Supplementary Materials

1. Supplementary Methods

Animal studies

Biospecimen collection: At the moment of sacrifice, blood was collected from the inferior vena cava under isoflurane anesthesia, and, following opening of the thoracic cavity to ensure that the animal is deceased, the kidneys were retrieved and sectioned in samples dedicated for histology and immunfluorescence (fixed in 10% neutral buffered formalin), protein and RNA analysis (flash-frozen in liquid nitrogen). Similarly, liver tissue sections from the left lateral lobe of the ANIT fed mice were fixed in neutral buffered formalin for histopathological processing, while other liver sections were flash-frozen in liquid nitrogen. Blood was collected from mice in heparinized tubes and plasma was separated following centrifugation at 7500 g for 5 minutes. Blood urea nitrogen (BUN) was measured using an InfinityUrea kit (Thermo Fisher Scientific, Wilmington, DE) and serum creatinine (SCr) was measured using a Creatinine Analyzer II (Beckman Coulter).

Human studies

Urine was collected from spontaneous voids or from indwelling Foley catheters. Urines dipstick analysis was performed (Multistix 8 SG, Bayer Corporation), followed by centrifugation at 3000g for 10 minutes and microscopic examination of the urine sediment (Olympus microscope). The urine supernatant was aliquoted into 1.8 mL eppendorf tubes and frozen within 4 hours of collection at -80°C. No additives or protease inhibitors were added. Urinary creatinine concentrations were measure using commercially available kit from Cayman Chemical.

Histology

Formalin fixed, paraffin embedded kidney sections were Masson Trichrome's stained and evaluated by a renal pathologist (Dr. Vanesa Bijol) under a light microscope in blinded fashion relative to sample group. Percent area of fibrosis relative to the total section area was evaluated. Sirius red staining of the liver sections was performed at the Michigan State University Investigative Histopathology Laboratory.

Immunofluorescence

Paraffin embedded kidney tissue sections (6 μm) were dewaxed and rehydrated by successive immersion for 5 min in 100% xylene, 1:1 xylene-ethanol, 100%, 90% and 70% ethanol solutions. Following heat-induced antigen retrieval, immunostaining was performed using antibodies from Abcam (rabbit polyclonal: anti- CDH11, GABRP, MRC1, PLD4, PLTP, SCN7A, STRA6) and Santa Cruz Biotechnology (rabbit polyclonal: anti- MGP, SMOC2; goat polyclonal: SYTL2). Primary antibodies were detected using species-specific Cy3 or FITC labeled secondary antibodies (Jackson ImmunoResearch Laboratories) and 4',6-Diamidino-2-phenylindole-containing mounting medium (Sigma-Aldrich) was used for nuclear staining. Images were captured at 630X magnification on a Carl Zeiss AxioImager.M2 using the AxioVision SE64 software.

Western blot

The sources of primary antibodies were: Abcam (rabbit polyclonal: anti- GABRP, MRC1, PLD4, PLTP, SCN7A, STRA6), Santa Cruz Biotechnology (rabbit polyclonal: anti- SMOC2; goat polyclonal: SYTL2), Life Technologies (mouse monoclonal: anti- CDH11), Enzo Life Sciences (mouse monoclonal: anti- MGP), Sigma (mouse monoclonal α-tubulin; assessed for loading control). Horseradish peroxidase–conjugated secondary antibodies against mouse, rabbit, or goat were from Jackson ImmunoResearch Laboratories. Images of the blots were taken using a ChemiDoc instrument and the analysis was performed using the ImageLab software provided by the manufacturer (BioRad).

RNA isolation and qRT-PCR

Total RNA was extracted from frozen kidney tissue using TRIzol reagent (Invitrogen). Following RNA concentration measurement by NanoDrop spectrophotometer (Thermo Fischer Scientific), 1 µg RNA was used for cDNA preparation using QuantiTect Reverse Transcription Kit from Qiagen (Valencia, CA). qRT- PCR using QuantiFast SYBR Green PCR Kit (Qiagen) was performed in 384-well plates on an Applied Biosystems 7900HT Fast Real-Time PCR System instrument with the following temperature profile: 3 min enzyme activation at 95°C followed by 40 cycles of 95°C for 10 s, and 55°C for 30 s. Primer pairs used are listed in Supplementary Table 1. Gapdh was used as reference gene for normalization. The SDS 2.4 software (Applied Biosystems) was used to compute the threshold cycle (Cq) and the relative expression for an mRNA was assessed using the $2^{-\Delta Cq}$ method.

SRM assays

Urine from control and CKD patient samples were randomized prior to sample preparation and mass spectrometry analysis. Urine was centrifuged at 10,000 *x g* for 10 min at room temperature; the pellet was discarded. 1 mL supernatant was depleted from the 14 most abundant plasma proteins using the multiple affinity removal system (MARS Hu-14, 4.6x100 mm, Agilent Technologies, Santa Clara, CA) according to the manufacturer's protocol. The depleted fraction was collected in 1.25 mL of MARS14 Buffer A and denatured by adding 600 mg urea to 8 M final concentration. Samples were reduced with 5 mM dithiothreitol (30 min, 55°C), alkylated with 14 mM iodoacetamide (30 min, room temperature and in the dark) and desalted using a GE HiPrep 26/10 column (GE HealthCare Life Sciences, Pittsburgh, PA) and a 1200 HPLC system (Agilent Technologies, Santa Clara, CA). The protein concentration of the desalted samples was determined by bicinchoninic acid (BCA) protein assay (Thermo-Fisher, Waltham, MA). Samples were digested with sequencing grade modified trypsin (Promega Corporation, Madison, WI) at 1:50 enzyme:substrate ratio at 37°C for 16h. The digest was dried under centrifugal evaporation (Savant, Thermo-Fisher Waltham, MA) and resolubilized in 1% formic acid to a concentration of 1.1 μg/μL.

39 proteotypic peptides that are unique to the 10 proteins studied and their respective SRM assays were obtained from SRMAtlas (www.srmatlas.org) (Table S2). The SRMAtlas is a publically accessible resource of complete proteome SRM assays for selected organisms. The human SRMAtlas build, constructed from quadrupole fragmentation of human peptides, was used to select the best proteotypic peptides for each protein to perform SRM (Kusebauch et al., *in preparation*). For each peptide sequence the heavy isotope labeled analogue with the C-terminal arginine as R[13C6; 15N4] or lysine as K[13C6; 15N2] and cysteine residues carbamidomethylated was synthesized as crude product (Thermo-Fisher, Rockford, IL) to allow for relative quantification. Samples were analyzed on a QTRAP 5500 LC-MS system equipped with a Nano Spray Source III and an Eksigent Nano LC 2D (AB Sciex, Foster City, CA). 2 μg urine digest spiked with an aliquot of the mixed standard peptides at a concentration between 45 fmol and 600 fmol for each individual peptide were loaded on a C18 ProteoCol trap column (0.3 x 10 mm, 300 μm, 3 μm d*p,* SGE, Victoria, Australia) in 0.1% formic acid in water (v/v) for 5 min at a flow rate of 5 μl/min. Chromatographic separations were performed with a C18 Acclaim PepMap 100 analytical column (15 cm, 75 μm, 3 μm, 100 Å, Thermo Scientific, Rockford, IL) using 0.1% formic acid in water (v/v) (A) and 0.1% formic acid in acetonitrile (v/v) (B) and a 60 min gradient from 3% to 33% B and 33% to 63% B at 60-67.5 min at a flow rate of 300 nL/min. The analytical column was connected to a PicoTip fused-silica emitter (360 μm x 20 μm with a 10 μm tip, New Objective, Woburn, MA). Peptides were analyzed in scheduled SRM mode with Q1 and Q3 set to unit resolution, a 2 s cycle time, a declustering potential of 70 and a retention time window of 360 s. SRM data and the transition list are available in the PASSEL data repository http://www.peptideatlas.org/PASS/PASS00647. SRM data were analyzed with Skyline (version 2.5.06157) and MSstats. SRM traces were integrated with default settings and manual inspected to verify correct peak assignment and co-elution of endogenous and isotope labeled standard peptides. The relative protein expression level is reported as ratio of endogenous light to the heavy standard.

2. Supplementary Figures

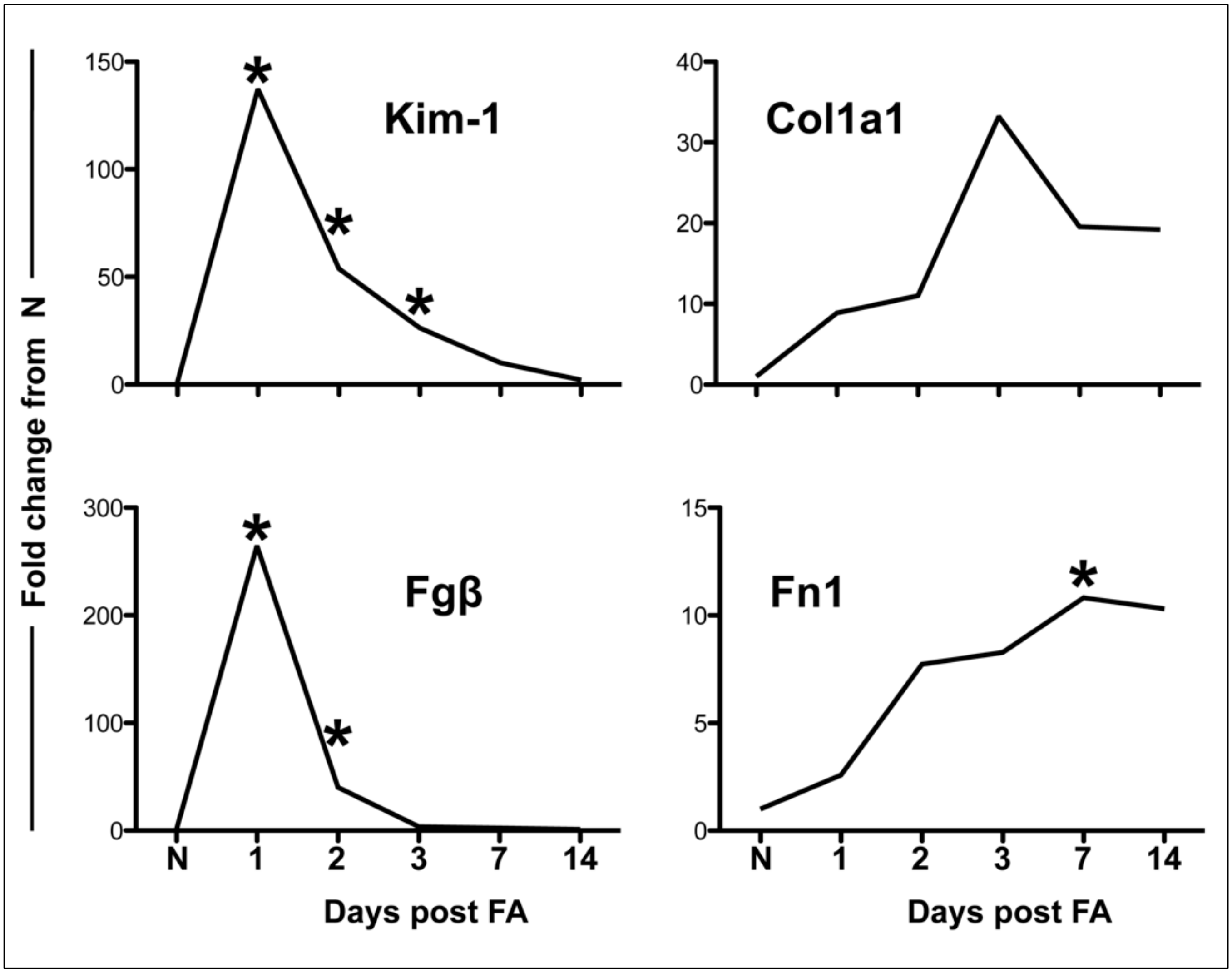

Figure S1. RNA-seq measurement of kidney gene expression for known markers of acute kidney injury (Kim-1, Fgβ) and kidney fibrosis (Col1a1, Fn1). Data is shown as the mean fold change from normal for the 3 samples included in RNA-seq at each time-point. * indicates time-points when $p<0.2$ for the fold change from normal.

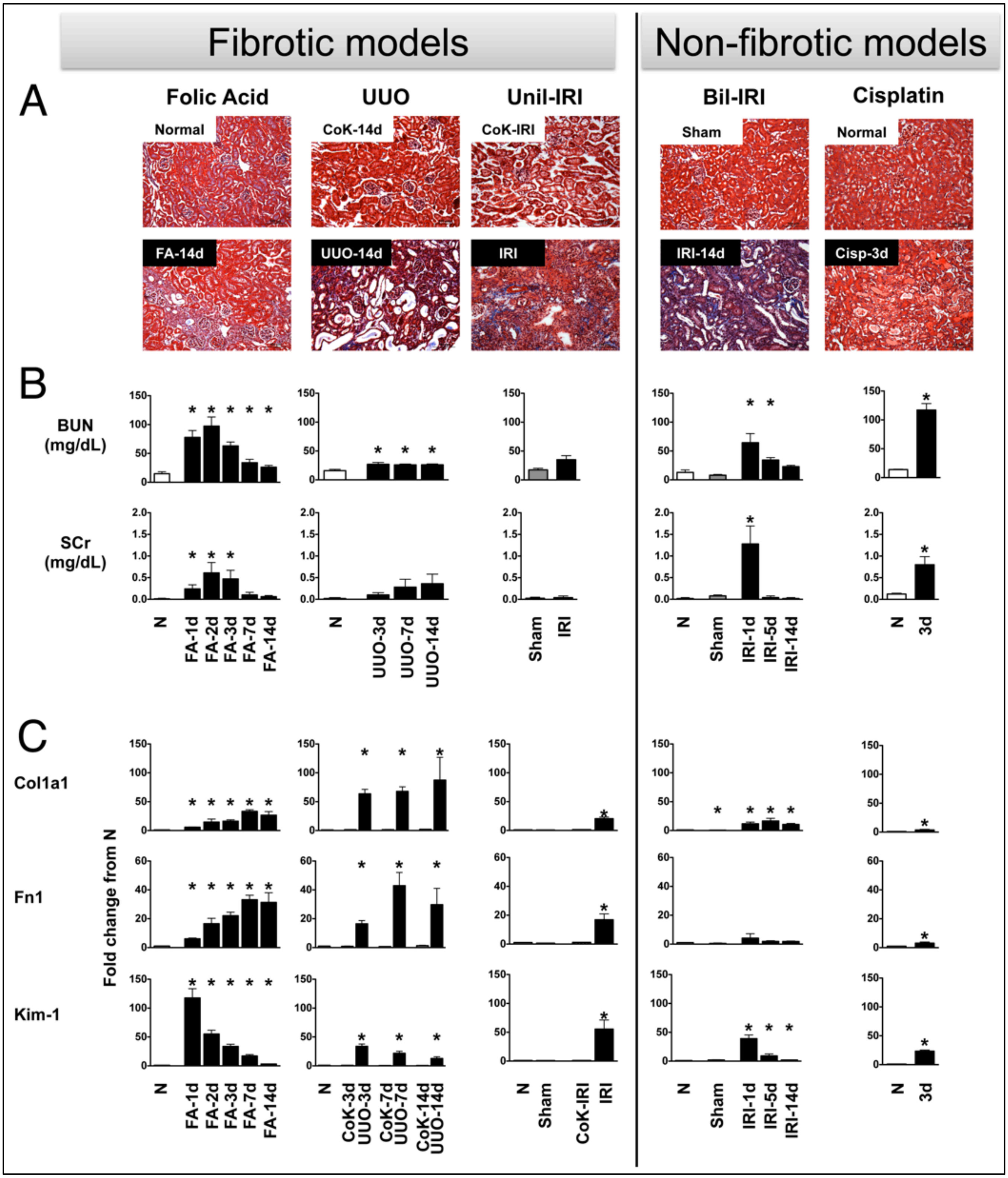

Figure S2. Histological, biochemical and molecular characteristics of mouse models of kidney fibrosis and acute kidney injury. (A) Masson's trichrome staining indicating if fibrosis has developed by the latest time-point recorded in the model compared to the appropriate controls for each model. Scale bars represent 100 µm. (B) Plasma levels of BUN and SCr. n= 7-10/group for the FA model, and 4-

5/group for other models. Data is presented as mean ± SEM. *p<0.05 when compared to N (or Sham for Unil-IRI model where samples were collected at 41 days). (C) qRT-PCR determination of kidney expression levels of fibrosis (Col1a1 and Fn1) and acute injury (Kim-1) markers. For FA nephropathy model n=6/group; for Unil-IRI model n=4 for Sham groups and 5 for IRI groups; for all other models n=5/group. Data was normalized to GAPDH and is presented as mean ± SEM of the fold change from normal (N) group in each model. For Unil-IRI N were the contralateral (CoK) kidneys from the sham-operated mice. *p<0.05 when compared to N.

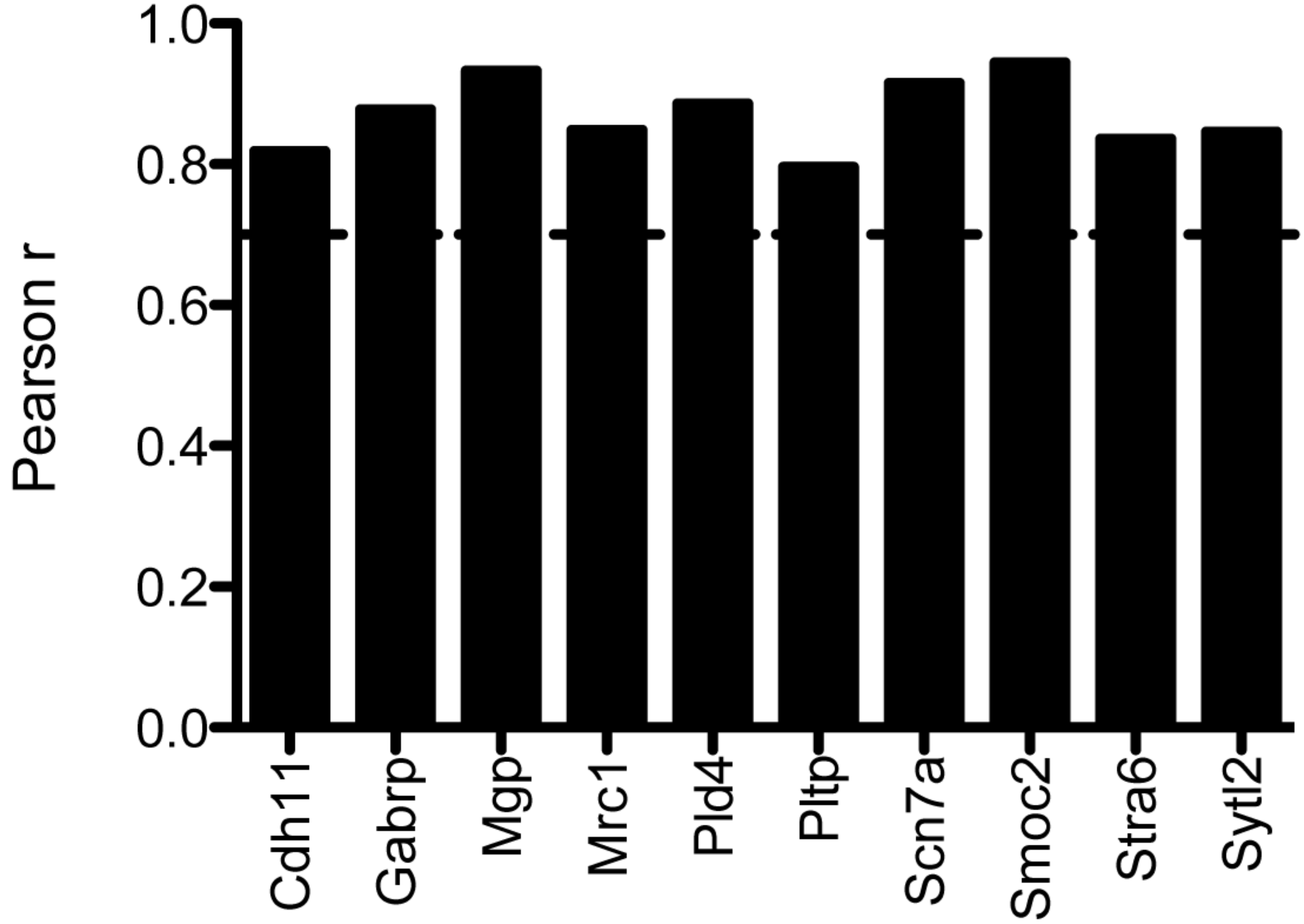

Figure S3. RNA-seq vs. qRT-PCR correlation of gene expression measurement for the 11 selected candidates. Pearson r correlation coefficients were calculated for all 18 measurements by the individual technique (3 samples X 6 groups). Horizontal line at 0.7 indicates a good level of correlation.

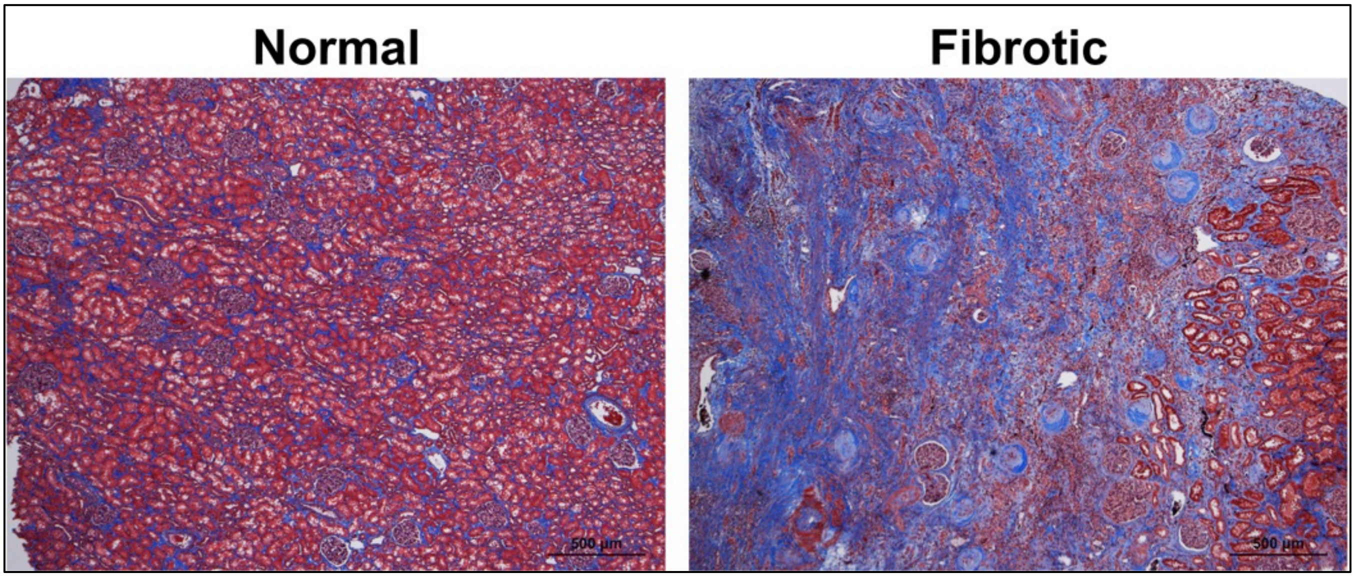

Figure S4. Histological characteristics of a normal vs fibrotic human kidney. Representative Masson's trichrome staining indicating the extent of fibrosis in normal patients vs patient with chronic kidney disease (n=5). Scale bars represent 500 µm.

3. Supplementary Tables

Table S1: List of genes identified by RNA-seq as significantly different from normal at least at one time-point in the FA nephropathy progression.

Data is presented as mean fold change from normal (n=3/group); gene symbols highlighted with yellow indicate the 10 candidates selected; gene symbols highlighted with gray indicate those that also met the selection criteria but were not chosen; fold changes highlighted with gray indicate p<0.2 at DESeq analysis.

Mgi symbol	Day 1	Day 2	Day 3	Day 7	Day 14
Aacs	0.23	0.08	0.20	0.51	1.01
Aadat	0.09	0.10	0.17	0.33	0.53
Abca13	0.07	0.10	0.25	0.70	1.01
Abca4	0.10	0.07	0.38	0.61	0.63
Abca8a	0.03	0.06	0.23	0.76	1.20
Abca9	0.09	0.09	1.25	2.83	1.85
Abp1	4.48	6.51	13.61	11.45	4.20
Acmsd	0.04	0.13	0.14	0.19	0.34
Acy1	0.07	0.10	0.24	0.24	0.62
Acy3	0.10	0.11	0.30	0.22	0.52
Adamts1	9.06	6.54	7.41	4.24	2.63
Adamts16	1.50	3.67	8.09	13.70	3.24
Adhfe1	0.13	0.21	0.36	0.39	0.67
Afap1l1	0.09	0.11	0.25	0.26	0.40
Agt	20.58	25.98	18.23	17.89	4.88
Agxt2l1	0.06	0.02	0.59	0.33	0.87
AI607873	1.76	3.41	7.73	20.17	6.63
Akap12	15.06	21.04	9.75	5.86	3.43
Akr1b8	79.97	65.26	30.92	44.39	15.01

Mgi symbol	Day 1	Day 2	Day 3	Day 7	Day 14
Akr1c14	0.04	0.06	0.26	0.13	0.46
Akr1c21	0.04	0.12	0.35	0.33	0.62
Akr1d1	0.07	0.10	0.20	0.31	1.00
Aldh1a2	24.56	10.24	6.58	19.53	14.25
Alox5ap	2.51	1.74	11.36	14.55	11.26
Amacr	0.11	0.14	0.70	0.28	0.61
Amica1	4.53	1.49	9.87	41.55	44.49
Ankrd1	30.01	14.30	29.13	10.98	6.12
Anln	5.84	16.30	7.69	3.82	1.98
Anpep	0.13	0.21	0.48	0.48	0.57
Anxa2	9.19	8.99	6.51	6.11	3.65
Apoc2	11.76	242.03	26.60	20.69	1.02
Arhgap11a	2.33	11.80	9.97	4.20	2.21
Arhgap36	1.24	2.75	33.05	149.84	36.77
Asns	16.36	6.46	11.45	7.44	3.09
Aspa	0.13	0.21	0.29	0.28	0.68
Aspdh	0.08	0.04	0.23	0.14	0.34
Ass1	0.10	0.10	0.19	0.31	0.59
Atp2a3	0.04	0.11	0.87	1.75	1.03
B3galnt1	0.09	0.17	0.38	0.76	0.99
Bag2	6.95	5.10	4.94	3.18	1.79
BC013712	0.06	0.06	0.76	1.14	0.83
BC089597	0.19	0.05	0.49	0.89	0.59
Bdh1	0.13	0.10	0.30	0.31	0.58
Birc3	6.13	5.71	6.88	11.37	3.18
C1qtnf3	0.03	0.07	0.37	0.14	0.45

Mgi symbol	Day 1	Day 2	Day 3	Day 7	Day 14
C3	82.12	185.03	275.58	173.67	43.48
C4b	7.86	9.71	10.37	5.93	3.91
C8a	0.08	0.01	0.19	0.22	0.38
Calb1	0.07	0.12	0.19	0.82	1.28
Capg	12.02	11.19	12.07	8.48	6.13
Cckar	0.10	0.51	0.45	0.38	0.56
Ccl2	18.46	41.17	134.97	198.61	73.50
Ccl5	1.12	9.92	26.96	21.36	7.61
Ccl6	0.93	0.82	5.02	14.89	5.47
Ccl9	2.11	3.65	7.69	11.22	5.02
Ccna2	4.06	10.99	11.07	3.17	1.43
Ccnb2	3.98	43.81	39.55	8.92	4.76
Ccr2	1.68	2.50	8.17	15.26	11.23
Cd14	49.17	22.10	48.26	25.68	9.02
Cd44	33.34	37.82	112.07	74.57	39.47
Cdh11	0.67	0.98	2.68	6.46	11.31
Ces1d	0.06	0.14	0.76	0.61	1.21
Ces1e	0.13	0.01	0.29	0.25	0.59
Ces1f	0.10	0.05	0.25	0.19	0.59
Cfi	16.17	17.72	17.40	17.28	11.52
Chrnb1	13.20	11.66	7.89	11.55	4.12
Ckap2l	8.29	47.27	67.64	12.41	6.79
Clcf1	27.11	36.77	23.13	11.34	5.79
Cldn3	6.26	5.05	5.50	10.71	2.06
Cldn4	4.83	10.31	6.93	3.78	3.06
Clec4n	5.93	8.59	9.94	25.40	19.94

Mgi symbol	Day 1	Day 2	Day 3	Day 7	Day 14
Clu	14.95	32.03	19.89	9.73	4.98
Cmbl	0.07	0.12	0.19	0.18	0.40
Cml1	0.05	0.09	0.30	0.44	0.85
Cndp1	0.08	0.15	0.35	0.42	0.82
Cntnap5a	0.05	0.04	0.15	0.10	0.56
Col19a1	0.02	0.01	0.01	0.02	0.22
Col3a1	3.30	2.93	6.98	11.08	13.34
Col6a6	0.15	0.13	0.10	0.13	0.36
Col8a1	5.29	5.34	5.34	14.30	7.99
Cp	13.38	24.07	17.99	13.92	5.59
Cpn1	5.79	14.80	13.04	18.05	9.08
Cpne4	0.01	0.11	0.26	0.04	0.31
Creb5	14.35	18.22	18.66	5.66	4.93
Csad	0.13	0.23	0.27	0.37	0.50
Csf1	18.25	12.77	18.53	14.82	5.53
Cstb	12.41	7.62	4.58	3.37	1.65
Ctnna2	0.06	0.05	0.32	0.17	0.68
Ctsl	8.23	5.63	4.16	2.24	2.04
Cxcl1	127.77	73.19	188.27	100.08	20.11
Cxcl10	9.35	8.90	27.50	5.51	5.61
Cxcl12	0.09	0.06	0.32	0.76	1.46
Cxcl2	26.16	30.16	123.70	59.78	16.85
Cyp2d26	0.03	0.02	0.12	0.32	0.54
Cyp2d9	0.12	0.01	0.21	0.24	0.81
Cyp2e1	0.07	0.04	0.18	0.26	0.54
Cyp2j11	0.06	0.06	0.21	0.29	0.64

Mgi symbol	Day 1	Day 2	Day 3	Day 7	Day 14
Cyp2j7-ps	0.01	0.21	0.14	0.43	0.57
Cyp51	0.09	0.07	0.10	0.20	0.44
Cyp7b1	0.14	0.05	0.11	0.22	0.44
D17H6S56E-5	6.95	9.37	16.67	9.58	4.24
D630024D03Rik	0.01	0.03	0.08	0.14	0.34
D630029K05Rik	0.05	0.07	0.31	0.22	0.72
Dcxr	0.06	0.24	0.23	0.26	0.46
Defb19	0.12	0.03	0.03	0.05	0.26
Diap3	4.48	10.56	6.29	3.13	1.97
Dnase1	0.20	0.02	0.04	0.09	0.58
Dpep1	0.04	0.05	0.13	0.34	0.67
Dpf3	0.04	0.04	0.21	0.24	0.23
Dtl	11.23	16.48	13.48	3.21	2.69
Dusp15	0.01	0.03	0.07	0.13	0.23
E2f8	4.99	15.63	7.41	8.49	2.09
Ear2	2.98	1.00	1.32	36.56	102.49
Eci3	0.09	0.04	0.11	0.11	0.30
Edn1	7.66	9.86	15.00	20.66	4.24
Egf	0.01	0.01	0.08	0.20	0.61
Egfl6	0.10	0.24	0.20	0.72	1.39
Egr2	20.16	17.85	17.11	53.69	44.00
Elf3	5.77	8.65	16.60	5.84	3.80
Emr1	0.35	0.26	4.39	13.66	7.73
Esm1	0.34	0.06	0.10	0.25	0.37
Fam107a	0.03	0.08	0.21	0.26	0.57
Fam151a	0.02	0.13	0.14	0.18	0.28

Mgi symbol	Day 1	Day 2	Day 3	Day 7	Day 14
Fam65c	0.06	0.52	0.62	1.26	1.25
Fbln1	0.10	0.08	0.93	1.22	1.18
Fbxo40	0.08	0.19	0.28	0.31	0.37
Fcamr	0.10	0.08	0.23	0.39	0.69
Fcgr1	9.39	6.00	22.31	39.89	31.91
Fcgr4	0.05	0.11	0.42	1.52	0.73
Fcrls	1.05	3.75	13.83	196.20	94.44
Fga	34.86	14.86	8.60	1.86	0.95
Fgb	264.53	40.24	3.56	2.39	1.00
Fgg	40.51	21.72	4.02	1.97	2.56
Fibin	0.09	0.10	0.09	0.10	0.31
Figf	0.11	0.39	0.61	1.71	1.25
Fitm1	0.07	0.10	0.40	0.83	0.71
Fmod	0.02	0.20	0.23	0.20	0.84
Fn1	2.58	7.73	8.28	10.82	10.31
Fn3k	0.07	0.11	0.25	0.38	0.57
Fndc4	13.11	13.41	2.86	3.99	2.98
Foxj1	49.71	22.09	34.44	32.56	16.49
Ftcd	0.09	0.08	0.32	0.11	0.44
G6pc	0.01	0.05	0.18	0.30	0.50
Gabrp	6.02	9.83	5.83	15.00	65.70
Galnt11	0.09	0.24	0.40	0.40	0.82
Gamt	0.07	0.36	0.27	0.48	0.65
Gatm	0.03	0.04	0.09	0.14	0.34
Gc	17.61	26.20	16.91	10.00	5.25
Gdf15	9.59	20.28	8.04	1.35	0.71

Mgi symbol	Day 1	Day 2	Day 3	Day 7	Day 14
Ggct	0.13	0.12	0.09	0.27	0.23
Gm10804	0.11	0.24	0.28	0.36	0.46
Gm11128	0.06	0.09	0.37	0.49	1.07
Gm11428	0.80	0.52	2.12	10.23	6.82
Gm11825	0.32	0.03	0.13	0.06	0.26
Gm11992	0.08	0.15	0.30	0.37	0.80
Gm12326	0.05	0.05	0.05	0.19	0.07
Gm13262	0.05	0.10	0.60	0.77	1.74
Gm15848	0.10	0.12	0.19	0.51	0.63
Gm15987	3.37	4.21	28.79	65.24	30.96
Gm20614	0.04	0.04	0.05	0.07	0.23
Gm4450	0.08	0.14	0.10	0.26	0.43
Gm4952	0.08	0.04	0.05	0.05	0.31
Gm4956	0.04	0.01	0.15	0.66	0.82
Gm5424	0.11	0.08	0.18	0.25	0.45
Gm5887	0.09	0.03	0.47	0.22	0.11
Gm8126	31.61	13.16	14.35	7.32	5.48
Gm853	0.21	0.36	0.33	0.12	0.31
Gm9732	24.08	1.53	8.94	11.84	14.82
Golm1	9.24	17.30	7.96	5.28	4.33
Gpr114	13.56	5.89	19.53	21.52	20.80
Gpx6	0.05	0.18	0.14	0.28	0.68
Gxylt2	16.28	12.14	14.04	7.30	12.54
Gyk	0.12	0.19	0.40	0.45	0.65
Gys2	0.04	0.29	0.31	0.33	0.39
H2-DMa	5.83	10.07	16.12	24.55	9.89

Mgi symbol	Day 1	Day 2	Day 3	Day 7	Day 14
H2-DMb1	1.95	4.44	6.68	10.89	8.21
Haao	0.13	0.08	0.16	0.21	0.37
Hao2	0.10	0.32	0.33	0.38	0.52
Hapln1	0.01	0.01	0.24	0.08	0.52
Havcr1	137.33	53.77	26.32	10.03	2.00
Hba-a1	0.13	0.56	0.05	0.26	0.45
Hba-a2	0.42	0.89	0.06	0.68	0.61
Hbb-b1	0.32	0.46	0.04	0.36	0.52
Hpcal4	4.09	9.66	2.91	4.59	1.33
Hpd	0.01	0.01	0.08	0.37	0.39
Icam1	16.30	24.35	20.70	9.29	5.87
Id1	5.53	10.02	3.26	2.47	1.55
Ido2	0.01	0.05	0.18	0.19	0.58
Igfbp1	0.01	0.04	0.13	0.18	0.40
Igj	0.27	0.02	0.33	0.81	0.42
Il1f6	2.45	10.46	27.71	10.99	10.49
Il1rn	42.57	51.91	88.49	62.43	29.62
Inmt	0.03	0.03	0.13	0.13	0.63
Inpp4b	0.23	0.06	0.29	0.92	0.71
Irx1	0.06	0.16	0.28	0.47	0.68
Itgam	10.37	10.62	31.52	65.37	35.56
Itih5	0.15	0.10	0.38	0.80	0.87
Kap	0.25	0.07	0.14	0.10	0.42
Kbtbd11	0.11	0.20	0.57	0.43	0.69
Kcng1	0.02	0.05	0.34	0.08	0.40
Kcnh4	0.03	0.20	0.80	0.41	0.34

Mgi symbol	Day 1	Day 2	Day 3	Day 7	Day 14
Kcnj1	0.12	0.18	0.49	0.55	0.84
Kcnj8	0.11	0.03	0.02	0.36	0.45
Kcnt1	0.01	0.09	0.25	0.16	0.20
Khk	0.12	0.19	0.39	0.33	0.66
Kif11	3.95	12.89	6.53	2.81	2.66
Kif18b	23.46	43.53	32.02	13.75	6.78
Kif4	7.35	17.87	20.69	3.59	7.27
Klf6	8.02	10.33	10.92	7.08	3.68
Kntc1	5.77	21.92	23.49	6.04	4.88
Krt20	99.65	40.80	65.31	49.83	23.54
Laptm5	1.62	2.12	8.68	10.60	8.39
Lbp	4.30	10.70	14.46	14.44	5.52
Lcn2	172.35	573.77	145.51	116.16	47.87
Lgals1	11.64	9.01	9.68	3.65	2.18
Lrg1	27.42	16.81	7.70	2.90	1.38
Lrrc66	0.04	0.07	0.29	0.20	1.07
Lyz1	1.01	1.02	13.19	13.96	93.62
Lyz2	2.49	2.57	10.50	26.25	25.76
Macrod2	0.12	0.10	0.22	0.21	0.42
Mcm6	14.09	40.99	11.80	3.87	6.63
Meox1	0.60	0.04	0.50	0.27	1.19
Mep1b	0.04	0.00	0.21	0.18	0.56
Mgp	0.85	0.55	3.30	9.97	9.57
Miox	0.04	0.05	0.21	0.25	0.49
Mir1943	0.04	0.04	0.37	0.34	0.20
Mki67	2.93	19.47	10.87	3.31	2.63

Mgi symbol	Day 1	Day 2	Day 3	Day 7	Day 14
Mmp27	55.82	13.03	15.58	2.66	3.55
Mmp7	4.72	12.29	10.09	24.03	29.14
Mpv17l	0.20	0.08	0.31	0.30	0.42
Mrc1	0.61	0.51	4.86	9.29	5.48
Mrvi1	0.04	0.08	0.50	1.01	1.75
Msi1	18.45	37.45	12.49	27.16	13.73
Mthfd2	17.65	10.04	19.94	11.54	1.37
Muc4	73.06	239.90	154.46	104.49	53.83
Mvp	10.42	7.90	4.41	3.04	2.27
Myct1	1.76	0.05	0.55	0.77	1.14
Nccrp1	0.00	0.00	0.00	0.07	0.28
Nckap1l	1.90	1.59	5.90	13.46	4.67
Nek6	8.68	4.74	4.62	2.17	2.61
Nfam1	3.49	24.67	19.48	59.18	68.60
Nfkbiz	11.90	10.97	12.66	9.70	5.33
Npas2	0.24	0.44	0.22	0.19	0.04
Npy	0.08	0.02	0.05	0.24	0.41
Npy6r	20.73	46.40	36.78	58.69	20.39
Pah	0.07	0.10	0.22	0.24	0.57
Pck1	0.11	0.17	0.48	0.68	1.24
Pde6a	0.04	0.02	0.08	0.10	0.60
Pdlim7	10.80	12.49	9.44	5.09	3.51
Pdpn	11.67	43.96	19.72	24.06	18.54
Pea15a	8.58	9.88	5.89	3.73	2.03
Pecr	0.12	0.13	0.23	0.30	0.49
Pfn3	0.02	0.13	0.44	0.47	0.41

Mgi symbol	Day 1	Day 2	Day 3	Day 7	Day 14
Pla1a	0.39	0.04	0.32	1.29	1.36
Plac8	9.91	5.10	17.08	17.41	5.99
Pld4	0.93	2.37	7.79	19.53	14.74
Plin2	50.30	21.47	11.95	4.65	2.72
Pltp	0.07	0.13	1.31	5.15	3.25
Ppp1r1a	0.09	0.13	0.30	0.95	1.15
Prox1	0.07	0.27	0.25	0.57	1.37
Proz	0.03	0.06	0.38	0.24	1.50
Psrc1	22.63	17.94	23.39	7.74	4.76
Ptgis	0.05	0.66	0.22	1.98	0.84
Pvalb	0.02	0.04	0.11	0.23	0.56
Pxmp2	0.05	0.15	0.42	0.37	0.65
Pzp	0.27	0.03	0.09	0.12	0.56
Rad51l1	37.27	7.51	23.21	20.85	17.35
Rcan1	7.81	6.35	3.48	2.13	1.26
Rras	8.93	8.77	7.99	4.42	4.46
Rrm2	9.69	26.46	26.37	3.25	3.28
S100g	0.12	0.07	0.07	0.49	1.23
Saa1	246.34	99.00	76.73	6.60	1.00
Sacs	10.20	5.88	4.39	3.26	2.93
Scn7a	0.19	0.11	1.21	2.79	4.42
Sectm1b	0.03	0.10	0.42	0.43	0.64
Sema3d	0.23	0.06	0.31	6.90	6.30
Serpina10	315.61	302.11	309.89	182.59	72.73
Serpina3n	101.28	251.85	99.04	111.79	98.42
Serpina7	99.83	49.78	20.22	18.24	3.58

Mgi symbol	Day 1	Day 2	Day 3	Day 7	Day 14
Serpine1	212.01	74.08	63.25	108.17	65.09
Serpine2	2.10	0.30	5.33	22.57	16.36
Sfrp1	0.15	0.33	0.71	0.84	1.24
Sirpb1c	1.87	1.59	2.96	15.66	8.93
Slc10a6	0.09	0.28	0.18	1.08	1.83
Slc12a1	0.04	0.06	0.21	0.51	0.83
Slc16a1	0.60	0.32	0.46	0.14	0.15
Slc16a7	0.11	0.09	0.17	0.58	0.86
Slc22a13	0.19	0.12	0.25	0.23	0.52
Slc22a19	0.26	0.05	0.16	0.34	0.54
Slc22a22	0.02	0.01	0.18	0.19	0.66
Slc22a26	0.16	0.02	0.12	0.14	0.34
Slc22a28	0.07	0.16	0.18	0.15	0.51
Slc22a30	0.08	0.08	0.20	0.15	0.44
Slc22a7	0.13	0.00	0.07	0.04	0.43
Slc22a8	0.22	0.07	0.20	0.27	0.66
Slc25a24	15.48	10.59	10.39	10.01	9.91
Slc28a1	0.02	0.19	0.18	0.44	0.55
Slc2a5	0.07	0.09	0.21	0.25	0.99
Slc34a1	0.05	0.11	0.33	0.30	0.58
Slc34a2	11.81	16.20	7.59	7.02	4.10
Slc34a3	0.05	0.05	0.09	0.20	0.33
Slc46a3	0.11	0.36	0.57	0.31	0.53
Slc4a1	0.11	0.09	0.18	0.35	0.92
Slc5a12	0.06	0.34	0.38	0.35	0.58
Slc5a4a	0.02	0.37	0.51	0.17	1.06

Mgi symbol	Day 1	Day 2	Day 3	Day 7	Day 14
Slc6a12	0.02	0.13	0.26	0.12	0.77
Slc7a13	0.02	0.02	0.11	0.10	0.48
Slco1a1	0.18	0.16	0.19	0.12	0.36
Smoc2	0.06	0.06	1.83	4.22	6.08
Smpdl3b	222.02	124.22	111.13	38.83	19.27
Snx31	0.06	0.05	0.07	0.07	0.27
Socs3	77.54	53.23	43.48	34.95	36.18
Sox4	12.86	13.93	11.69	11.09	7.60
Sox9	24.10	49.89	52.43	30.72	8.17
Spaca7	27.30	74.80	18.32	30.89	11.81
Spink6	46.74	13.93	9.16	5.47	1.77
Spp1	113.22	174.85	63.01	37.70	10.75
Spred3	6.01	11.03	8.99	3.82	5.60
Spsb1	11.68	13.04	4.64	8.93	4.14
Sptlc3	0.07	0.11	1.02	1.25	0.68
St8sia2	3.07	2.10	10.17	26.47	2.02
Stil	13.84	32.74	10.68	3.57	0.95
Stk32a	10.38	7.59	5.33	2.72	1.64
Stra6	1.19	1.95	8.56	22.31	14.59
Susd2	0.18	0.07	0.32	0.28	0.51
Sycn	0.07	0.07	0.07	0.07	0.22
Synpr	0.23	0.02	0.01	0.01	0.18
Sytl2	3.75	5.53	8.20	11.81	6.72
Tagln2	8.92	6.40	4.86	4.01	2.37
Tbx10	0.06	0.10	0.08	0.03	0.44
Timd2	7.27	2.97	1.47	0.68	0.67

Mgi symbol	Day 1	Day 2	Day 3	Day 7	Day 14
Timp1	175.24	194.76	60.56	67.32	61.27
Tlr2	6.43	12.76	34.62	15.78	7.34
Tmem207	0.01	0.02	0.14	0.35	1.20
Tmem25	0.11	0.34	0.39	0.53	0.53
Tmem26	0.10	0.07	0.16	0.16	0.49
Tmsb10	19.04	18.72	9.84	9.28	5.31
Tnc	13.27	9.63	9.00	16.74	18.78
Tnfaip3	1.97	3.85	6.38	8.79	3.95
Tnfrsf23	18.16	7.62	5.65	2.21	1.75
Top2a	5.38	15.75	10.49	5.58	3.30
Tpx2	3.87	10.97	7.65	2.93	2.69
Tril	0.07	0.43	0.69	2.07	0.97
Tsc22d1	8.11	6.92	4.34	2.18	2.00
Ttc36	0.04	0.10	0.34	0.34	0.67
Ttr	0.05	0.04	0.15	0.56	0.78
Tyrobp	1.26	1.65	4.90	16.29	10.29
Ugt3a1	0.18	0.07	0.17	0.22	0.46
Uhrf1	16.90	31.75	12.11	3.81	3.48
Upp2	0.25	0.11	0.21	0.69	1.34
Vcam1	13.66	30.80	121.91	63.51	36.46
Vill	0.09	0.28	0.18	0.20	0.36
Vmn1r-ps11	0.02	0.03	0.73	0.11	0.51
Vmn1r18	0.02	0.01	0.14	0.27	0.87
Vmn1r19	0.03	0.02	0.52	0.73	1.04
Vmn1r20	0.02	0.34	0.31	0.27	0.79
Vstm2a	0.04	0.05	0.04	0.20	0.60

Mgi symbol	Day 1	Day 2	Day 3	Day 7	Day 14
Vtcn1	64.93	44.16	28.37	15.70	7.44
Vwce	0.06	0.08	0.42	1.03	0.85
Wfdc15b	0.02	0.05	0.06	0.27	0.90
Ybx2	0.08	0.12	0.18	0.72	0.44
2310042D19Rik	0.09	0.08	0.47	0.46	0.95
4930533I22Rik	0.11	0.09	0.22	0.25	0.74
4933417A18Rik	0.04	0.07	0.49	0.41	0.67
7SK RNA	0.04	0.04	0.08	0.08	1.35
8430408G22Rik	0.09	0.23	0.34	1.23	0.79
9030619P08Rik	0.01	0.05	0.02	0.03	0.25

Table S2. List of peptides used for selected reaction monitoring (SRM) assays.

	Peptide Sequence	Protein Accession	Gene Symbol
1	LHSDIDSGDGNIK	P55287	CDH11
2	FIFSLPPEIIHNPNFTVR		
3	VLDVNDNAPK		
4	VEAANVHIDPK		
5	LSLPGFENLTAGYNK	O00591	GABRP
6	SFLHEVTVGNR		
7	IVDYFTIQNPSNVDHYSK		
8	LFSNGTVLYALR		
9	NANTFISPQQR	P08493	MGP
10	YAMVYGYNAAYNR		
11	SKPVHELNR		
12	IYGTTDNLCSR	P22897	MRC1
13	TGIAGGLWDVLK		
14	NDTLLGIK		
15	ALGGDLASINNK		
16	VFIVPVGNHSNIPFSR	Q96BZ4	PLD4
17	SLQALSNPAANVSVDVK		
18	TSTDLQVLAAR		
19	FQPFHGLFDGVPTTAYFSASPPALCPQGR		
20	VSNVSCQASVSR	P55058	PLTP
21	EGHFYYNISEVK		
22	IYSNHSALESLALIPLQAPLK		
23	AVEPQLQEEER		

	Peptide Sequence	Protein Accession	Gene Symbol
24	YSPLDFIPTLQTAR	Q01118	SCN7A
25	LGGSNIFITVK		
26	AYFSNGWYR		
27	WPQENENETLHNR		
28	LSEPDPSHTLEER	Q9H3U7	SMOC2
29	NSVSSCDQEHQSALEEAK		
30	YPTLWTEQVK		
31	SISVQELMGCLGVAK		
32	GAALDLSPLHR	Q9BX79	STRA6
33	GLQSSYSEEYLR		
34	AATLDPGYYTYR		
35	HGFLSWAR		
36	GNIQFAIEYVESLK	Q9HCH5	SYTL2
37	IVSPGLTIHER		
38	LTNQFLGGLR		
39	SVPAFLQDESDDR		

Table S3: List of primers used for mouse qRT-PCR

Gene	F/R	Sequence
Cdh11	F	TGC CAA TCT TCT TTT CGT TCT T
	R	CCT TGA AAG GTC CAT TGC TG
Gabrp	F	TGT GGA GGT CAG CAG AAG TG
	R	CAG TGC TAT CCG AAC TGG GT
Mgp	F	AGG CAG ACT CAC AGG ACA CC
	R	AGG ACT CCA TGC TTT CGT GA
Mrc1	F	CCT CTT AAT TCA GCA TCA CTT GC
	R	TGC ATT GCC CAG TAA GGA GT
Pld4	F	ATT CTG GGT TGT GGA TGG G
	R	CAA GGT CTT GAG CCA GGT TG
Pltp	F	TGA GGG GCG TGT CAC TAC TT
	R	CGA GAT CAT CCA CAG AAC TGC
Scn7a	F	AAA TGA AAC GCT GCA CAA CA
	R	CAG CAT CTG TCC TGT TGC C
Smoc2	F	ACT GCG ACA TGA ACA ATG ACA
	R	ACT TTC AGC ATT TCC TCT GGG
Stra6	F	TGC CTT CCT TCT ATC CTG TCC

Gene	**F/R**	**Sequence**
	R	AGG ACC ACA AAG ACA GCA GC
Sytl2	F	TGA AGG AAT GCC TTG ACC TC
	R	ACA GCT CTT GTC TTC TGG CG
Col1a1	F	TGA CTG GAA GAG CGG AGA GT
	R	GTT CGG GCT GAT GTA CCA GT
Fn1	F	ATG TGG ACC CCT CCT GAT AGT
	R	GCC CAG TGA TTT CAG CAA AGG
Kim-1	F	GGA AGT AAA GGG GGT AGT GGG
	R	AAG CAG AAG ATG GGC ATT GC
Gapdh	F	GAA TAC GGC TAC AGC AAC AGG
	R	GGT CTG GGA TGG AAA TTG TG

Table S4: List of primers used for human qRT-PCR

Gene	F/R	Sequence
Cdh11	F	AGG GAC AAC CAA AGT GAC GA
	R	GGC TGC TTC TGA CAC AGA CA
Gabrp	F	TAG TCA CCA GAT CGC AGC AG
	R	GAA CAT TCC TCC GAA GCT CA
Mgp	F	ACG AAA CCA TGA AGA GCC TG
	R	AAC TGA AAC GAT ATC AAA GCC G
Mrc1	F	AGG AAA AGC TGC CAA CAA CA
	R	TCC TGA GGT CAA GGA ACT GG
Pld4	F	CAG GTG CAG CCC AAG GAC
	R	GGA TGC TTT CCA CAA GGA CA
Pltp	F	CGG TCC TGC TCA ACT CCC
	R	GAA GTC CAT GTC CAG GTT GC
Scn7a	F	AGC CCT TGG AAG ATG TGG AC
	R	AAG CCG CAT TGA ATC TGA AG
Smoc2	F	CCG TAC AAG AAC TGA TGG GC
	R	CTT TCA GCA TGA CCT CTG GG
Stra6	F	CTC CAG ACC CTG ACC TCT CA

Gene	**F/R**	**Sequence**
	R	AGC AGG ACA AGA CCA AGG CT
Sytl2	F	CCA GTA TGT CCC AGA GCC AG
	R	TGA CTT CCC CTT AGC AGT GG
Col1a1	F	AGG CTG GTG TGA TGG GAT T
	R	GGA ACA CCT CGC TCT CCA G
Gapdh	F	ATT GCC CTC AAC GAC CAC TTT G
	R	TCT CTC TTC CTC TTG TGC TCT TGC