

SUPPLEMENTARY FIGURES LEGENDS

Supplementary Figure 1. scRNA-seq demonstrates increased proportion of urothelial cells and increased urothelial gene expression during UUO.

a Graph shows the proportion of *Upk1a*, *Upk1b*, *Upk2*, *Upk3a*, *Krt5*, and *Krt14* expressing urothelial cells at baseline (POD0) and at UUO POD2, POD4, POD6, POD10, and POD14. **b** Dotplot of canonical urothelial marker genes at baseline and UUO.

Supplementary Figure 2. UUO leads to increased UPK1A and UPK1B which are altered during conditional manipulation of PPAR γ .

a-c Representative micrographs show anti-UPK1A, -UPK1B, -KRT5, and Hoechst labeling (and individual color channels) in the renal urothelium of SHAM and POD7 kidneys (**a**), *Pparg*^{fl/fl} and *Upk2*^{CreERT2};*Pparg*^{fl/fl} (*Pparg*^{LOF}) mice at POD7 (**b**), and *VP16-Pparg*^{fl} and *Upk2*^{CreERT2};*VP16-Pparg*^{fl} (*Pparg*^{GOF}) mice at POD7 (**c**). White dashed line: renal urothelium basement membrane; L: lumen; Yellow arrowhead: UPK1A+ UPK1B+ cell. SHAM (n=4 mice), POD7 (n=4 mice).

Supplementary Figure 3. UUO leads to increased UPK3A and FABP4 which are altered during conditional manipulation of PPAR γ .

a Representative micrographs show anti-FABP4, -UPK3A, -KRT5, and Hoechst labeling (and individual color channels) in the renal urothelium of SHAM and POD7 kidneys. White dashed line: renal urothelium basement membrane; L: lumen; Red arrowhead: FABP4+ UPK+ cell. **b** Graph shows the relative fold change of *Upk3a* mRNA levels in the kidneys of SHAM and POD7 mice normalized to *Gapdh*. Sham (n=4 mice), POD7 (n=4 mice). Bars: mean; Error bars: SD; P values: Unpaired Two-Tailed T test. **c** Representative micrographs show anti-FABP4, -UPK3A, -

KRT5, and Hoechst labeling (and individual color channels) in the renal urothelium of *Pparg*^{fl/fl} and *Upk2*^{CreERT2};*Pparg*^{fl/fl} (*Pparg*^{LOF}) mice at POD7. White dashed line: renal urothelium basement membrane; L: lumen; Red arrowhead: FABP4+ UPK+ cell. **d** Graph shows the relative fold change of *Upk3a* mRNA levels in the kidneys of *Pparg*^{fl/fl} and *Upk2*^{CreERT2};*Pparg*^{fl/fl} (*Pparg*^{LOF}) mice at POD7, normalized to *Gapdh*. *Pparg*^{fl/fl} (n=4 mice), *Pparg*^{LOF} (n=6 mice). Bars: mean; Error bars: SD; P values: Unpaired Two-Tailed T test. **e** Representative micrographs show anti-FABP4, -UPK3A, -KRT5, and Hoechst labeling (and individual color channels) in the renal urothelium of *VP16-Pparg*^{fl} and *Upk2*^{CreERT2};*VP16-Pparg*^{fl} (*Pparg*^{GOF}) mice at POD7. White dashed line: renal urothelium basement membrane; L: lumen; Red arrowhead: FABP4+ UPK+ cell. **f** Graph shows the relative fold change of *Upk3a* mRNA levels in the kidneys of *VP16-Pparg*^{fl} and *Upk2*^{CreERT2};*VP16-Pparg*^{fl} (*Pparg*^{GOF}) mice at POD7, normalized to *Gapdh*. *VP16-Pparg*^{fl} (n=7 mice), *Pparg*^{GOF} (n=5 mice). Bars: mean; Error bars: SD; P values: Mann-Whitney test was used due to nonparametric data distribution in *VP16-Pparg*^{fl} cohort.

Supplementary Figure 4. Conditional manipulation of PPAR γ alters both PPAR γ and UPK3A expression.

a Representative micrographs show anti-PPARG, -UPK3A, -KRT5 labeling in bladder, contralateral kidney (normal) renal urothelium and POD7 renal urothelium in *Pparg*^{fl/fl} and *Upk2*^{CreERT2};*Pparg*^{fl/fl} (*Pparg*^{LOF}) mice. White dashed line: urothelium basement membrane; L: lumen. White Arrowhead: PPARG+ UPK+ cell. **b** Representative micrographs show anti-PPARG, -UPK3A, -KRT5 labeling in bladder, contralateral kidney (normal) renal urothelium and POD7 renal urothelium in *VP16-Pparg*^{fl} and *Upk2*^{CreERT2};*VP16-Pparg*^{fl} (*Pparg*^{GOF}) mice. White dashed line: urothelium basement membrane; L: lumen. White Arrowhead: PPARG+ UPK+ cell. **c**

Representative sonograph shows kidneys in *Pparg*^{fl/fl} and *Pparg*^{LOF} mice without UUO. **d**

Representative sonograph shows kidneys in *VPI6-Pparg*^{fl} and *Pparg*^{GOF} mice without UUO.

Supplementary Figure 5. Annotation of sonograms for renal parenchyma measurements.

Annotated longitudinal images of POD7 kidneys. Images are captured at the largest longitudinal plane of the kidney. Dashed white line: longitudinal renal length (LRL – to which all measurements lines are perpendicular); red line: transverse renal width (TRW); white line: renal pelvis diameter (RPD); blue line: renal papilla width (RPW); Asterisk (*): renal pelvis. The fractional percentage of parenchyma is calculated as $([TRW - RPD] + RPW)/TRW$.