

Supplemental material Table of Contents

Supplemental Figure 1. Diagram of the glomerular structure

Supplemental Figure 2. Unbiased clustering reveals the major cell types of the glomerulus

Supplemental Figure 3. Mapping of FSGS and CKD susceptibility gene expression to glomerular cell types

Supplemental Figure 4. Nephrotoxic serum nephritis in C57BL/6J mice

Supplemental Figure 5. scRNA-Seq analysis of glomerular cells from nephritic mice

Supplemental Figure 6. Induction of *Ccl2* expression in nephrotoxic serum nephritis

Supplemental Figure 7. Conditional deletion of TAZ and YAP

Supplemental Figure 8. scRNA-Seq analysis of glomerular cells from diabetic, doxorubicin-treated, and CD2AP-deficient mice

Supplemental Figure 9. Validation of previously reported mesangial cell-specific genes

Supplemental Figure 10. Glomerular cells show distinct responses to different types of injury

Supplemental Table 1. Genes differentially expressed between two podocyte sub-clusters (2 and 4) in Supplemental Figure 2A

Supplemental Table 2. List of canonical cell type markers used to determine the identity of cell clusters

Supplemental Table 3. Composition of glomerular cells from a C57BL/6J mouse analyzed by scRNA-Seq

Supplemental Table 4. Top 50 cell type marker genes

Supplemental Table 5. Genes differentially expressed between mesangial cells (cluster 3) and SMCs/JG cells (cluster 5)

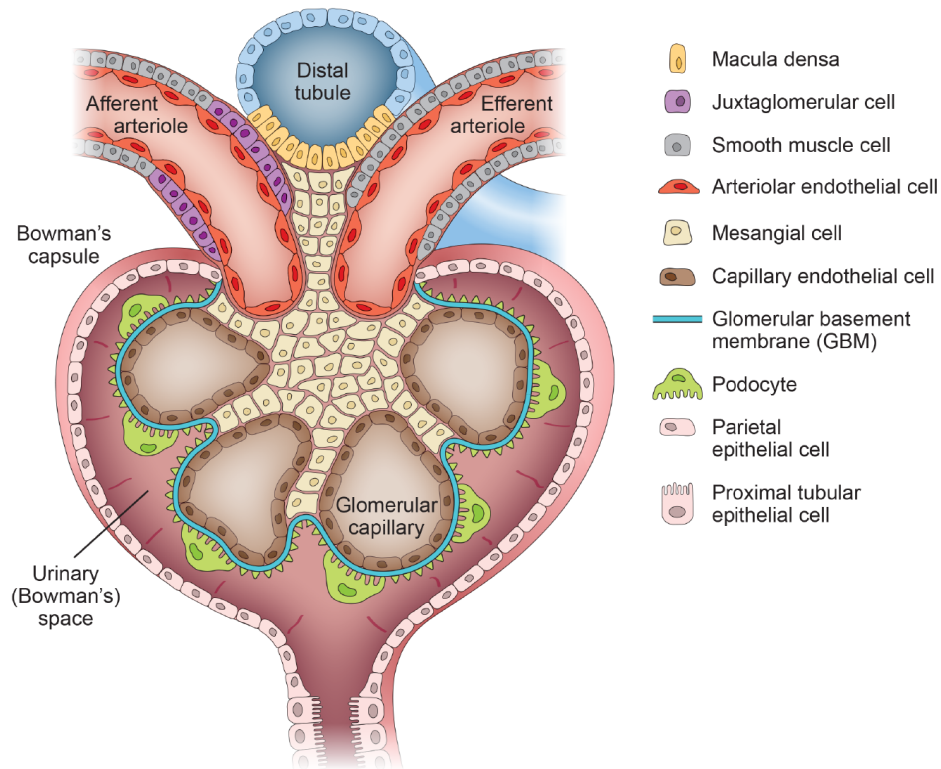
Supplemental Table 6. Genes enriched in mesangial cells

Supplemental Table 7. Number of differentially expressed genes in nephritic mice

Supplemental Table 8. Comparison of kidney single cell datasets

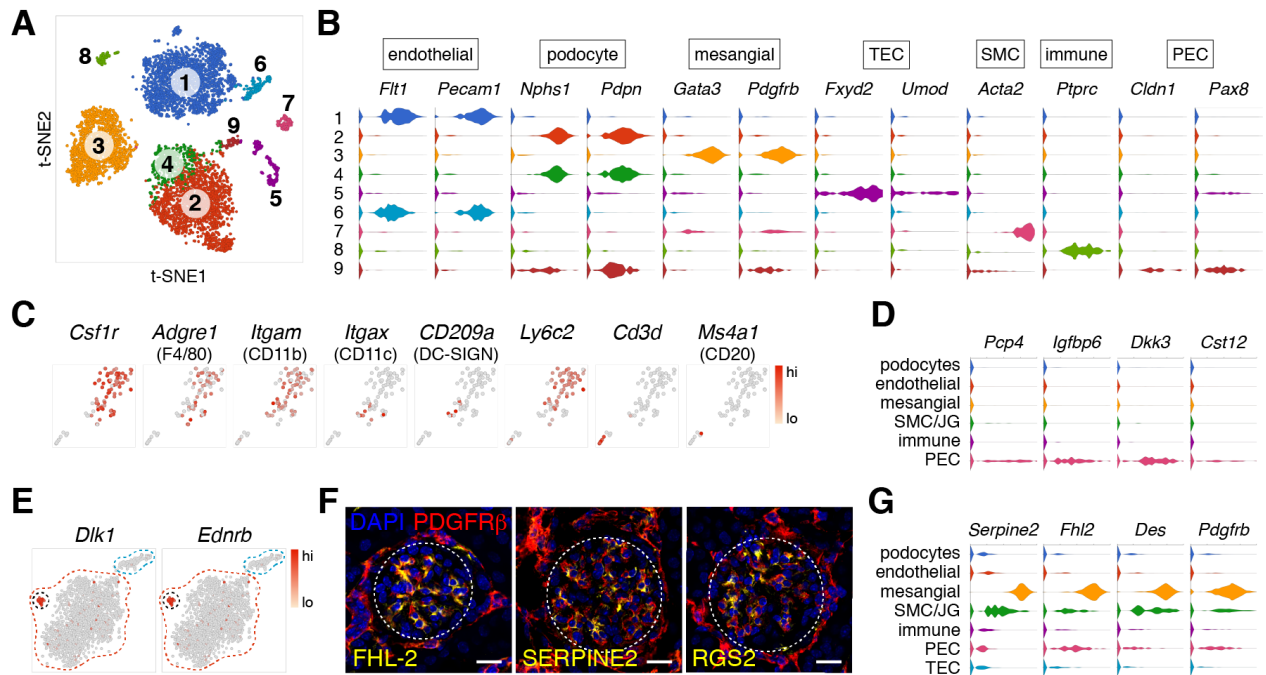
Supplemental Table 9. Genes commonly induced in mesangial cells after different injury types

Supplemental Figure 1



Supplemental Figure 1. Diagram of the glomerular structure. The glomerulus is a capillary tuft that is supplied by the afferent arteriole and drained by the efferent arteriole. Mesangial cells provide structural support for the glomerular capillaries, which are lined by specialized fenestrated endothelial cells that allow water and soluble molecules to pass. Blood is filtered through the glomerular basement membrane (GBM) and between the branched foot processes of podocytes. The primary filtrate is collected in the Bowman's capsule, which is lined with a layer of parietal epithelial cells, then further processed in the downstream tubules to produce urine. The juxtaglomerular apparatus (JGA) is composed of the macula densa that senses changes in salt levels in the tubules and sends signals to regulate constriction of the afferent arterioles by vascular smooth muscle cells (SMCs) and secretion of renin by juxtaglomerular (JG) cells.

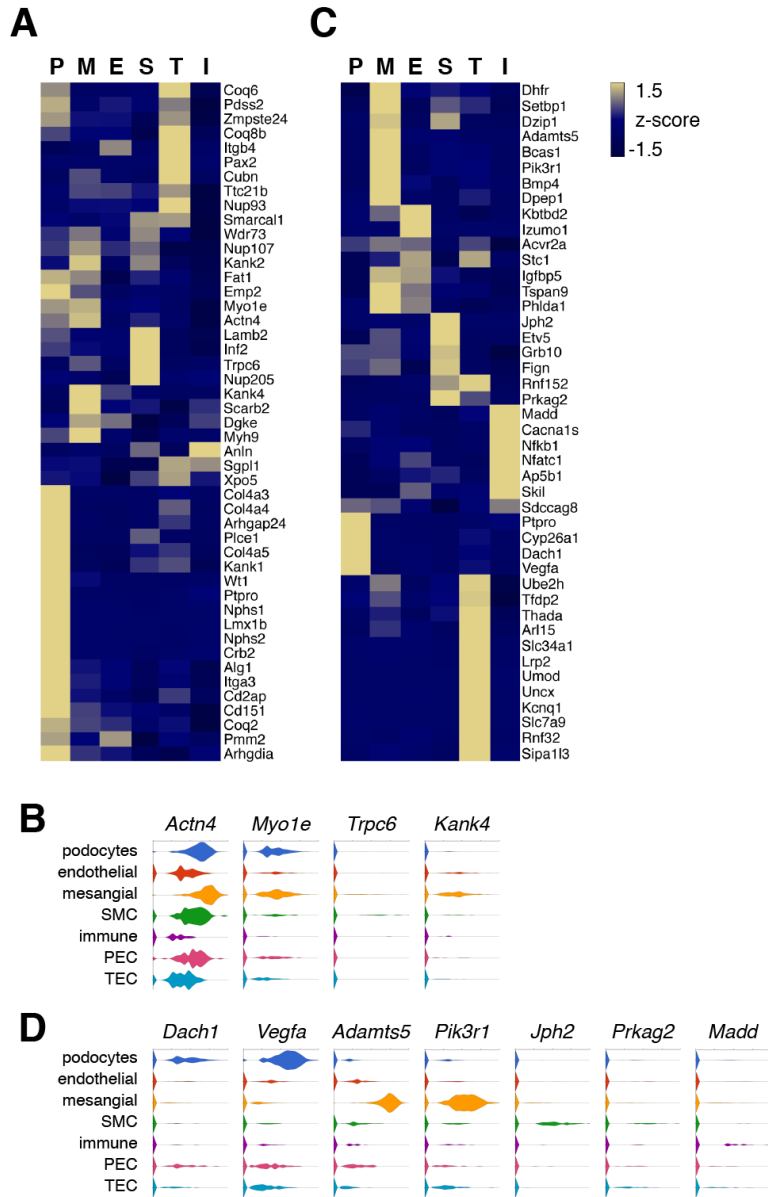
Supplemental Figure 2



Supplemental Figure 2. Unbiased clustering reveals the major cell types of the glomerulus. **A.** t-SNE representation of 5,488 glomerular cells isolated from a C57BL/6J mouse. Labels indicate clusters identified by unsupervised clustering analysis *before* removal of dissociation-induced genes and tubular epithelial cells. Analysis of the two podocyte sub-clusters (2 and 4) showed that the sub-clustering was driven by immediate early genes known to be induced by enzymatic tissue dissociation (Supplemental Table 1). **B.** Violin plots of marker gene expression in each cluster shown in **A**. **C.** Expression levels of immune cell marker genes are shown in a t-SNE plot of immune cells. Majority of the cells express the monocyte/macrophage markers *Csflr*, *Adgre1*, *Itgam*, and *Ly6c2*. **D.** Violin plots showing expression levels of novel PEC marker genes. **E.** *Dlk1* and *Ednrb* are highly expressed in a sub-cluster of glomerular endothelial cells

(outlined in black). Expression levels are shown in a t-SNE plot of endothelial cells. Capillary endothelial cells are outlined in red, arteriolar endothelial cells are outlined in blue. **F.** Immunofluorescence staining of kidney sections shows mesangial expression of the identified marker genes. PDGFR β , which stains mesangial cells in the glomerulus (dotted circle) and stromal cells outside the glomerulus, was used as reference. Scale bars, 20 μ m. **G.** Examples of ‘mesangial-enriched’ genes that are also expressed in SMC/JG cells. Normalized expression levels are shown in the violin plots. SMC: smooth muscle cells, JG: juxtaglomerular cells, PEC: parietal epithelial cells, TEC: tubular epithelial cells.

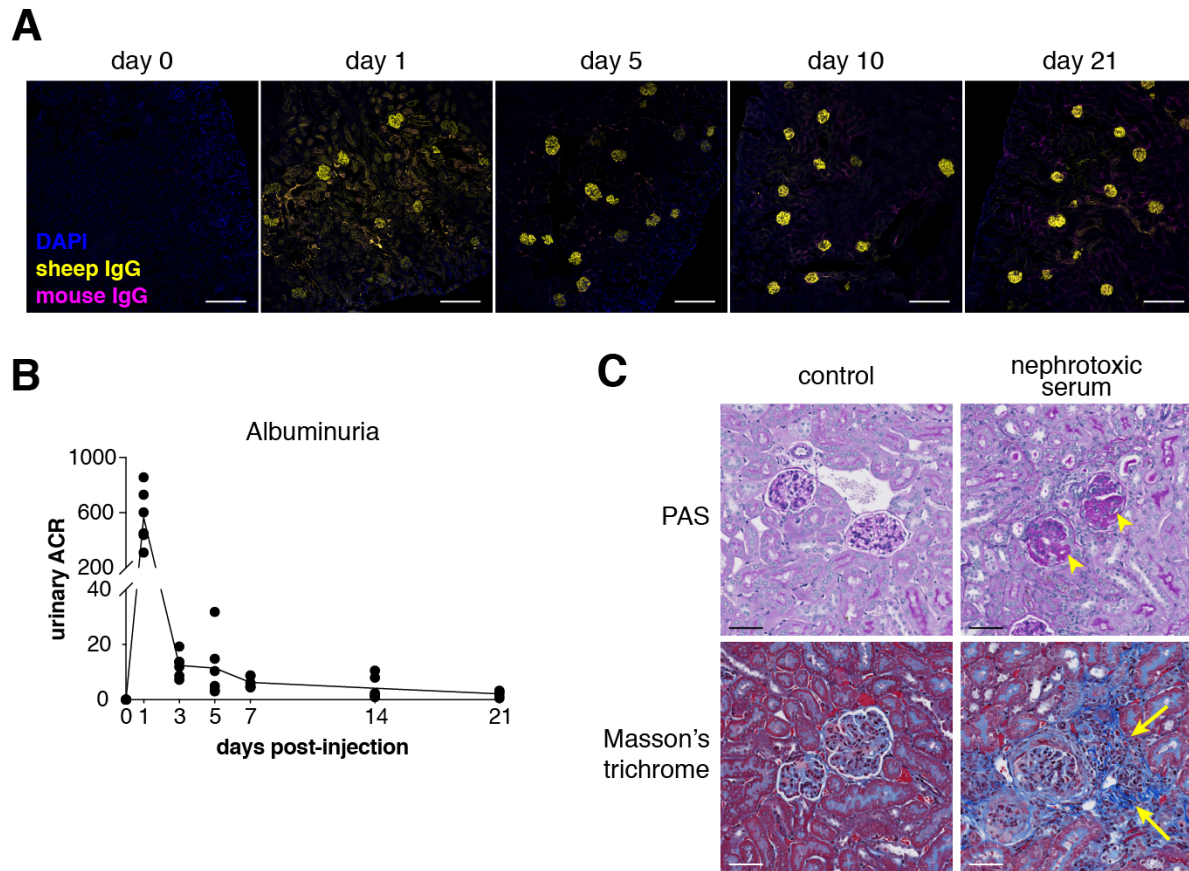
Supplemental Figure 3



Supplemental Figure 3. Mapping of FSGS and CKD susceptibility gene expression to glomerular cell types. **A, C.** Heatmaps showing the expression levels of **(A)** FSGS genes and **(C)** CKD susceptibility genes in each cell type. Each column represents a cell type, each row represents a gene. Results are depicted in z-score. P: podocytes, M: mesangial cells, E: endothelial cells, S: smooth muscle cells, T: tubular epithelial cells, I: immune cells. **B, D.** Violin

plots showing expression of **(B)** FSGS and **(D)** CKD susceptibility genes. Normalized expression levels are shown in the violin plots.

Supplemental Figure 4

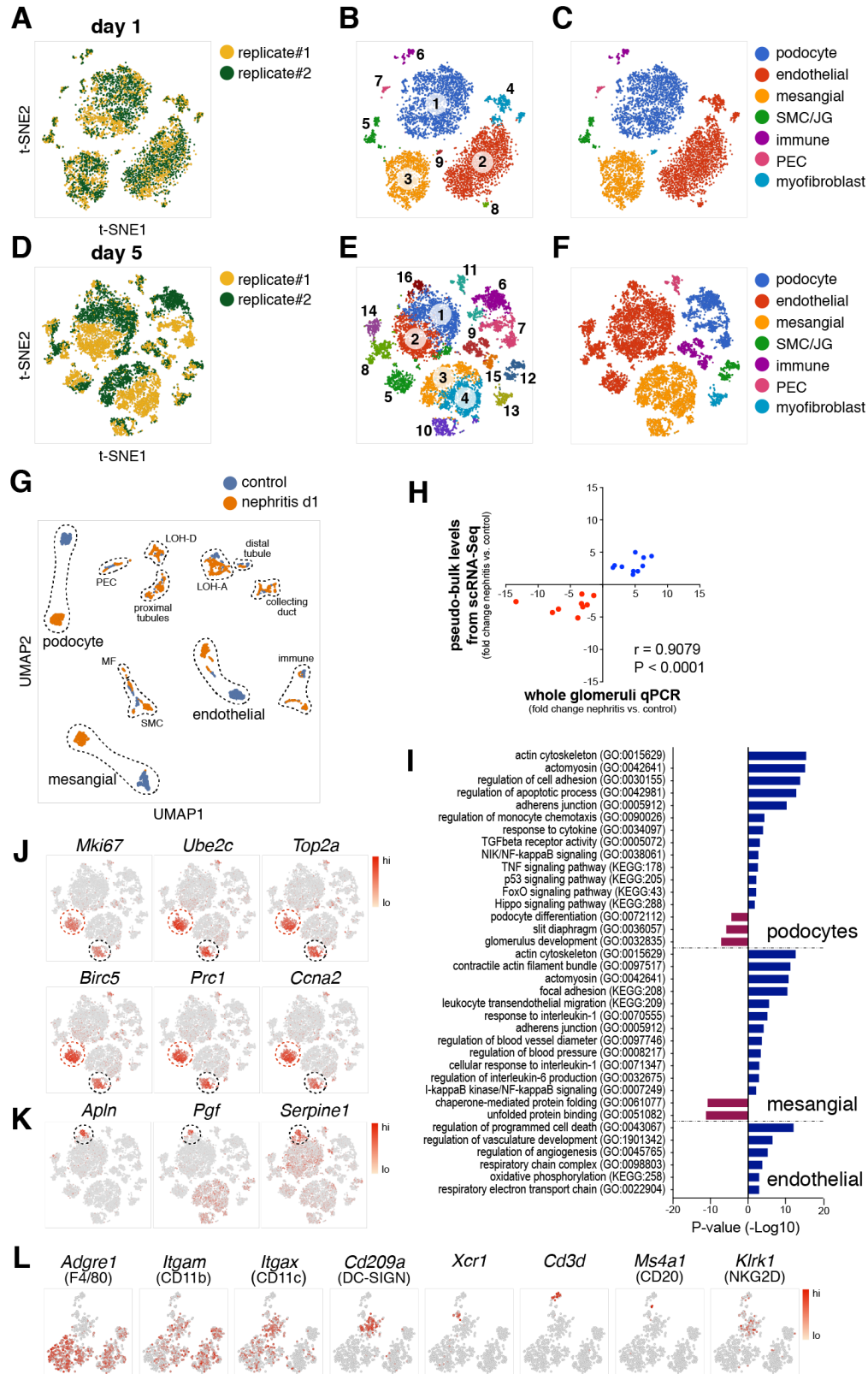


Supplemental Figure 4. Nephrotoxic serum nephritis in C57BL/6J mice. **A.**

Immunofluorescence staining of kidney sections shows deposition of the nephrotoxic antibodies (sheep IgG) in the glomerulus. Glomerular deposition of mouse IgG was not observed at any time point. Scale bar, 200 μ m. **B.** Albumin/creatinine ratios measured from spot urine collected at the indicated time points after nephrotoxic serum injection. n=5. **C.** Representative light microscopy of PAS and Masson's trichrome stained kidney sections from control and nephrotoxic serum-injected mice show glomerulosclerosis (arrowheads) and periglomerular

fibrosis (arrows) in the nephritic mice. Kidneys were analyzed 5 weeks after injection. Scale bars, 50 μm .

Supplemental Figure 5



Supplemental Figure 5. scRNA-Seq analysis of glomerular cells from nephritic mice. **A-F.**

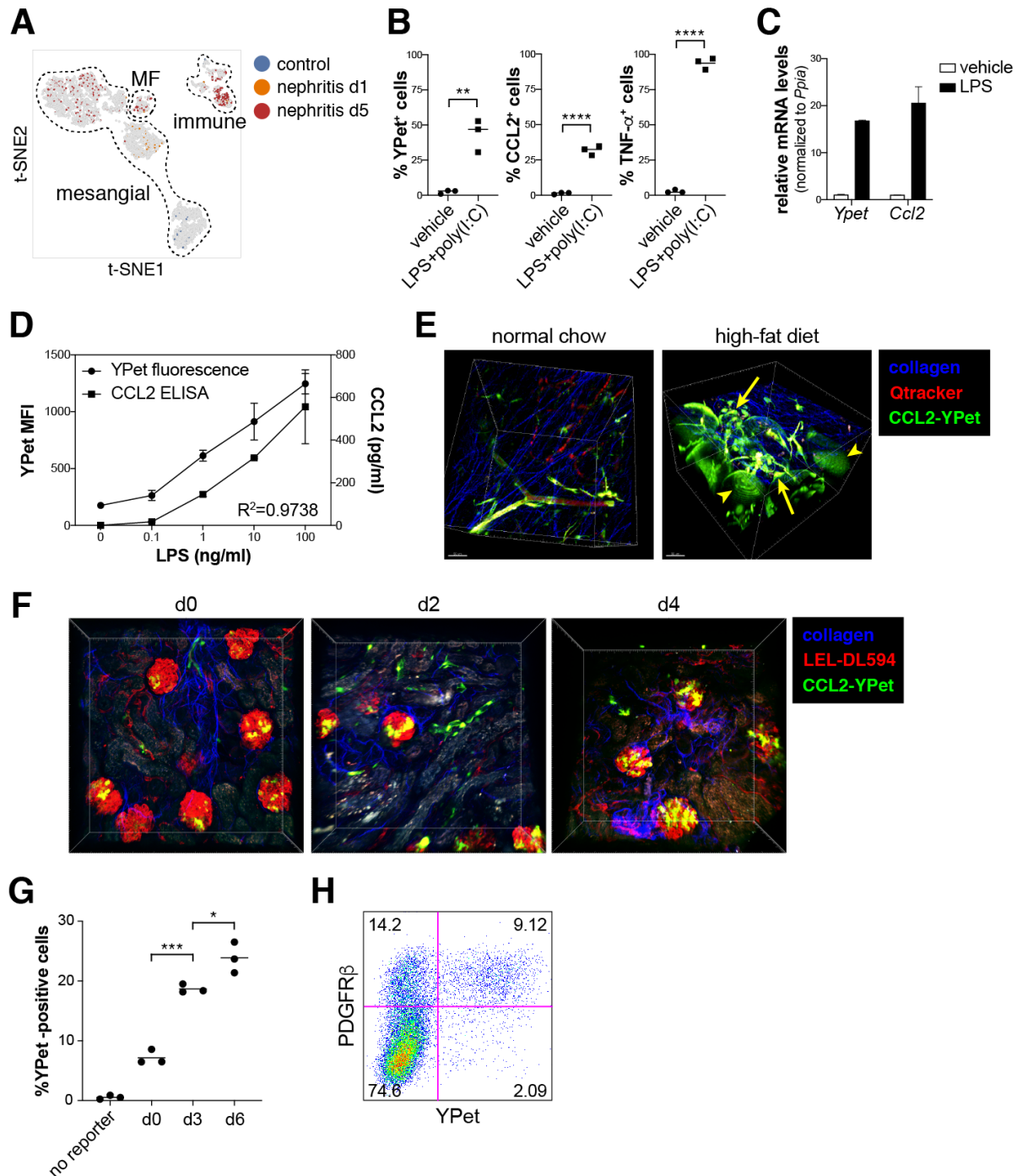
Unsupervised clustering analysis reveals the major glomerular cell types in cells isolated from mice at **(A-C)** 1 day or **(D-F)** 5 days after nephrotoxic serum injection. t-SNE plots were generated from cells isolated at each time point and are labeled to show **(A, D)** replicate samples, **(B, E)** clusters identified by clustering analyses, and **(C, F)** cell types. **G.** Down-sampling analysis of nephritic glomerular cells. Since podocytes, mesangial cells, and endothelial cells comprise ~90% of the cells in the dataset, they have a larger effect on the outcome of clustering analyses compared to the remaining cell types. To reduce this bias, clustering analysis was performed after podocytes, mesangial cells, and endothelial cells were randomly down-sampled to match the number of the remaining cell types. The results are shown as a UMAP plot.

Nephritic podocytes, mesangial cells, endothelial cells still form distinct clusters from control cells, while PECs, SMCs, and tubular epithelial cells from normal and nephritic mice are grouped as single clusters. This supports the conclusion that the distinct clustering of nephritic podocytes, mesangial cells, and endothelial cells in Figure 2A is not due to batch effect. **H.**

qPCR validation of DE genes from freshly isolated glomeruli. A subset of genes identified to be up-regulated (blue) or down-regulated (red) from scRNA-Seq analysis were analyzed by real-time qPCR using cDNA prepared from isolated glomeruli. qPCR results (normalized to *Rpl13a* levels) are plotted against pseudo-bulk (podocyte, mesangial, endothelial) expression levels calculated from scRNA-Seq data and shown as fold change nephritis vs. control. **I.** Pathways up-regulated (blue) or down-regulated (red) after nephrotoxic injury are shown. **J.** Expression levels of cell cycle genes reveal sub-clusters of proliferating mesangial cells (black dotted circle) and endothelial cells (red dotted circle) 5 days after nephrotoxic injury. t-SNE plot is identical to **(E)**. **K.** Expression levels of *Apln*, *Pgf*, and *Serpine1* in a sub-cluster of endothelial cells

(outlined) found at day 5. t-SNE plot is identical to **(E)**. **L**. Expression levels of immune cell marker genes overlaid on the t-SNE plot shown in Figure 2E.

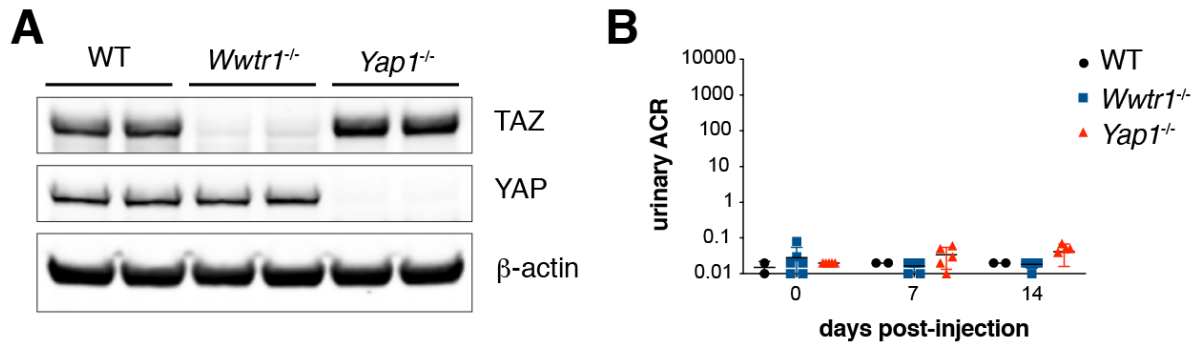
Supplemental Figure 6



Supplemental Figure 6. Induction of *Ccl2* expression in nephrotoxic serum nephritis. **A.** t-SNE plot of mesangial cells, myofibroblasts (MF), and immune cells from control and nephritic

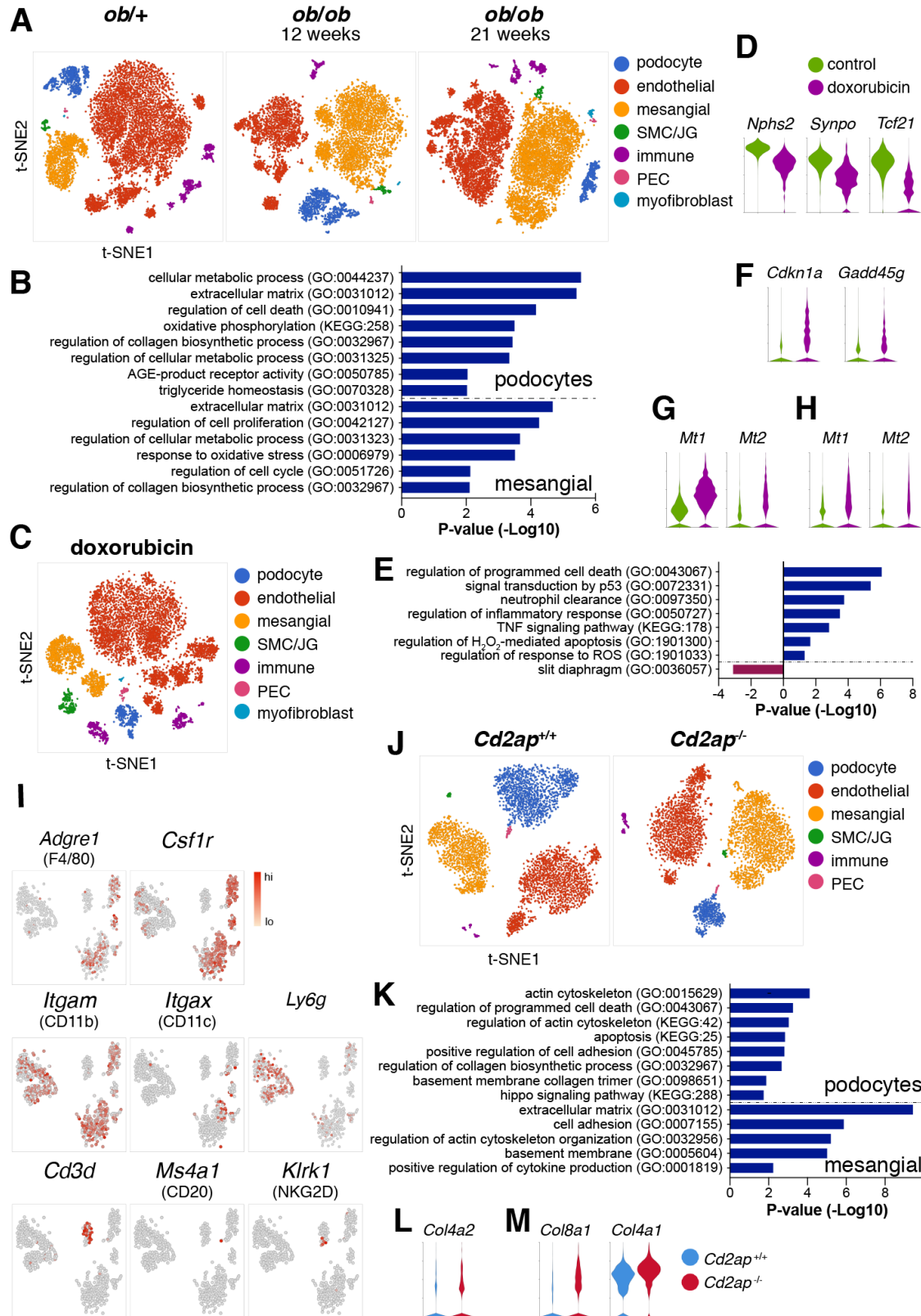
glomeruli shows increased number of *Ccl2*-expressing cells after nephrotoxic injury. *Ccl2*-positive cells are labeled in color and *Ccl2*-negative cells are in gray. **B.** Induction of the YPet reporter in peritoneal macrophages isolated from CCL2-reporter mice upon *in vitro* stimulation with LPS and poly(I:C). Results represent three individual experiments analyzed by two-tailed Student's *t* test (** $P < 0.01$, **** $P < 0.0001$). **C.** qPCR analysis shows similar fold-induction of YPet and *Ccl2* transcript levels in peritoneal macrophages isolated from CCL2-reporter mice after *in vitro* LPS stimulation. Results are representative of 2 individual experiments. **D.** Expression of YPet reporter correlates well with CCL2 production/secretion. Peritoneal macrophages isolated from CCL2-reporter mice were treated *in vitro* with increasing concentrations of LPS. Cells were analyzed by FACS to measure YPet fluorescence; the culture supernatant was used to measure secreted CCL2 protein levels. Pearson's correlation $R^2 = 0.9738$, $P = 0.0018$. **E.** Images of adipose tissue from control and HFD-fed CCL2-reporter mice obtained using 2-photon microscopy. YPet expression is only detected in peri-vascular cells in normal chow-fed mice. In the HFD-fed mice, reporter expression is induced in fat cells (arrowheads) and macrophages (arrows). **F.** Images of glomeruli from control and nephritic CCL2-reporter mice obtained by 2-photon microscopy show progressive increase in YPet expression after nephrotoxic injury. **G.** Glomerular cells were isolated from CCL2-reporter mice at the indicated time points after nephrotoxic serum injection and analyzed by flow cytometry to determine the percentage of YPet-expressing cells. Three mice from two individual experiments were analyzed by multiple *t* tests using the two-stage linear step-up method (* $q < 0.05$, *** $q < 0.001$). **H.** CCL2 is expressed in mesangial cells. Glomerular cells isolated from CCL2-reporter mice were stained for the mesangial cell marker PDGFR β and analyzed by flow cytometry. >80% of YPet-positive cells are PDGFR β -positive mesangial cells.

Supplemental Figure 7



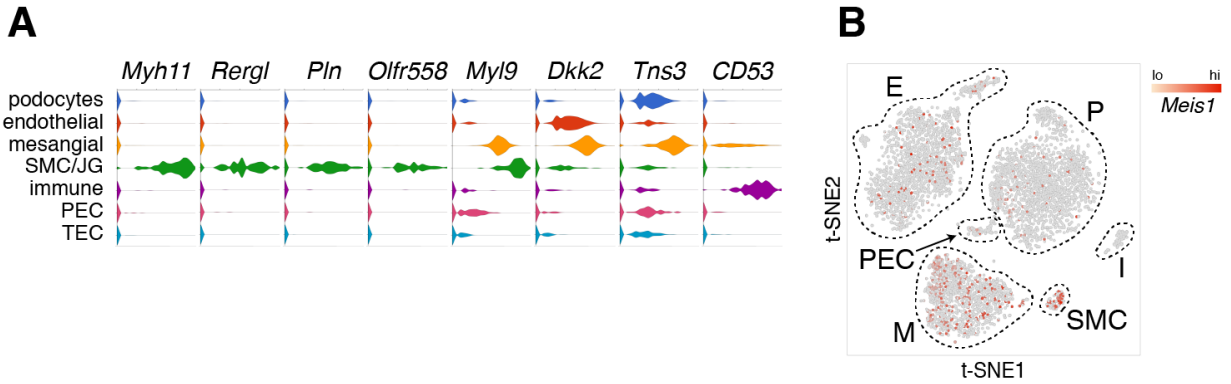
Supplemental Figure 7. Conditional deletion of TAZ and YAP. **A.** Wild-type (Rosa26.CreERT2, *Wwtr1*^{+/+}, *Yap1*^{+/+}), TAZ conditional knockout (Rosa26.CreERT2, *Wwtr1*^{flx/flx}, *Yap1*^{+/+}), and YAP conditional knockout (Rosa26.CreERT2, *Wwtr1*^{+/+}, *Yap1*^{flx/flx}) mice were given 5 daily injections of tamoxifen. Glomerular lysates were prepared one week after the final injection and immunoblotted for TAZ and YAP. β-actin was used as loading control. **B.** Deletion of TAZ or YAP does not cause proteinuria. WT, *Wwtr1*^{-/-}, and *Yap1*^{-/-} mice were injected with sterile saline. Albumin/creatinine ratios (ACR) were measured from spot urine collected at the indicated time points.

Supplemental Figure 8



Supplemental Figure 8. scRNA-Seq analysis of glomerular cells from diabetic, doxorubicin-treated, and CD2AP-deficient mice. **A.** t-SNE plot of glomerular cells from control (*ob/+*) and diabetic mice (*ob/ob*). **B.** Pathways up-regulated in podocytes and mesangial cells in diabetic mice are shown. **C.** t-SNE plot of glomerular cells from doxorubicin-treated mice. **D.** Violin plots show down-regulation of podocyte-specific genes in podocytes after doxorubicin treatment. **E.** Pathways up-regulated (blue) or down-regulated (red) in podocytes after doxorubicin treatment are shown. **F.** Violin plots show induction of p53 signaling target genes in podocytes after doxorubicin treatment. **G, H.** Violin plots show induction of *Mt1* and *Mt2* in **(G)** mesangial cells and **(H)** endothelial cells after doxorubicin treatment. **I.** Expression of immune cell markers in control and doxorubicin-treated mice. t-SNE plot is identical to Figure 4D. **J.** t-SNE plot of glomerular cells from 3 week-old wild-type and *Cd2ap*^{-/-} mice. **K.** Pathways up-regulated in podocytes and mesangial cells in *Cd2ap*^{-/-} mice are shown. **L, M.** Violin plots show increased expression of matrix genes in **(L)** podocytes and **(M)** mesangial cells. Normalized expression levels are shown in violin plots.

Supplemental Figure 9

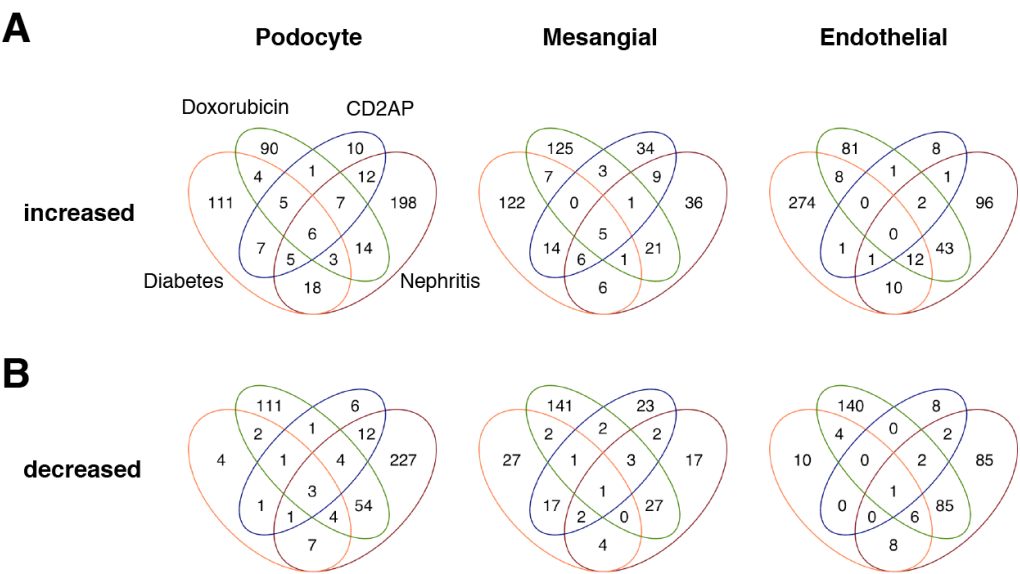


Supplemental Figure 9. Validation of previously reported mesangial cell-specific genes. **A.**

Violin plots showing expression of previously reported mesangial-specific genes. Normalized expression levels are shown. **B.** Expression level of *Meis1* overlaid on a t-SNE plot of

glomerular cells (identical to Figure 1A). *Meis1* is broadly expressed in non-mesangial cells, including vascular SMCs, endothelial cells, and podocytes. P: podocytes, M: mesangial cells, E: endothelial cells, SMC: vascular smooth muscle cells, PEC: parietal epithelial cells, I: immune cells.

Supplemental Figure 10



Supplemental Figure 10. Glomerular cells show distinct responses to different types of injury.

A, B. Venn diagrams showing the number of **(A)** up-regulated and **(B)** down-regulated genes commonly altered in different injury models in podocytes, mesangial cells, and endothelial cells.

Supplemental Table 1

podocyte	mesangial	endothelial	PEC	SMC	immune	TEC
<i>Nphs1</i>	<i>Pdgfrb</i>	<i>Flt1</i>	<i>Cldn1</i>	<i>Acta2</i>	<i>Ptpcr</i>	<i>Fxyd2</i>
<i>Nphs2</i>	<i>Gata3</i>	<i>Tie1</i>	<i>Pax8</i>	<i>Myh11</i>	<i>Lyz1</i>	<i>Slc12a1</i>
<i>Pdpm</i>	<i>Des</i>	<i>Pecam1</i>		<i>Tagln</i>	<i>Csf1r</i>	<i>Slc12a3</i>
<i>Wt1</i>	<i>Itga8</i>	<i>Kdr</i>			<i>Itgam</i>	<i>Slc14a2</i>
<i>Mafb</i>		<i>Emcn</i>			<i>Cd3d</i>	<i>Aqp1</i>
<i>Synpo</i>					<i>Ms4a1</i>	<i>Aqp2</i>
<i>Cdkn1c</i>						<i>Umod</i>
<i>Ptpro</i>						

PEC: parietal epithelial cell, SMC: smooth muscle cell, TEC: tubular epithelial cell

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Supplemental Table 1. List of canonical cell type markers used to determine the identity of cell clusters.

Supplemental Table 2

Gene symbol	Adj p-value	Fold change (4 vs. 2)	Mean (cluster 4)	Mean (cluster 2)	Dissociation-induced gene
<i>Fos</i>	0.00E+00	6.65	51.53	7.75	Y
<i>Cyr61</i>	3.24E-213	5.29	25.21	4.77	Y
<i>Ier2</i>	2.12E-279	5.02	13.92	2.77	Y
<i>Atf3</i>	5.48E-125	4.69	7.59	1.62	Y
<i>Junb</i>	1.49E-244	4.54	19.51	4.30	Y
<i>Fosb</i>	4.18E-169	4.26	6.12	1.44	Y
<i>Hspa1a</i>	2.75E-234	4.06	97.50	24.02	Y
<i>Dusp1</i>	2.15E-204	3.79	18.03	4.76	Y
<i>Jun</i>	1.16E-183	3.61	32.85	9.09	Y
<i>Egr1</i>	8.96E-126	3.59	7.63	2.13	Y
<i>Hspb1</i>	2.76E-107	3.25	15.87	4.89	Y
<i>Nr4a1</i>	2.54E-110	2.98	6.09	2.05	Y
<i>Hspa1b</i>	9.08E-123	2.97	7.79	2.62	Y
<i>Btg2</i>	1.91E-119	2.92	9.61	3.29	Y
<i>Hsp25-ps1</i>	1.05E-82	2.81	6.61	2.35	
<i>Ubc</i>	6.39E-180	2.74	36.36	13.29	Y
<i>Dnajb1</i>	1.76E-70	2.70	5.27	1.95	Y
<i>Nfkbia</i>	3.54E-80	2.57	7.02	2.73	Y
<i>Slc38a2</i>	1.44E-123	2.45	6.09	2.48	Y
<i>Klf6</i>	6.89E-70	2.38	4.75	1.99	Y
<i>Hsp90aa1</i>	3.17E-78	2.36	8.08	3.43	Y
<i>Zfp36</i>	2.29E-70	2.30	4.32	1.88	Y
<i>Btg1</i>	4.64E-71	2.29	5.00	2.18	Y
<i>Gadd45b</i>	2.46E-54	2.29	4.17	1.82	
<i>Hes1</i>	1.88E-26	2.12	4.06	1.92	
<i>Ier3</i>	1.27E-49	2.02	7.42	3.66	Y
<i>Ppp1r15a</i>	6.54E-59	1.99	4.13	2.08	Y
<i>Socs3</i>	8.01E-28	1.95	2.91	1.50	Y
<i>Jund</i>	2.93E-62	1.93	24.14	12.49	Y
<i>Pnrc1</i>	8.25E-54	1.89	4.16	2.20	Y
<i>Sertad1</i>	4.97E-47	1.88	4.71	2.51	
<i>Phl1a1</i>	3.41E-25	1.86	4.02	2.16	Y
<i>Hspe1</i>	3.21E-41	1.82	4.09	2.24	Y
<i>Txnip</i>	3.83E-44	1.80	5.62	3.12	
<i>Ccn11</i>	1.63E-43	1.80	3.26	1.81	Y
<i>Klf2</i>	6.09E-16	1.79	2.97	1.65	Y

<i>Adm</i>	1.02E-34	1.79	7.87	4.41	
<i>Cited2</i>	1.28E-28	1.70	4.77	2.81	
<i>Dnajb4</i>	7.70E-40	1.69	3.66	2.17	Y
<i>CT009757.7</i>	8.00E-61	1.67	3.35	2.01	
<i>Arrdc3</i>	8.60E-55	1.64	3.42	2.08	
<i>Hsph1</i>	1.45E-17	1.61	2.63	1.63	Y
<i>Srf</i>	8.00E-61	1.61	2.13	1.32	Y
<i>Csrnp1</i>	1.63E-16	1.58	2.01	1.27	Y
<i>Hspa8</i>	3.48E-36	1.57	5.83	3.72	Y
<i>Rhob</i>	5.09E-21	1.55	3.40	2.19	Y
<i>Clk1</i>	6.59E-32	1.54	3.61	2.35	
<i>Gm12346</i>	1.04E-19	1.53	1.95	1.27	
<i>Ifrd1</i>	2.72E-09	1.50	2.45	1.63	Y

Supplemental Table 2. Genes differentially expressed between two podocyte sub-clusters (2 and 4) in Supplemental Figure 2A. 38 of

49 differentially expressed genes are dissociation-induced genes.

Supplemental Table 3

Cell type	# of cells	% of total
podocyte	1930	35.17%
endothelial cells	1858	33.86%
mesangial cells	1197	21.81%
tubular epithelial cells	207	3.77%
vascular SMCs	109	1.99%
immune cells	98	1.79%
parietal epithelial cells	89	1.62%
total	5488	100.00%

5 **Supplemental Table 3.** Composition of glomerular cells from a C57BL/6J mouse analyzed by scRNA-Seq.

Supplemental Table 4

podocyte	mesangial	endothelial	vascular SMCs	immune	PECs	TECs
<i>Cdkn1c</i>	<i>Sfrp2</i>	<i>Ly6c1</i>	<i>Acta2</i>	<i>Lyz2</i>	<i>Gpx3</i>	<i>Umod</i>
<i>H2-Q6</i>	<i>Ptn</i>	<i>Emcn</i>	<i>Rgs5</i>	<i>Cd74</i>	<i>Lsp1</i>	<i>Fxyd2</i>
<i>Clic3</i>	<i>Serpine2</i>	<i>Plpp1</i>	<i>Tagln</i>	<i>Il1b</i>	<i>Cpe</i>	<i>Spp1</i>
<i>Nphs2</i>	<i>Adamts5</i>	<i>Pi16</i>	<i>Tpm2</i>	<i>Tyrobp</i>	<i>Pcp4</i>	<i>Atp1b1</i>
<i>Enpep</i>	<i>Bgn</i>	<i>Cd24a</i>	<i>Myh11</i>	<i>Fcer1g</i>	<i>Igsf5</i>	<i>Slc12a1</i>
<i>H2-Q7</i>	<i>Fhl2</i>	<i>Cyp4b1</i>	<i>Sparcl1</i>	<i>Lgals3</i>	<i>Igfbp6</i>	<i>Defb1</i>
<i>Nphs1</i>	<i>Agtr1a</i>	<i>Gimap6</i>	<i>Mustn1</i>	<i>Cd52</i>	<i>Dkk3</i>	<i>Wfdc15b</i>
<i>Tcf21</i>	<i>Igfbp4</i>	<i>Egfl7</i>	<i>Rergl</i>	<i>Plac8</i>	<i>Igfbp2</i>	<i>Klk1</i>
<i>Dpp4</i>	<i>Gata3</i>	<i>Kdr</i>	<i>Akr1b7</i>	<i>Ccl4</i>	<i>Ptgis</i>	<i>Apela</i>
<i>Mafb</i>	<i>Ctgf</i>	<i>Gimap4</i>	<i>Map3k7cl</i>	<i>Ctss</i>	<i>Cst12</i>	<i>mt-Nd1</i>
<i>Rab3b</i>	<i>Itga8</i>	<i>Ctla2a</i>	<i>Fxyd1</i>	<i>Cd14</i>	<i>Stc2</i>	<i>Ppp1r1a</i>
<i>Cldn5</i>	<i>Lhfp</i>	<i>Ly6e</i>	<i>Pln</i>	<i>Clec4e</i>	<i>Pamr1</i>	<i>Cdh16</i>
<i>Pth1r</i>	<i>Rgs2</i>	<i>Pecam1</i>	<i>Nrip2</i>	<i>Coro1a</i>	<i>Lbp</i>	<i>mt-Cytb</i>
<i>Rhpn1</i>	<i>Sept4</i>	<i>Cd300lg</i>	<i>Ppp1r14a</i>	<i>Wfdc17</i>	<i>Cacna1g</i>	<i>Wfdc2</i>
<i>Wt1</i>	<i>Mfge8</i>	<i>Ehd3</i>	<i>Cox4i2</i>	<i>Ccl3</i>	<i>Plppr4</i>	<i>Ldhb</i>
<i>Sema3g</i>	<i>Myl9</i>	<i>Ramp2</i>	<i>Lmod1</i>	<i>Lyz1</i>	<i>Mir147</i>	<i>Epcam</i>
<i>Thsd7a</i>	<i>Plvap</i>	<i>Fabp4</i>	<i>Cnn1</i>	<i>Ccl9</i>	<i>Efemp1</i>	<i>Tmem213</i>
<i>Angptl2</i>	<i>Maf</i>	<i>Ly6a</i>	<i>Olfr558</i>	<i>Plek</i>	<i>Ms4a2</i>	<i>Pdzklip1</i>
<i>Fgfbp1</i>	<i>Gdf10</i>	<i>AU021092</i>	<i>Gm13861</i>	<i>Ifi2712a</i>	<i>Wnt16</i>	<i>Tmem52b</i>
<i>Col4a3</i>	<i>Serpini1</i>	<i>Plk2</i>	<i>Pdlim3</i>	<i>Ms4a6c</i>	<i>AA467197</i>	<i>Kng2</i>
<i>Hs3st6</i>	<i>Prkca</i>	<i>Srgn</i>	<i>Ptgis</i>	<i>Slfn2</i>	<i>Col6a1</i>	<i>Mal</i>
<i>Cd59a</i>	<i>Art3</i>	<i>Plpp3</i>	<i>Atp1a2</i>	<i>Chil3</i>	<i>Vit</i>	<i>Kcnj1</i>
<i>Arhgap24</i>	<i>Lmo7</i>	<i>Cdh5</i>	<i>Ramp1</i>	<i>Alox5ap</i>	<i>Scrn1</i>	<i>Plet1</i>
<i>Tmem150c</i>	<i>Pdgfrb</i>	<i>Sgk1</i>	<i>Aoc3</i>	<i>Laptm5</i>	<i>Fam180a</i>	<i>Cldn8</i>
<i>Synpo</i>	<i>Apoe</i>	<i>Flt1</i>	<i>Rgs7bp</i>	<i>Cybb</i>	<i>Nkain4</i>	<i>Kl</i>
<i>Pak1</i>	<i>Dkk2</i>	<i>Cdkn1a</i>	<i>Kcna5</i>	<i>Spi1</i>	<i>Gxylt2</i>	<i>Sostdc1</i>
<i>Itgb5</i>	<i>Nt5e</i>	<i>Cavin2</i>	<i>Itga7</i>	<i>Tnf</i>	<i>Tagln</i>	<i>Paqr5</i>
<i>Cmtm7</i>	<i>Gucyl1a3</i>	<i>Cd200</i>	<i>Jph2</i>	<i>Ccl6</i>	<i>Col6a2</i>	<i>Cldn4</i>
<i>Eif3m</i>	<i>Ndufa4l2</i>	<i>Cd9</i>	<i>Kcnab1</i>	<i>Lsp1</i>	<i>Loxl1</i>	<i>Pcbd1</i>
<i>Htra1</i>	<i>Rasgrp2</i>	<i>Sox17</i>	<i>Heyl</i>	<i>Samsn1</i>	<i>Pebp4</i>	<i>Sfrp1</i>
<i>Metrn1</i>	<i>Aldh2</i>	<i>Gimap5</i>	<i>Lmo1</i>	<i>Cd83</i>	<i>Sod3</i>	<i>Cdh1</i>
<i>Podxl</i>	<i>Gpc3</i>	<i>Cmtm8</i>	<i>Gpc6</i>	<i>Ctsc</i>	<i>Ogn</i>	<i>1700011H14Rik</i>
<i>Aplp1</i>	<i>Cald1</i>	<i>Hsp25-ps1</i>	<i>Susd5</i>	<i>Lilrb4a</i>	<i>Pax8</i>	<i>Slc16a7</i>
<i>Npnt</i>	<i>Cpm</i>	<i>Tspan7</i>	<i>Ppp1r12b</i>	<i>Lst1</i>	<i>Clstn2</i>	<i>Gm45886</i>
<i>Ptpro</i>	<i>Slc12a2</i>	<i>Mmrn2</i>	<i>1700120C14Rik</i>	<i>Cd44</i>	<i>Cldn1</i>	<i>Cyfp2</i>
<i>Pdpn</i>	<i>Vcl</i>	<i>Rasip1</i>	<i>Fbxl22</i>	<i>Ifitm6</i>	<i>Prss23</i>	<i>Krt18</i>
<i>Mmp23</i>	<i>Col4a1</i>	<i>AC160962.1</i>	<i>Adamts11</i>	<i>Cytip</i>	<i>Osr2</i>	<i>Clcnkb</i>

<i>Gas1</i>	<i>Sorbs2</i>	<i>Adgrf5</i>	<i>Sh3bgr</i>	<i>Hp</i>	<i>Proser2</i>	<i>Cldn7</i>
<i>Snx31</i>	<i>Ebfl</i>	<i>Gimap1</i>	<i>Grip2</i>	<i>Rac2</i>	<i>Rspo1</i>	<i>Car2</i>
<i>Ezr</i>	<i>Mecom</i>	<i>Icam1</i>	<i>Asb2</i>	<i>Mir5107</i>	<i>C3</i>	<i>Wwc1</i>
<i>Itm2b</i>	<i>Slpr3</i>	<i>Adgrl4</i>	<i>Ldb3</i>	<i>Ms4a6b</i>	<i>Pla2g7</i>	<i>Kcnj16</i>
<i>Ddn</i>	<i>Pcp4l1</i>	<i>Lmo2</i>	<i>Thsd4</i>	<i>Ms4a4c</i>	<i>Ncam1</i>	<i>Rbm47</i>
<i>Aifl1</i>	<i>Gstm1</i>	<i>Esam</i>	<i>Kcnk3</i>	<i>Cd68</i>	<i>Msmg</i>	<i>Wnk4</i>
<i>Nupr1</i>	<i>Atp1b2</i>	<i>CT010498.1</i>	<i>Prkg2</i>	<i>Tlr2</i>	<i>Sp6</i>	<i>Eps8l2</i>
<i>P3h2</i>	<i>Col4a2</i>	<i>Hbegf</i>	<i>Nkx3-1</i>	<i>Napsa</i>	<i>Acot1</i>	<i>Tfcp2l1</i>
<i>Vegfa</i>	<i>Scarf2</i>	<i>Ramp3</i>	<i>Synpo2</i>	<i>Ptafr</i>	<i>Bdh2</i>	<i>Cdkl1</i>
<i>Nes</i>	<i>Scn1b</i>	<i>Icam2</i>	<i>Dhx58os</i>	<i>Bcl2a1d</i>	<i>Ccdc3</i>	<i>Aldh1l1</i>
<i>Col4a4</i>	<i>Rasl11b</i>	<i>Pde2a</i>	<i>Rbm24</i>	<i>C5ar1</i>	<i>Dgkg</i>	<i>Cox7a1</i>
<i>Gsn</i>	<i>Csrp1</i>	<i>Gm45837</i>	<i>Gpr20</i>	<i>Pld4</i>	<i>Smim5</i>	<i>Elovl7</i>
<i>Shisa3</i>	<i>Pik3r1</i>	<i>Tie1</i>	<i>Cap2</i>	<i>Pou2f2</i>	<i>Adra2c</i>	<i>Ppargc1a</i>

Supplemental Table 4. Top 50 cell type marker genes. Genes are listed in order of greatest fold-change compared to all other cell types.

Supplemental Table 5

Gene symbol	Adj p-value (5 vs. 3)	Fold change (5 vs. 3)	Mean (cluster 5)	Mean (cluster 3)
<i>Ren1</i>	1.33E-177	126.85	153.49	1.21
<i>Acta2</i>	0.00E+00	90.80	146.81	1.62
<i>Tagln</i>	0.00E+00	61.45	77.07	1.25
<i>Crip1</i>	0.00E+00	26.30	72.39	2.75
<i>Rgs5</i>	0.00E+00	24.93	68.51	2.75
<i>Myh11</i>	0.00E+00	22.87	23.63	1.03
<i>Sparcl1</i>	0.00E+00	21.13	24.36	1.15
<i>Rergl</i>	0.00E+00	12.23	12.41	1.01
<i>Tpm2</i>	0.00E+00	11.15	48.94	4.39
<i>Sncg</i>	0.00E+00	10.80	13.82	1.28
<i>Map3k7cl</i>	0.00E+00	10.15	10.30	1.01
<i>Pln</i>	0.00E+00	9.82	9.97	1.02
<i>Akr1b7</i>	0.00E+00	9.73	14.00	1.44
<i>Mustn1</i>	0.00E+00	8.58	21.91	2.55
<i>Nrip2</i>	0.00E+00	7.39	7.63	1.03
<i>Cd9</i>	1.11E-194	7.32	8.59	1.17
<i>Fxyd1</i>	0.00E+00	6.18	13.57	2.20
<i>Palld</i>	1.74E-251	6.17	8.31	1.35
<i>Lmod1</i>	0.00E+00	6.16	6.32	1.03
<i>Cnn1</i>	0.00E+00	5.90	5.94	1.01
<i>Lgals1</i>	2.50E-267	5.85	19.83	3.39
<i>Cavin3</i>	1.02E-134	5.75	9.51	1.65
<i>Ppp1r14a</i>	0.00E+00	5.38	6.71	1.25
<i>Olfr558</i>	0.00E+00	5.28	5.32	1.01
<i>Actn1</i>	1.23E-198	5.12	10.01	1.95
<i>Zfhx3</i>	2.11E-172	4.99	8.98	1.80
<i>Chchd10</i>	1.78E-113	4.90	5.64	1.15
<i>Rasd1</i>	2.12E-106	4.63	4.86	1.05
<i>Cavin1</i>	9.47E-127	4.60	10.98	2.39
<i>Cox4i2</i>	0.00E+00	4.59	6.88	1.50
<i>Id2</i>	1.17E-66	4.33	9.62	2.22
<i>Gm13861</i>	0.00E+00	4.28	5.05	1.18
<i>Pdlim3</i>	0.00E+00	4.27	4.31	1.01
<i>Ptgis</i>	0.00E+00	4.24	4.32	1.02
<i>Dstn</i>	5.72E-94	4.24	10.29	2.43
<i>Nrarp</i>	4.62E-156	4.18	5.41	1.29

<i>Coll8a1</i>	2.76E-73	4.11	5.17	1.26
<i>Atp1a2</i>	0.00E+00	3.95	3.98	1.01
<i>Hspb2</i>	2.47E-257	3.95	4.09	1.04
<i>Uba2</i>	2.42E-102	3.94	8.94	2.27
<i>Nme2</i>	2.04E-86	3.84	8.58	2.23
<i>Tpm1</i>	1.32E-94	3.84	26.22	6.83
<i>Ramp1</i>	0.00E+00	3.83	3.86	1.01
<i>Mef2c</i>	4.99E-114	3.81	11.75	3.08
<i>Filip1l</i>	2.38E-173	3.78	4.76	1.26
<i>Eln</i>	8.62E-84	3.72	3.89	1.05
<i>Aoc3</i>	0.00E+00	3.67	4.07	1.11
<i>Cenpa</i>	1.49E-264	3.63	3.90	1.07
<i>Rgs7bp</i>	0.00E+00	3.62	3.68	1.02
<i>Kcna5</i>	0.00E+00	3.56	3.59	1.01
<i>Mylk</i>	4.71E-70	3.38	27.94	8.28
<i>Ppp1r12a</i>	2.01E-86	3.29	8.27	2.51
<i>Cd200</i>	4.41E-59	3.26	5.13	1.57
<i>Gng1l</i>	3.11E-47	3.24	16.39	5.05
<i>Tuba1c</i>	4.56E-78	3.22	4.71	1.46
<i>Mgst3</i>	2.36E-64	3.20	4.71	1.47
<i>Cav1</i>	8.28E-73	3.20	3.44	1.07
<i>Myl9</i>	4.62E-105	3.18	91.43	28.77
<i>Csrp2</i>	6.22E-49	3.17	4.62	1.46
<i>Tsc22d1</i>	5.28E-55	3.05	18.45	6.04
<i>Nbl1</i>	3.19E-69	3.05	3.69	1.21
<i>Cd24a</i>	4.47E-62	3.02	5.85	1.93
<i>Nexn</i>	8.28E-117	3.00	3.98	1.32
<i>Angptl4</i>	2.75E-71	-3.02	1.26	3.81
<i>Pdlim2</i>	2.22E-69	-3.03	1.57	4.77
<i>Coil</i>	4.24E-74	-3.03	1.18	3.59
<i>Gpsm3</i>	8.76E-72	-3.07	1.29	3.94
<i>Bst2</i>	1.91E-55	-3.07	1.66	5.11
<i>Mrc1</i>	2.73E-155	-3.08	1.07	3.30
<i>Cp</i>	2.17E-102	-3.10	1.00	3.10
<i>Gm9844</i>	2.01E-71	-3.11	1.33	4.14
<i>Eva1b</i>	7.90E-79	-3.14	2.64	8.28
<i>Mxd4</i>	1.93E-76	-3.15	2.24	7.06
<i>Srgn</i>	5.86E-91	-3.19	1.41	4.51
<i>Psen2</i>	3.69E-100	-3.21	1.06	3.40
<i>Cpm</i>	5.66E-168	-3.22	1.57	5.04

<i>Cxcl13</i>	1.13E-31	-3.22	1.05	3.39
<i>Col4a1</i>	3.01E-92	-3.23	3.05	9.85
<i>Tmsb4x</i>	9.84E-241	-3.25	41.44	134.81
<i>Sgkl</i>	7.74E-72	-3.31	2.37	7.86
<i>Rgl1</i>	4.33E-71	-3.31	1.20	3.97
<i>Marcks11</i>	5.40E-63	-3.43	1.81	6.21
<i>S100a10</i>	2.22E-71	-3.50	1.46	5.11
<i>Slc12a2</i>	2.98E-168	-3.51	1.38	4.85
<i>Igfbp7</i>	7.31E-183	-3.52	54.72	192.44
<i>Cd53</i>	1.18E-76	-3.53	1.15	4.07
<i>Nupr1</i>	6.62E-72	-3.62	1.78	6.42
<i>Anxa2</i>	4.76E-118	-3.70	2.35	8.68
<i>Agtr1a</i>	0.00E+00	-3.72	4.01	14.91
<i>Ifitm3</i>	5.16E-142	-3.75	8.71	32.65
<i>Tmsb10</i>	5.46E-109	-3.78	1.73	6.53
<i>Gstm1</i>	8.36E-114	-3.78	3.28	12.39
<i>Cited2</i>	1.41E-55	-3.78	2.24	8.49
<i>Nrpl</i>	9.46E-177	-3.79	5.29	20.07
<i>Fhl2</i>	2.23E-304	-3.83	4.23	16.19
<i>Gm13588</i>	7.58E-110	-3.90	1.63	6.34
<i>Gpc3</i>	4.58E-169	-3.95	1.61	6.37
<i>Ets1</i>	3.39E-107	-3.96	1.61	6.36
<i>H2-D1</i>	2.97E-203	-4.00	3.54	14.18
<i>Lmo7</i>	8.47E-232	-4.02	1.98	7.98
<i>Serpine2</i>	1.08E-228	-4.06	8.56	34.77
<i>Igfbp5</i>	5.37E-97	-4.12	7.90	32.53
<i>Tns3</i>	7.06E-121	-4.13	2.41	9.95
<i>Gata3</i>	2.94E-287	-4.14	3.02	12.52
<i>Gm22133</i>	3.38E-210	-4.16	8.30	34.52
<i>Fil1</i>	2.42E-214	-4.18	8.49	35.49
<i>Ehd3</i>	8.11E-111	-4.20	2.25	9.47
<i>B2m</i>	1.76E-170	-4.29	5.94	25.45
<i>Maf</i>	2.37E-216	-4.33	1.84	7.96
<i>Nt5e</i>	1.97E-271	-4.58	1.24	5.67
<i>Dkk2</i>	1.79E-173	-4.61	4.75	21.86
<i>F2r</i>	3.96E-129	-4.67	2.13	9.96
<i>Sept4</i>	0.00E+00	-4.93	2.28	11.22
<i>Itga8</i>	0.00E+00	-5.59	2.09	11.68
<i>Apoe</i>	9.23E-174	-5.68	2.08	11.83
<i>Art3</i>	2.84E-300	-5.86	1.11	6.48

<i>Cd34</i>	9.36E-177	-5.98	1.30	7.75
<i>Ctgf</i>	2.04E-267	-6.17	2.46	15.19
<i>Eng</i>	9.89E-281	-6.21	2.18	13.54
<i>Prkca</i>	5.07E-227	-6.63	1.51	10.00
<i>Plscr2</i>	5.66E-232	-6.88	1.85	12.73
<i>Plvap</i>	3.42E-318	-8.33	1.21	10.09
<i>Adamts5</i>	0.00E+00	-8.56	2.53	21.63
<i>Sfrp2</i>	0.00E+00	-11.63	3.87	45.03
<i>Igfbp4</i>	0.00E+00	-14.36	1.56	22.37
<i>Ptn</i>	0.00E+00	-19.08	2.10	40.00

Supplemental Table 5. Genes differentially expressed between mesangial cells (cluster 3) and SMCs/JG cells (cluster 5)

Supplemental Table 6

Gene symbol	Adj p-value	Fold change (mesangial vs. rest)	Mean (mesangial)	Mean (rest)	Mean (podocyte)	Mean (endothelial)	Mean (SMC)	Mean (PEC)	Mean (immune)	Mean (TEC)
<i>Sfrp2</i>	0.00E+00	22.75	44.97	1.98	1.56	1.52	3.82	1.70	1.63	1.64
<i>Ptn</i>	0.00E+00	20.79	39.94	1.92	1.80	1.78	2.09	2.53	1.67	1.66
<i>Igfbp4</i>	0.00E+00	12.72	22.34	1.76	1.33	2.89	1.57	1.82	1.43	1.50
<i>Serpine2</i>	0.00E+00	12.45	34.77	2.79	1.62	2.00	8.05	1.71	1.80	1.59
<i>Adamts5</i>	0.00E+00	11.36	21.61	1.90	1.33	2.25	2.37	2.62	1.42	1.42
<i>Itga8</i>	0.00E+00	8.41	11.67	1.39	1.25	1.29	2.08	1.25	1.22	1.24
<i>Agtr1a</i>	0.00E+00	8.08	14.91	1.85	1.25	1.25	3.86	2.23	1.21	1.27
<i>Gata3</i>	0.00E+00	7.72	12.51	1.62	1.22	1.27	2.94	1.28	1.20	1.82
<i>Plvap</i>	0.00E+00	7.42	10.07	1.36	1.21	1.91	1.22	1.26	1.38	1.17
<i>Ctgf</i>	0.00E+00	7.38	15.18	2.06	1.77	1.41	2.36	3.78	1.33	1.68
<i>Dkk2</i>	0.00E+00	7.26	21.85	3.01	1.35	8.02	4.50	1.37	1.45	1.38
<i>Sept4</i>	0.00E+00	7.09	11.20	1.58	1.17	1.43	2.24	1.38	1.15	2.11
<i>Fhl2</i>	0.00E+00	6.82	16.20	2.38	1.26	1.31	3.93	4.89	1.39	1.48
<i>Lhfp</i>	0.00E+00	6.55	11.37	1.74	1.24	1.37	3.80	1.58	1.21	1.22
<i>Bgn</i>	0.00E+00	6.46	28.85	4.46	1.64	2.71	12.92	5.99	1.85	1.68
<i>Des</i>	0.00E+00	6.23	15.29	2.45	1.33	1.25	7.67	1.96	1.34	1.17
<i>Mfge8</i>	0.00E+00	6.03	32.16	5.34	3.88	3.66	16.23	3.53	2.13	2.57
<i>Prkca</i>	0.00E+00	5.86	9.99	1.70	1.70	1.87	1.42	1.64	2.20	1.39
<i>Art3</i>	0.00E+00	5.70	6.47	1.14	1.07	1.22	1.11	1.16	1.13	1.12
<i>Rgs2</i>	0.00E+00	5.69	15.20	2.67	1.45	1.95	6.45	1.62	2.80	1.77
<i>Lmo7</i>	0.00E+00	5.20	7.99	1.54	1.14	1.62	1.75	1.34	1.11	2.27
<i>Nt5e</i>	0.00E+00	4.98	5.67	1.14	1.11	1.14	1.21	1.08	1.15	1.14
<i>Gdf10</i>	0.00E+00	4.95	7.12	1.44	1.12	1.16	2.97	1.11	1.15	1.12
<i>Serpini1</i>	0.00E+00	4.39	7.77	1.77	1.14	1.43	4.53	1.07	1.23	1.23
<i>Igfbp5</i>	0.00E+00	4.32	32.48	7.52	2.12	27.86	8.00	2.25	2.31	2.56
<i>Maf</i>	0.00E+00	4.25	7.96	1.87	1.06	1.37	1.83	3.86	1.74	1.38
<i>Slc12a2</i>	0.00E+00	4.06	4.84	1.19	1.07	1.23	1.39	1.12	1.10	1.25
<i>Gucy1a3</i>	0.00E+00	4.01	6.01	1.50	1.13	1.16	3.35	1.17	1.06	1.12
<i>Cpm</i>	0.00E+00	3.94	5.04	1.28	1.12	1.20	1.58	1.07	1.33	1.37
<i>Gpc3</i>	0.00E+00	3.93	6.37	1.62	1.60	1.16	1.59	2.82	1.10	1.43
<i>Cd34</i>	0.00E+00	3.90	7.75	1.98	1.21	5.69	1.27	1.34	1.21	1.19
<i>Col4a1</i>	0.00E+00	3.87	9.83	2.54	1.22	3.53	3.05	3.96	1.39	2.08
<i>F2r</i>	0.00E+00	3.79	9.95	2.63	2.05	5.11	2.12	3.82	1.28	1.39

<i>Epas1</i>	0.00E+00	3.75	13.64	3.64	1.81	8.00	6.49	2.04	1.73	1.78
<i>Rasgrp2</i>	0.00E+00	3.69	7.49	2.03	1.11	2.02	4.23	1.21	2.45	1.14
<i>Mecom</i>	0.00E+00	3.68	5.92	1.61	1.06	1.83	2.33	1.10	1.07	2.27
<i>Tns3</i>	0.00E+00	3.62	9.94	2.74	3.77	2.51	2.40	3.25	2.00	2.52
<i>Ebfl</i>	0.00E+00	3.58	10.86	3.04	1.14	4.11	9.02	1.28	1.49	1.18
<i>Pdgfrb</i>	0.00E+00	3.51	6.98	1.99	1.30	1.19	4.34	2.74	1.24	1.12
<i>Nrp1</i>	0.00E+00	3.47	20.06	5.78	2.91	18.91	5.08	4.18	1.79	1.84
<i>Vcl</i>	0.00E+00	3.45	7.17	2.08	1.59	1.72	2.78	2.65	1.54	2.20
<i>Scn1b</i>	0.00E+00	3.43	4.09	1.19	1.05	1.21	1.62	1.06	1.04	1.17
<i>Col4a2</i>	0.00E+00	3.37	7.23	2.15	1.17	2.76	3.10	3.03	1.24	1.56
<i>Scarf2</i>	0.00E+00	3.33	3.91	1.17	1.05	1.07	1.38	1.39	1.04	1.11
<i>Cxcl13</i>	2.92E-166	3.26	3.38	1.04	1.03	1.03	1.05	1.06	1.04	1.02
<i>Eva1b</i>	0.00E+00	3.22	8.28	2.57	2.68	4.23	2.50	2.63	1.35	2.06
<i>Angptl4</i>	0.00E+00	3.18	3.80	1.19	1.16	1.09	1.27	1.39	1.08	1.18
<i>Amotl1</i>	0.00E+00	3.14	5.01	1.60	1.18	2.53	1.96	1.35	1.27	1.28
<i>Pik3r1</i>	0.00E+00	3.12	4.74	1.52	1.32	1.32	1.81	1.46	1.38	1.82
<i>Aldh2</i>	0.00E+00	3.10	10.02	3.23	1.75	2.24	4.69	3.39	4.61	2.71
<i>Isyna1</i>	0.00E+00	3.10	7.07	2.28	2.08	1.89	2.96	2.76	1.74	2.27
<i>Mrc1</i>	0.00E+00	3.06	3.29	1.08	1.06	1.04	1.07	1.03	1.20	1.06
<i>Coil</i>	0.00E+00	3.02	3.58	1.19	1.12	1.35	1.19	1.14	1.22	1.10
<i>Ets1</i>	0.00E+00	3.02	6.36	2.11	1.52	4.36	1.53	1.66	2.23	1.36

Supplemental Table 6. Genes enriched in mesangial cells. Genes with very low expression levels (Mean < 2) in all non-mesangial cell types are in bold.

Supplemental Table 7

	up-regulated		down-regulated	
	day 1	day 5	day1	day 5
podocytes	263	80	312	132
mesangial	85	101	56	99
endothelial	165	206	189	248

5 **Supplemental Table 7.** Number of differentially expressed genes in nephritic mice (> 1.5 FC vs. control, adjusted p-value < 0.01)

Supplemental Table 8

	Karaikos <i>et al.</i>²³	Fu <i>et al.</i>²⁴	Park <i>et al.</i>²⁸	Ransick <i>et al.</i>⁴⁶	Wu <i>et al.</i>⁴⁷				Lake <i>et al.</i>⁴⁸	this study
species	mouse	mouse	mouse	mouse	mouse				human	mouse
sample	purified glomeruli (cells)	purified glomeruli (cells)	whole kidney (cells)	whole kidney (cells)	whole kidney (cells)	whole kidney (nuclei)	whole kidney (nuclei)	whole kidney (nuclei)	whole kidney (nuclei)	purified glomeruli (cells)
method	Drop-Seq	Fluidigm C1	10X	10X	Drop-Seq	DroNc-Seq	Drop-Seq	10X	snDrop-Seq	10X
detected genes/cell (median)	626	3457	940	1571	812	937	736	757	589	2878*
mitochondrial reads % (median)	4.92%	10.91%	19.26%	1.02%	22.77%	NA	NA	NA	NA	0.72*
# of podocytes	10,364	48	78	24	0	45	75	107	859	11,431
# of total cells	12,954	644	43,745	31,265	3,535	2,772	3,056	2,159	17,659	74,149
% podocyte of total cells	80.01%	7.45%	0.18%	0.08%	0.00%	1.62%	2.45%	4.96%	4.86%	15.42%
notes	skewed cell population conflated vSMCs and mesangial cell low yield (required 32 mice to obtain ~13,000 cells)	low cell numbers conflated vSMCs and mesangial cells	low detection of glomerular cells did not identify mesangial cells	low detection of glomerular cells did not identify mesangial cells	did not distinguish glomerular/non-glomerular endothelial cells					*values calculated from healthy B6 sample. values are similar for all samples

Supplementary Table 8. Comparison of kidney single cell datasets.

Supplemental Table 9

D, C, O, N	D, O, N	C, O, N	D, C, O	D, C, N
<i>Spink8</i>	<i>Spink8</i>	<i>Acta2</i>	<i>Spink8</i>	<i>Spink8</i>
<i>Lgals1</i>	<i>F2r</i>	<i>P2rx1</i>	<i>Lgals1</i>	<i>Lgals1</i>
<i>Vegfd</i>	<i>Lgals1</i>	<i>Tagln</i>	<i>Vegfd</i>	<i>Vegfd</i>
<i>Acta2</i>	<i>Vegfd</i>	<i>Lgals1</i>	<i>Acta2</i>	<i>Tpm2</i>
<i>Ccnd1</i>	<i>Acta2</i>	<i>Ankrd1</i>	<i>Ccnd1</i>	<i>Acta2</i>
	<i>Ccnd1</i>	<i>Spon2</i>		<i>Ccnd1</i>
		<i>Enho</i>		
		<i>Spink8</i>		
		<i>Vegfd</i>		
		<i>Ccnd1</i>		

D: doxorubicin

C: *Cd2ap*^{-/-}

O: BTBR ob/ob

N: nephrotoxic serum nephritis

- 5 **Supplemental Table 9.** List of genes induced in mesangial cells in 3 or more injury models. Genes involved in wound healing response are in bold.