

Fig. S1. Differentially expressed genes and gene enrichment analysis for UNx-Renin mice compared to UNx mice in both glomeruli and kidney cortex samples. (A) Total number of DEGs in glomeruli and kidney cortex in UNx-Renin mice compared to UNx mice. (B) Venn diagram depicting shared and separate DEGs in glomeruli and kidney cortex. (C) Reactome pathway gene enrichment analysis in glomeruli and kidney cortex. Degree of perturbation is presented as the $-\log_{10}(\text{p-value})$ after correction for gene-wise multiple testing ($n=5-13$).

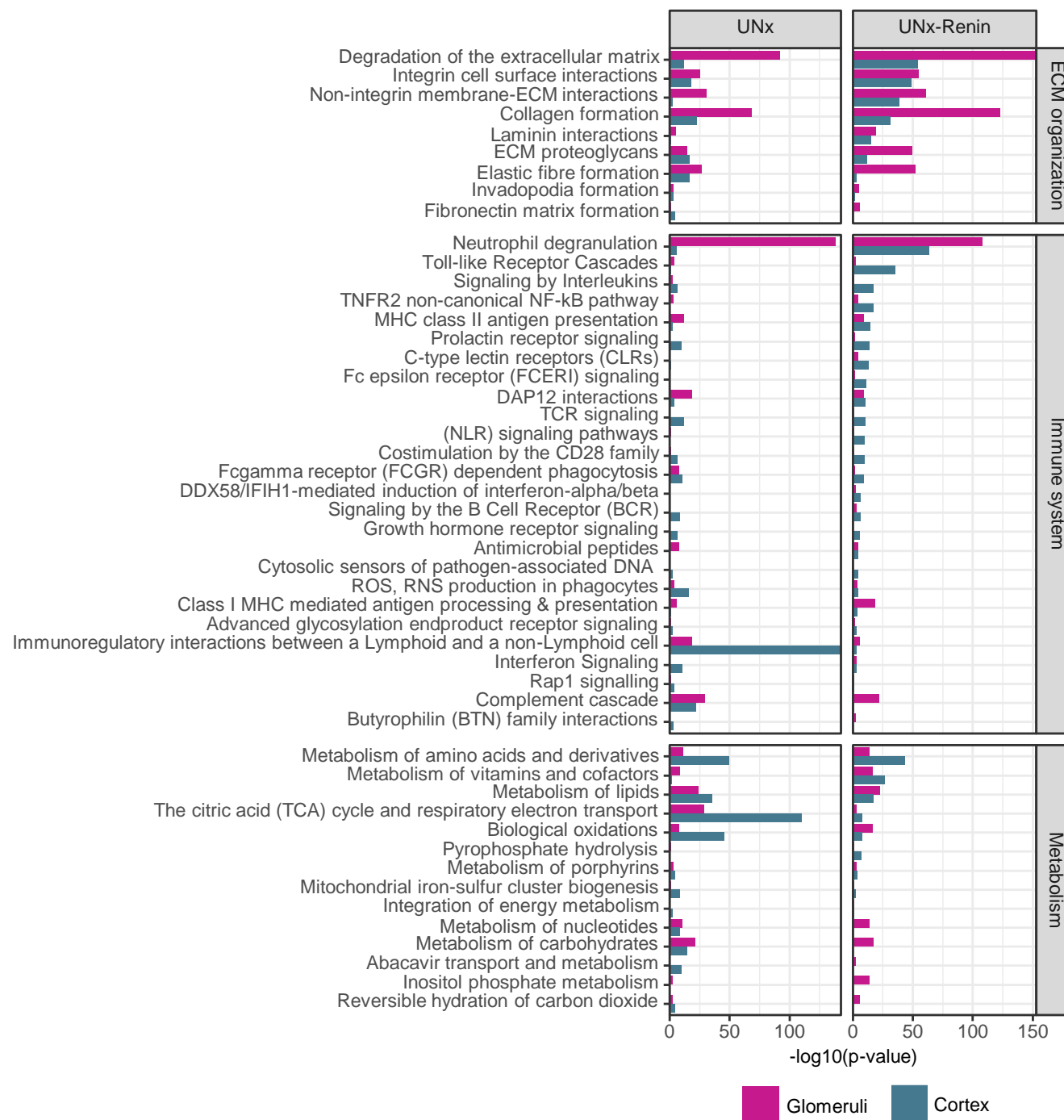


Fig. S2. Gene enrichment analysis using Reactome of sub-pathways for UNx or UNx-Renin mice compared to db/m controls. Degree of perturbation is presented as the $-\log_{10}(\text{p-value})$ after correction for gene-wise multiple testing (n=5-13).

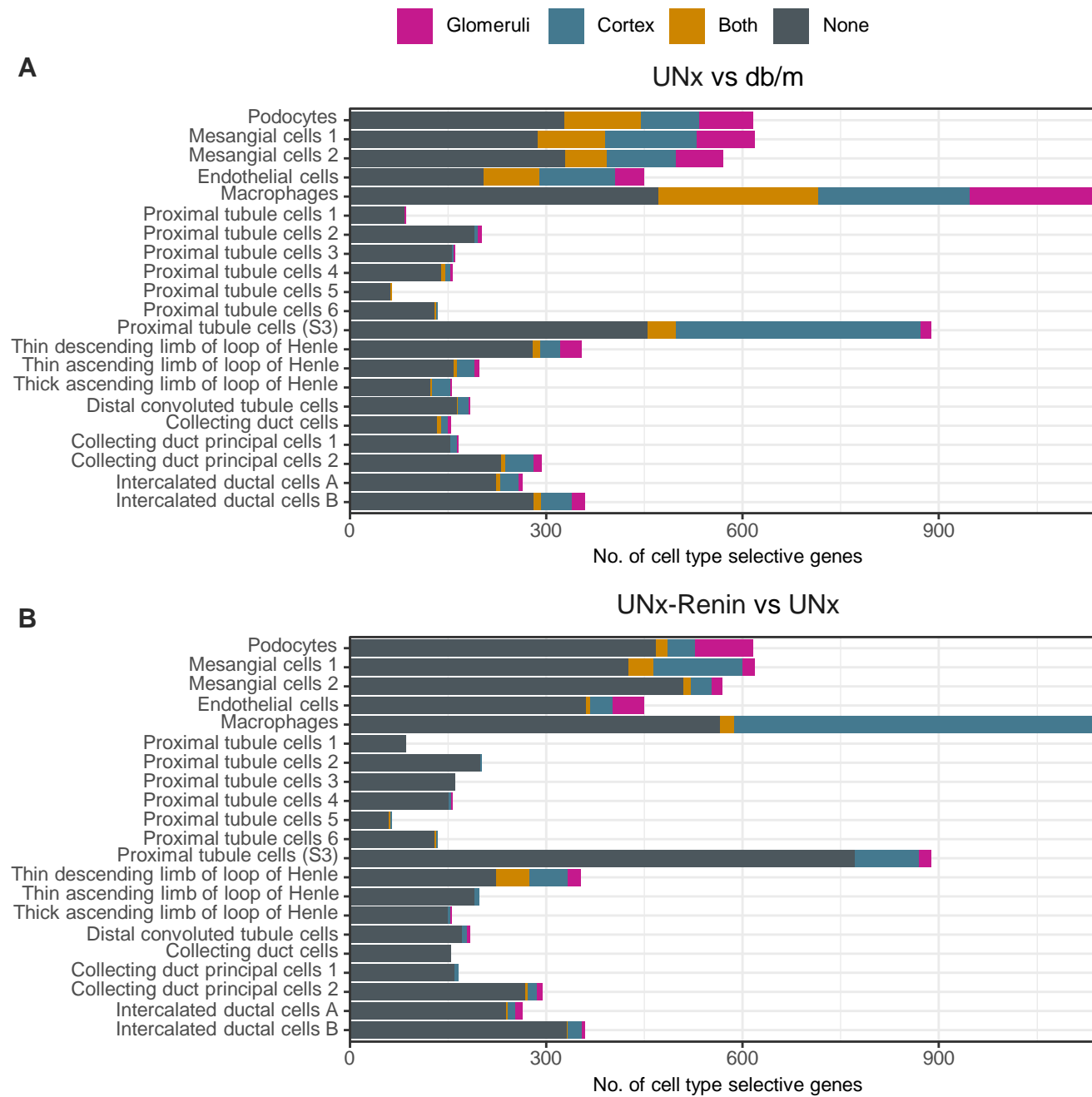


Fig. S3. DEGs mapped to specific cell types. (A) Number of cell type specific DEGs between UNx mice and db/m controls, or (B) between UNx-Renin and UNx mice, in glomeruli, cortex, both or none of the two tissue areas. Genes were defined as specific to the cell population with the highest average expression level, if the expression level was increased by 2-fold as compared to the cell population with the second highest expression level.

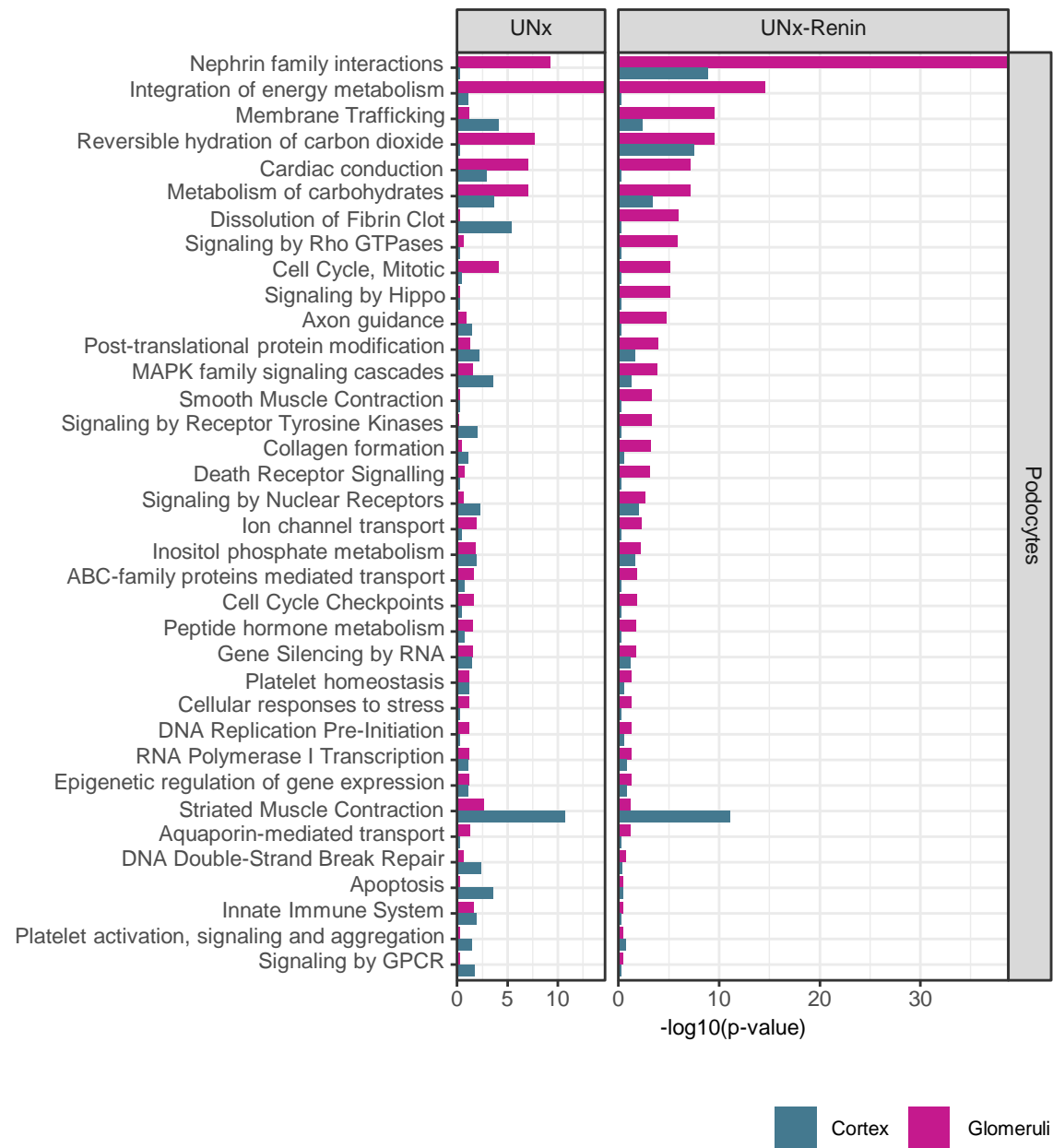


Fig. S4. Podocyte- specific DEGs found in kidney cortex and glomeruli of UNx and UNx-Renin mice compared to db/m controls. Degree of perturbation is presented as the $-\log_{10}(\text{p-value})$ after correction for gene-wise multiple testing (n=5-13).

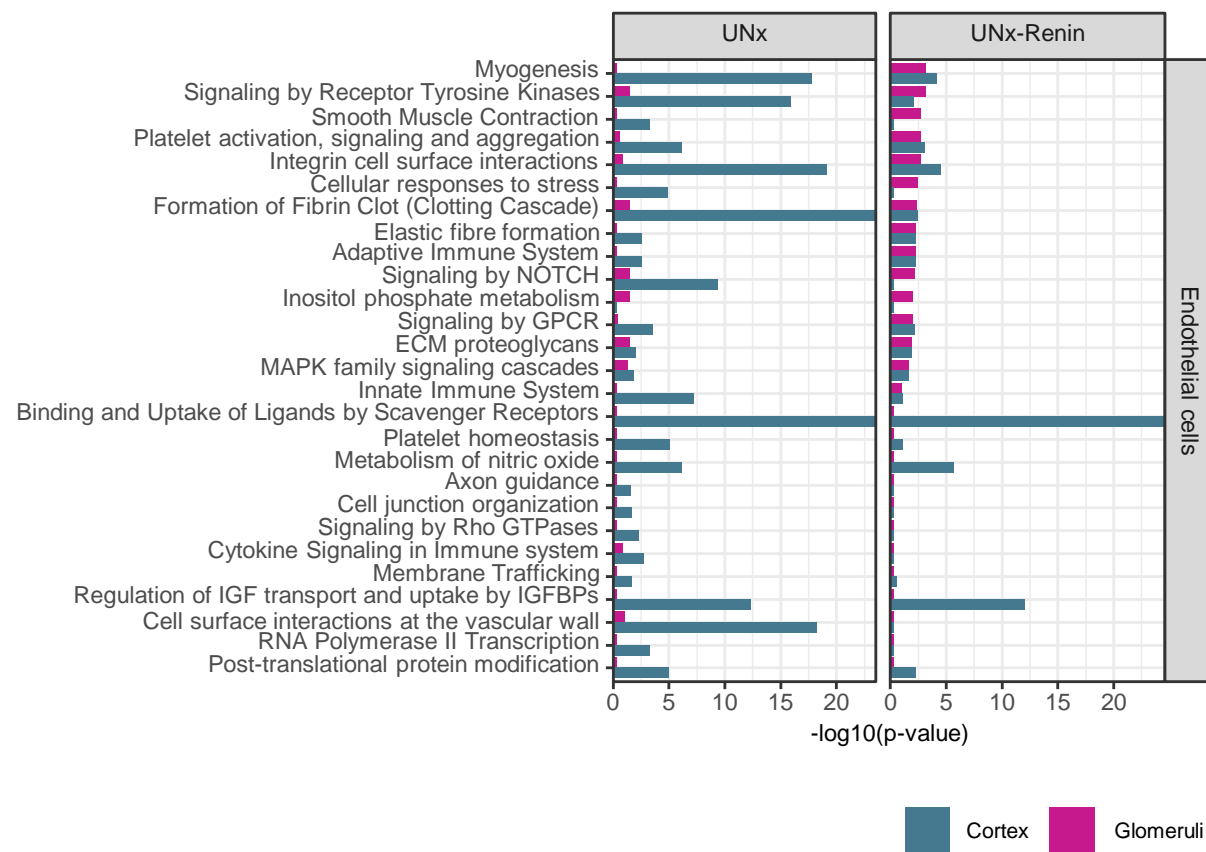


Fig. S5. Endothelial cell- specific DEGs found in kidney cortex and glomeruli of UNx and UNx-Renin mice compared to db/m controls. Degree of perturbation is presented as the $-\log_{10}(\text{p-value})$ after correction for gene-wise multiple testing (n=5-13).



Fig. S6. Mesangial cell- specific DEGs found in kidney cortex and glomeruli of UNx and UNx-Renin mice compared to db/m controls. Degree of perturbation is presented as the $-\log_{10}(\text{p-value})$ after correction for gene-wise multiple testing (n=5-13).

Table S1. Selected differential expressed genes (DEGs) in kidney cortex

Summary of selected DEGs in kidney cortex and comparison to relevant transcriptomic studies of human DKD (Woroniccka *et al.*, 2011; Ju *et al.*, 2013; Levin *et al.*, 2020; Fan *et al.*, 2019; Verzola *et al.*, 2014; Sircar *et al.*, 2018) including use of the Nephroseq database. Fold change, FC; NA, not applicable; NS, non-significant.

Gene Name	Gene Description	UNx vs db/m	UNx-Renin vs db/m	UNx-Renin vs UNx	Human DKD Transcriptomics
		Log ₂ FC (p-value)	Log ₂ FC (p-value)	Log ₂ FC (p-value)	
<i>Adamts4</i>	a disintegrin-like and metallopeptidase (reprolysin type) with thrombospondin type 1 motif, 4	0.5 (0.13)	1.3 (0.001)	0.8 (0.07)	NA
<i>C3</i>	complement component 3	0.0 (0.87)	1.8 (5.54E-11)	1.8 (7.08E-11)	Upregulated in tubulointerstitium in Woroniccka <i>et al.</i> , 2011 and Ju <i>et al.</i> , 2013.
<i>C6</i>	complement component 6	1.3 (0.0006)	2.7 (3.09E-10)	1.4 (0.002)	Upregulated in tubulointerstitium in Woroniccka <i>et al.</i> , 2011 and Ju <i>et al.</i> , 2013.
<i>C7</i>	complement component 7	0.9 (0.0004)	1.9 (1.98E-08)	1.0 (0.01)	Upregulated in tubulointerstitium in Woroniccka <i>et al.</i> , 2011; Ju <i>et al.</i> , 2013 and Sircar <i>et al.</i> , 2018.
<i>Col1a1</i>	collagen, type I, alpha 1	-0.9 (0.01)	1.1 (0.03)	2.0 (2.49E-05)	Upregulated in tubulointerstitium in Woroniccka <i>et al.</i> , 2011; Ju <i>et al.</i> , 2013 and Levin <i>et al.</i> , 2020.
<i>Col3a1</i>	collagen, type III, alpha 1	-1.4 (2.26E-05)	0.6 (0.25)	2.0 (1.38E-05)	Upregulated in tubulointerstitium in Woroniccka <i>et al.</i> , 2011 and Ju <i>et al.</i> , 2013.
<i>Col5a1</i>	collagen, type V, alpha 1	-0.7 (2.47E-08)	0.2 (0.25)	0.9 (6.83E-08)	Upregulated in tubulointerstitium in Woroniccka <i>et al.</i> , 2011 and Ju <i>et al.</i> , 2013.
<i>Col5a3</i>	collagen, type V, alpha 3	0.2 (0.47)	1.1 (7.61E-06)	0.9 (0.0004)	NS regulated in Ju <i>et al.</i> , 2013, while downregulated in Woroniccka <i>et al.</i> , 2011.

<i>Col6a1</i>	collagen, type VI, alpha 1	-0.2 (0.09)	0.6 (0.0001)	0.9 (2.36E-07)	Downregulated in tubulointerstitium in Woroniecka <i>et al.</i> , 2011 and Ju <i>et al.</i> , 2013.
<i>Col6a2</i>	collagen, type VI, alpha 2	-0.2 (0.24)	0.9 (6.16E-06)	1.1 (4.98E-08)	Upregulated in tubulointerstitium in Woroniecka <i>et al.</i> , 2011 and NS regulated in Ju <i>et al.</i> , 2013.
<i>Cxcl1</i>	chemokine (C-X-C motif) ligand 1	1.2 (0.08)	3.8 (3.23E-06)	2.6 (0.003)	Upregulated in whole kidney in Fan <i>et al.</i> , 2019 and in tubulointerstitium in Woroniecka <i>et al.</i> , 2011 and Ju <i>et al.</i> , 2013.
<i>Cxcl2</i>	chemokine (C-X-C motif) ligand 2	1.0 (0.21)	5.1 (2.28E-13)	4.2 (5.50E-10)	Downregulated in whole kidney in Fan <i>et al.</i> , 2019 and NS regulated in tubulointerstitium in Woroniecka <i>et al.</i> , 2011 and Ju <i>et al.</i> , 2013.
<i>Cyp2d9</i>	cytochrome P450, family 2, subfamily d, polypeptide 9	2.8 (3.72E-50)	2.4 (1.60E-20)	-0.4 (0.20)	NA
<i>Fn1</i>	fibronectin 1	-0.5 (0.008)	0.7 (0.008)	1.3 (2.25E-06)	Upregulated in tubulointerstitium in Woroniecka <i>et al.</i> , 2011 and Ju <i>et al.</i> , 2013.
<i>Lox</i>	lysyl oxidase	0.1 (0.81)	1.4 (8.50E-07)	1.3 (8.62E-06)	NS regulated in tubulointerstitium in Woroniecka <i>et al.</i> , 2011, while downregulated in Ju <i>et al.</i> , 2013.
<i>Mapk12</i>	mitogen-activated protein kinase 12	-0.5 (7.55E-08)	-0.7 (1.64E-08)	-0.2 (0.18)	NS regulated in tubulointerstitium in Ju <i>et al.</i> , 2013.
<i>Mmp12</i>	matrix metalloproteinase 12	0.8 (0.02)	3.2 (3.22E-23)	2.4 (2.78E-14)	NS regulated in tubulointerstitium in Woroniecka <i>et al.</i> , 2011 and Ju <i>et al.</i> , 2013.
<i>Mmp14</i>	matrix metalloproteinase 14 (membrane-inserted)	-0.3 (0.06)	0.7 (0.001)	1.1 (2.05E-06)	NS regulated in tubulointerstitium in Ju <i>et al.</i> , 2013, while downregulated in Woroniecka <i>et al.</i> , 2011.
<i>Mmp3</i>	matrix metalloproteinase 3	-0.1 (0.86)	1.1 (0.16)	1.3 (0.13)	NS regulated in tubulointerstitium in Woroniecka <i>et al.</i> , 2011 and Ju <i>et al.</i> , 2013.

<i>Mmp7</i>	matrix metalloproteinase 7	-2.1 (0.16)	2.7 (0.15)	4.8 (0.01)	Upregulated in whole kidney in Fan <i>et al.</i> , 2019 and in tubulointerstitium in Woroniecka <i>et al.</i> , 2011 and Ju <i>et al.</i> , 2013.
<i>Mmp8</i>	matrix metalloproteinase 8	0.9 (0.42)	2.2 (0.08)	1.2 (0.36)	NS regulated in tubulointerstitium in Ju <i>et al.</i> , 2013, while downregulated in Woroniecka <i>et al.</i> , 2011.
<i>Nphs1</i>	nephrosis 1, nephrin	-0.1 (0.59)	-0.5 (0.001)	-0.4 (0.01)	Downregulated in tubulointerstitium in Woroniecka <i>et al.</i> , 2011 and Ju <i>et al.</i> , 2013.
<i>Nphs2</i>	nephrosis 2, podocin	0.1 (0.58)	-0.1 (0.81)	-0.1 (0.50)	NS regulated in tubulointerstitium in Woroniecka <i>et al.</i> , 2011, while downregulated in Ju <i>et al.</i> , 2013.
<i>Rbp2</i>	retinol binding protein 2, cellular	3.4 (0.0003)	2.7 (0.04)	-0.7 (0.63)	NA
<i>Serpine1</i>	serine (or cysteine) peptidase inhibitor, clade E, member 1	0.0 (0.89)	1.1 (0.0001)	1.0 (0.0004)	Downregulated in tubulointerstitium in Woroniecka <i>et al.</i> , 2011 and Ju <i>et al.</i> , 2013.
<i>Timp1</i>	tissue inhibitor of metalloproteinase 1	-0.6 (0.51)	2.1 (0.04)	2.6 (0.008)	Upregulated in tubulointerstitium in Woroniecka <i>et al.</i> , 2011 and Ju <i>et al.</i> , 2013.
<i>Tlr4</i>	toll-like receptor 4	-0.1 (0.52)	0.6 (0.03)	0.7 (0.006)	Upregulated in tubulointerstitium in Verzola <i>et al.</i> , 2014, and Ju <i>et al.</i> , 2013.
<i>Ugt1a10</i>	UDP glycosyltransferase 1 family, polypeptide A10	1.8 (3.58E-30)	1.8 (2.08E-18)	0.1 (0.88)	NA
<i>Vcam1</i>	vascular cell adhesion molecule 1	-0.4 (0.02)	2.4 (3.57E-29)	2.8 (2.53E-40)	Upregulated in tubulointerstitium in Woroniecka <i>et al.</i> , 2011 and Ju <i>et al.</i> , 2013.

Table S2. Selected differential expressed genes (DEGs) in glomeruli

Summary of selected DEGs in glomeruli and comparison to relevant transcriptomic studies of human DKD (Woroniccka <i>et al.</i> , 2011; Ju <i>et al.</i> , 2013; Levin <i>et al.</i> , 2020; Verzola <i>et al.</i> , 2014) including use of the Nephroseq database. Fold change, FC; NA, not applicable; NS, non-significant.					
Gene Name	Gene Description	UNx vs db/m	UNx-Renin vs db/m	UNx-Renin vs UNx	Comments
		Log ₂ FC (p-value)	Log ₂ FC (p-value)	Log ₂ FC (p-value)	
<i>Adamts4</i>	a disintegrin-like and metallopeptidase (reprolysin type) with thrombospondin type 1 motif, 4	3.8 (1.39E-11)	3.4 (1.89E-09)	-0.4 (0.74)	NA
<i>C3</i>	complement component 3	-0.1 (0.94)	2.2 (1.48E-05)	2.3 (5.39E-05)	Upregulated in glomeruli in Woroniccka <i>et al.</i> , 2011; Ju <i>et al.</i> , 2013 and Levin <i>et al.</i> , 2020.
<i>C6</i>	complement component 6	5.2 (1.22E-08)	3.0 (0.003)	-2.2 (0.03)	NS regulated in glomeruli in Woroniccka <i>et al.</i> , 2011, while downregulated in Ju <i>et al.</i> , 2013.
<i>C7</i>	complement component 7	1.4 (0.30)	2.1 (0.08)	0.6 (0.81)	Upregulated in glomeruli in Woroniccka <i>et al.</i> , 2011, while NS regulated in Ju <i>et al.</i> , 2013.
<i>Col1a1</i>	collagen, type I, alpha 1	1.1 (0.37)	2.7 (0.003)	1.7 (0.25)	Upregulated in glomeruli in Woroniccka <i>et al.</i> , 2011; Ju <i>et al.</i> , 2013 and Levin <i>et al.</i> , 2020.
<i>Col3a1</i>	collagen, type III, alpha 1	0.7 (0.12)	2.1 (8.98E-09)	1.4 (0.002)	Upregulated in glomeruli in Ju <i>et al.</i> , 2013, while NS regulated in Woroniccka <i>et al.</i> , 2011.
<i>Col5a1</i>	collagen, type V, alpha 1	1.0 (8.24E-16)	1.4 (1.54E-31)	0.4 (0.01)	Upregulated in glomeruli in Woroniccka <i>et al.</i> , 2011 and Ju <i>et al.</i> , 2013.
<i>Col5a3</i>	collagen, type V, alpha 3	3.3 (2.74E-10)	5.2 (1.03E-25)	1.9 (0.0002)	NS regulated in glomeruli in Woroniccka <i>et al.</i> , 2011 and Ju <i>et al.</i> , 2013.
<i>Col6a1</i>	collagen, type VI, alpha 1	-0.3 (0.52)	2.0 (4.74E-08)	2.3 (8.54E-10)	Upregulated in glomeruli in Woroniccka <i>et al.</i> , 2011, while NS regulated in Ju <i>et al.</i> , 2013.

<i>Col6a2</i>	collagen, type VI, alpha 2	0.0 (0.97)	1.7 (8.35E-06)	1.7 (8.50E-05)	Upregulated in glomeruli in Woroniecka <i>et al.</i> , 2011 and Ju <i>et al.</i> , 2013.
<i>Cxcl1</i>	chemokine (C-X-C motif) ligand 1	1.4 (0.01)	3.1 (5.48E-10)	1.6 (0.01)	Upregulated in glomeruli in Ju <i>et al.</i> , 2013, while NS regulated in Woroniecka <i>et al.</i> , 2011.
<i>Cxcl2</i>	chemokine (C-X-C motif) ligand 2	1.3 (0.20)	3.4 (2.19E-05)	2.1 (0.04)	NS regulated in glomeruli in Woroniecka <i>et al.</i> , 2011 and Ju <i>et al.</i> , 2013.
<i>Cyp2d9</i>	cytochrome P450, family 2, subfamily d, polypeptide 9	1.9 (0.22)	1.3 (0.43)	-0.6 (0.86)	NA
<i>Fn1</i>	fibronectin 1	2.7 (1.58E-07)	4.2 (8.82E-19)	1.6 (0.01)	Upregulated in glomeruli in Woroniecka <i>et al.</i> , 2011 and Ju <i>et al.</i> , 2013.
<i>Lox</i>	lysyl oxidase	1.3 (0.0001)	3.2 (1.89E-29)	2.0 (2.39E-11)	Downregulated in glomeruli in Woroniecka <i>et al.</i> , 2011 and Ju <i>et al.</i> , 2013.
<i>Mapk12</i>	mitogen-activated protein kinase 12	-0.1 (0.51)	-0.5 (0.0002)	-0.4 (0.03)	NS regulated in glomeruli in Ju <i>et al.</i> , 2013.
<i>Mmp12</i>	matrix metalloproteinase 12	5.7 (3.78E-36)	6.3 (8.38E-46)	0.7 (0.08)	NS regulated in glomeruli in Woroniecka <i>et al.</i> , 2011 and Ju <i>et al.</i> , 2013.
<i>Mmp14</i>	matrix metalloproteinase 14 (membrane-inserted)	0.7 (1.74E-10)	0.8 (6.79E-15)	0.1 (0.59)	NS regulated in glomeruli in Woroniecka <i>et al.</i> , 2011, while downregulated in Ju <i>et al.</i> , 2013.
<i>Mmp3</i>	matrix metalloproteinase 3	2.1 (1.96E-05)	2.2 (4.96E-06)	0.1 (0.96)	in glomeruli in Woroniecka <i>et al.</i> , 2011, while NS regulated in Ju <i>et al.</i> , 2013.
<i>Mmp7</i>	matrix metalloproteinase 7	3.6 (0.27)	6.4 (0.02)	2.8 (0.58)	Upregulated in glomeruli in Woroniecka <i>et al.</i> , 2011 and Ju <i>et al.</i> , 2013.
<i>Mmp8</i>	matrix metalloproteinase 8	3.7 (2.48E-06)	3.0 (0.0002)	-0.7 (0.69)	NS regulated in glomeruli in Woroniecka <i>et al.</i> , 2011.
<i>Nphs1</i>	nephrosis 1, nephrin	-0.3 (0.02)	-0.8 (3.99E-16)	-0.6 (1.86E-06)	Downregulated in glomeruli in Woroniecka <i>et al.</i> , 2011 and Ju <i>et al.</i> , 2013.
<i>Nphs2</i>	nephrosis 2, podocin	0.1 (0.40)	-0.4 (0.002)	-0.5 (7.09E-05)	Downregulated in glomeruli in Woroniecka <i>et al.</i> , 2011, while NS regulated in Ju <i>et al.</i> , 2013.
<i>Rbp2</i>	retinol binding protein 2, cellular	3.0 (0.24)	0.9 (0.73)	-2.1 (0.42)	NA
<i>Serpine1</i>	serine (or cysteine) peptidase inhibitor, clade E, member 1	0.6 (0.02)	2.1 (1.58E-26)	1.5 (2.38E-13)	NS regulated in glomeruli in Woroniecka <i>et al.</i> , 2011.
<i>Timp1</i>	tissue inhibitor of metalloproteinase 1	2.0 (0.0007)	3.0 (3.01E-08)	1.0 (0.26)	NS regulated in glomeruli in Woroniecka <i>et al.</i> , 2011, while upregulated in Ju <i>et al.</i> , 2013.
<i>Tlr4</i>	toll-like receptor 4	0.6 (0.005)	0.7 (0.0002)	0.1 (0.75)	NS regulated in Ju <i>et al.</i> , 2013, but upregulated in Verzola <i>et al.</i> , 2014.
<i>Ugt1a10</i>	UDP glycosyltransferase 1 family, polypeptide A10	1.4 (0.68)	2.8 (0.41)	1.3 (0.69)	NA
<i>Vcam1</i>	vascular cell adhesion molecule 1	-0.4 (0.08)	0.4 (0.04)	0.8 (0.0001)	Upregulated in glomeruli in Woroniecka <i>et al.</i> , 2011 and Ju <i>et al.</i> , 2013.