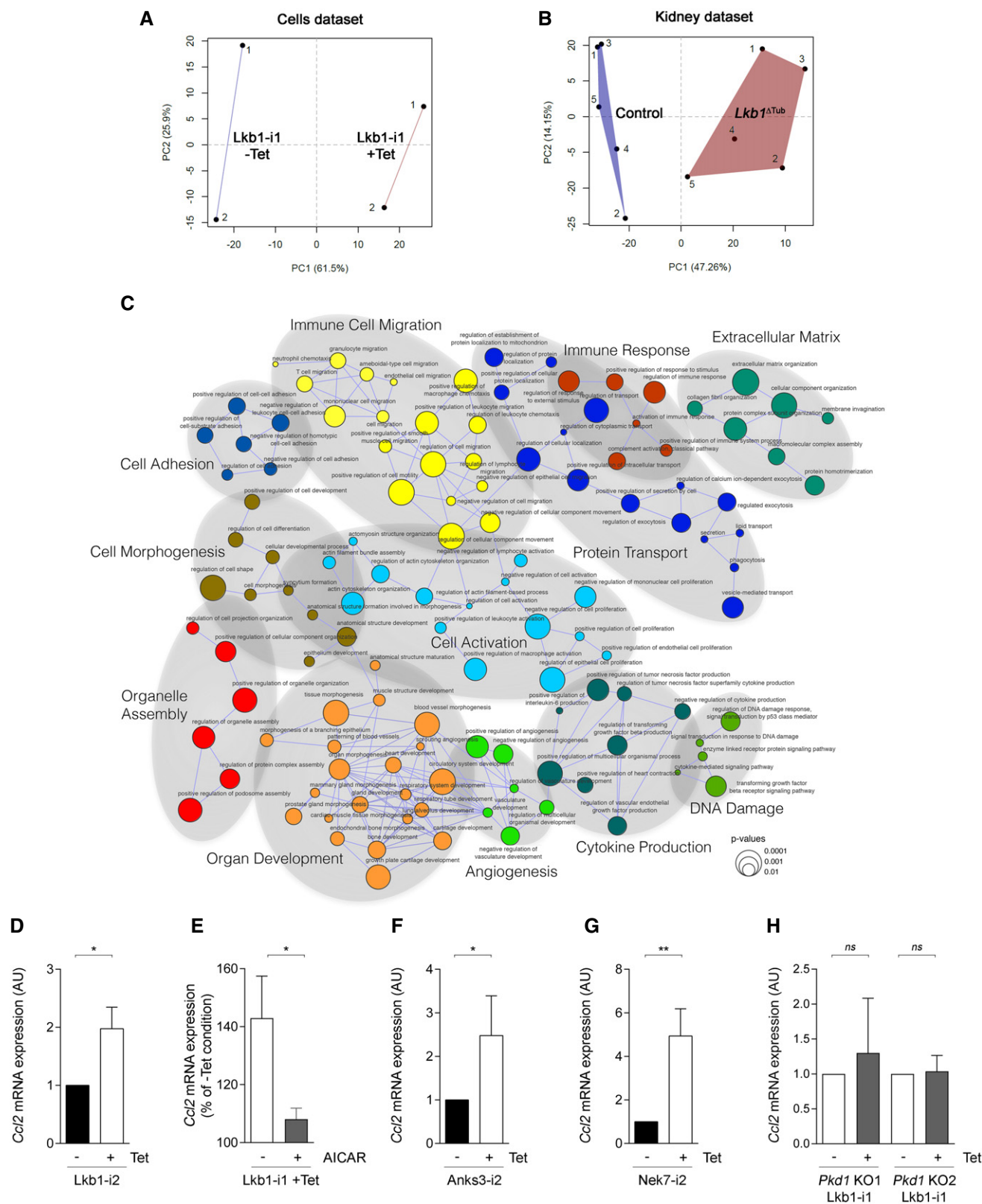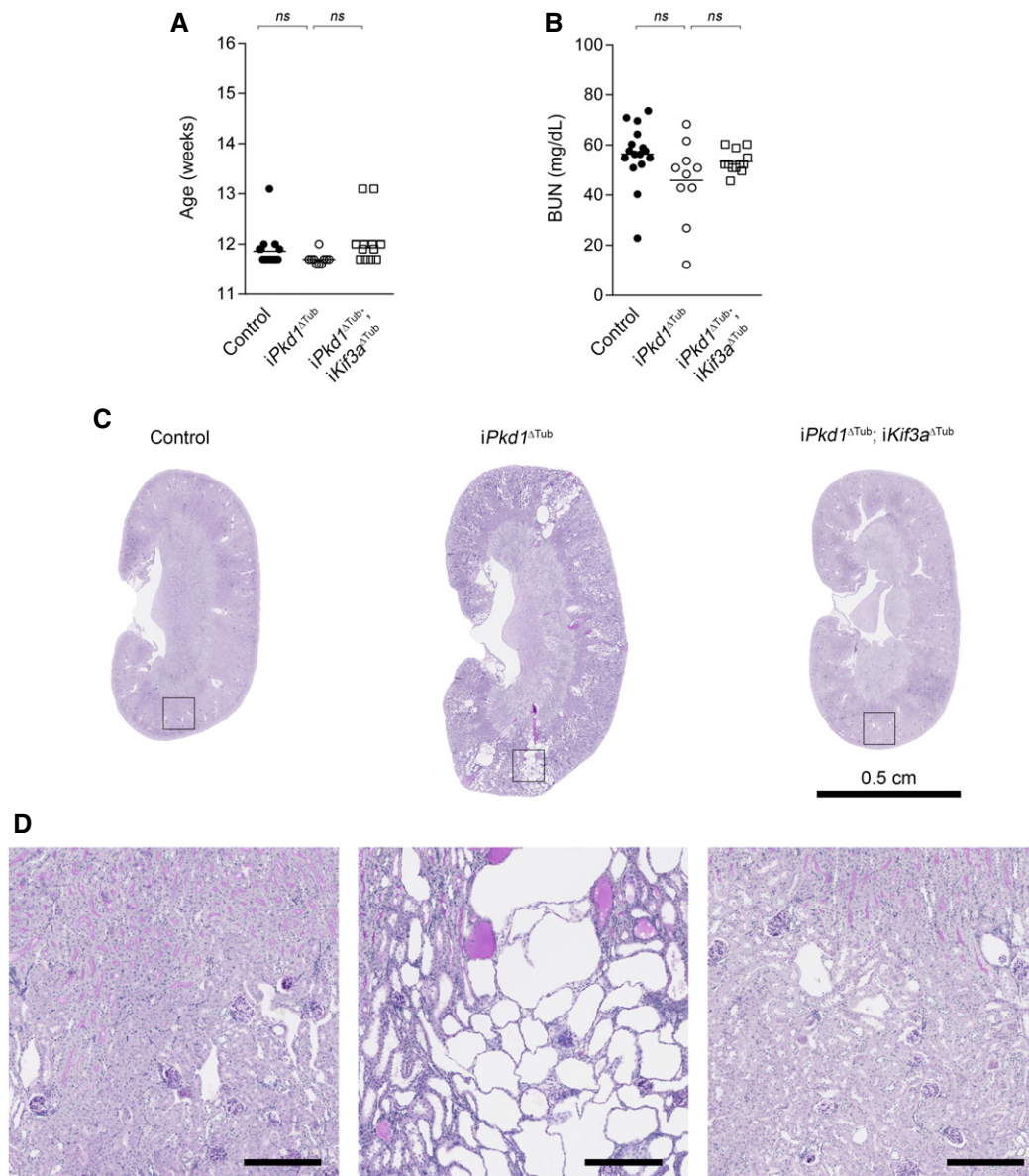Data information: In (D−H), mean ± SD. Paired *t*-test, **P* < 0.05, ***P* < 0.01, *ns*: not statistically different.

Figure EV3.

Figure EV4. *Kif3a* ablation ameliorates cyst formation in *Pkd1* mutant mice.

A   Age from control, iPkd1$^{\Delta Tub}$, and iPkd1$^{\Delta Tub}$;iKif3a$^{\Delta Tub}$ mice.

B   Plasma blood urea nitrogen (BUN) from control (n = 16), iPkd1$^{\Delta Tub}$ (n = 10), and iPkd1$^{\Delta Tub}$;iKif3a$^{\Delta Tub}$ (n = 12) mice at 12 weeks.

C   Representative periodic acid–Schiff (PAS)-stained kidney sections from control, iPkd1$^{\Delta Tub}$, and iPkd1$^{\Delta Tub}$;iKif3a$^{\Delta Tub}$ mice at 12 weeks.

D   Higher magnification of PAS-stained sections. Scale bar: 250 μm.

Data information: In (A, B), each dot represents one individual mouse. Bars indicate mean. ANOVA followed by the Tukey–Kramer test, *ns*: not statistically different.
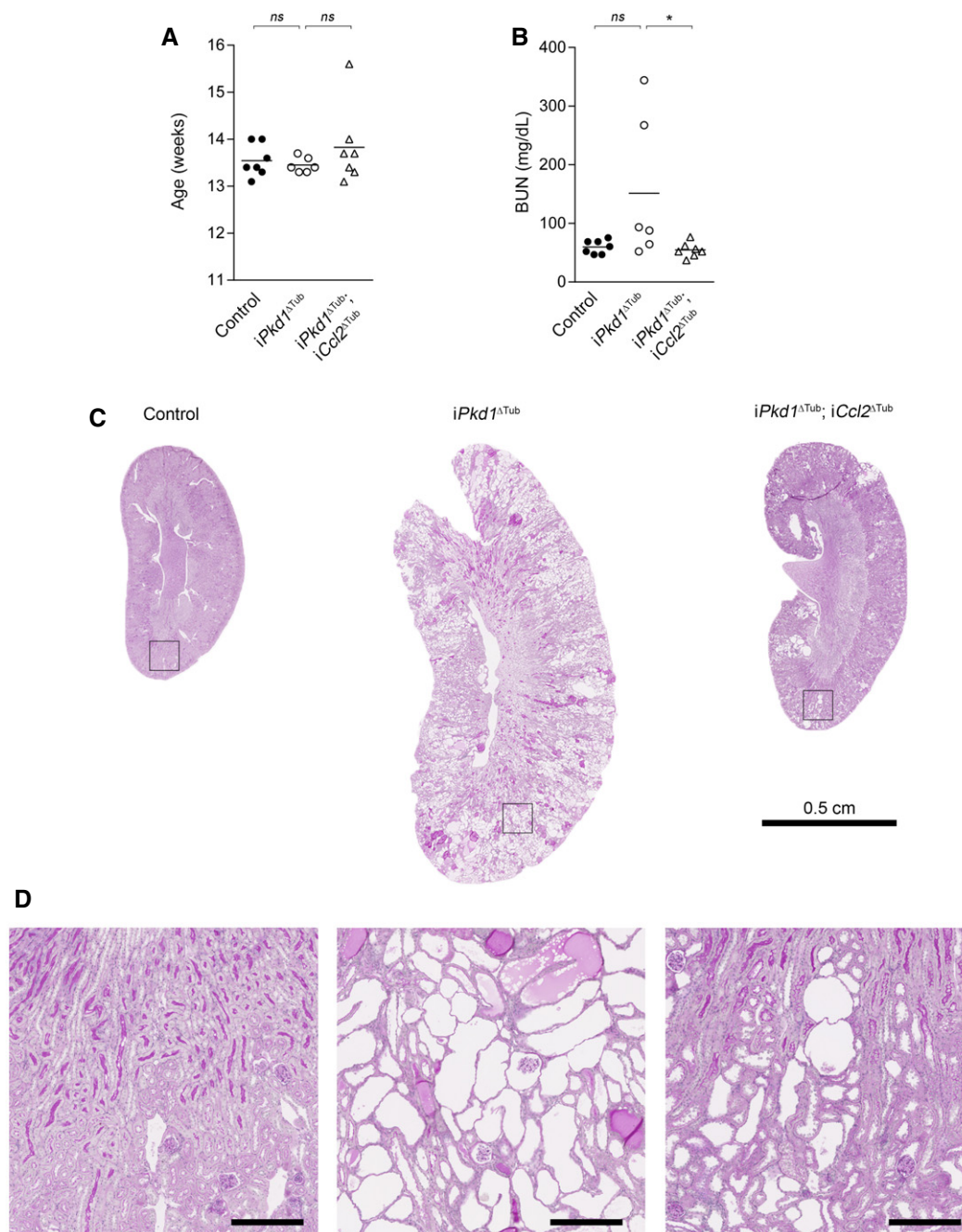
Figure EV5. *Ccl2* ablation reduces cyst formation in *Pkd1* mutant mice.

A   Age from control, iPkd1$^{\Delta Tub}$, and iPkd1$^{\Delta Tub}$;iCcl2$^{\Delta Tub}$ mice.

B   Plasma blood urea nitrogen (BUN) from control, iPkd1$^{\Delta Tub}$, and iPkd1$^{\Delta Tub}$;iCcl2$^{\Delta Tub}$ mice at 13.5 weeks.

C   Representative periodic acid–Schiff (PAS)-stained kidney sections from control (n = 7), iPkd1$^{\Delta Tub}$ (n = 6), and iPkd1$^{\Delta Tub}$;iCcl2$^{\Delta Tub}$ (n = 7) mice at 13.5 weeks.

D   Higher magnification of PAS-stained sections. Scale bar: 250 μm.

Data information: In (A, B), each dot represents one individual mouse. Bars indicate mean. ANOVA followed by the Tukey–Kramer test. *P < 0.05, *ns*: not statistically different.