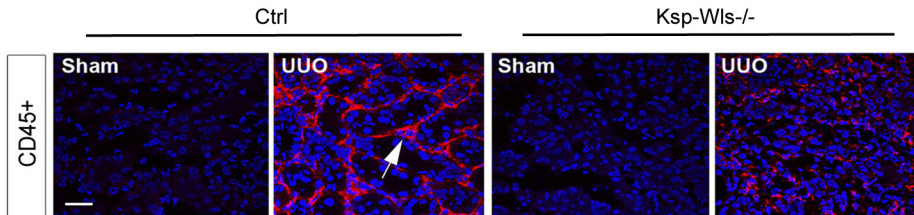
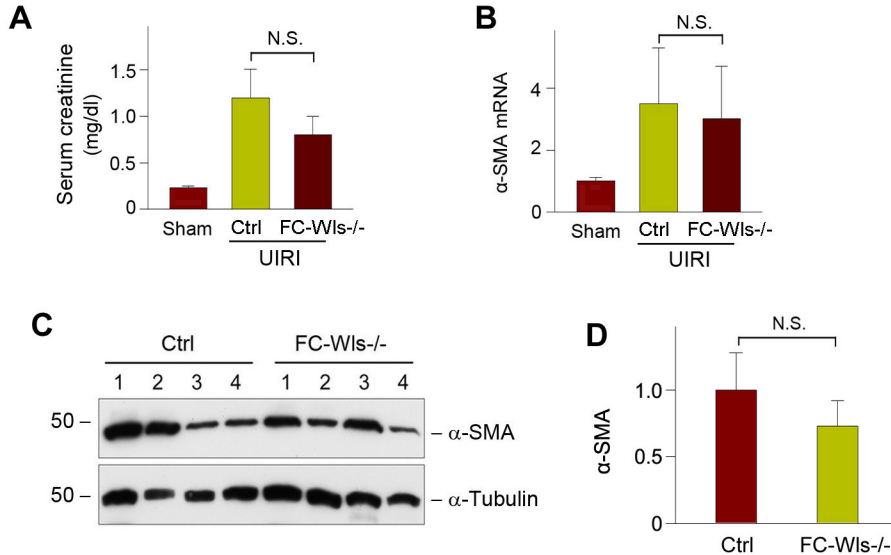


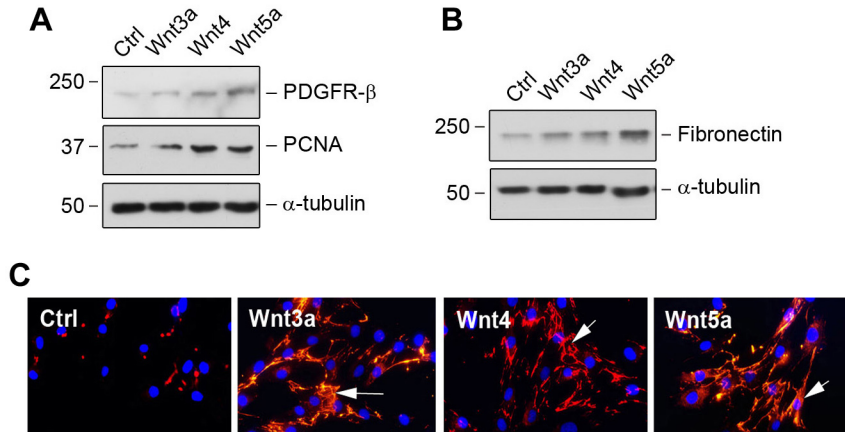
Supplementary Figure 1. Wnts also induce tubular cell injury by an autocrine mechanism. (A) Preparation of tubular cell conditioned medium rich in Wnts ligands. Human kidney proximal tubular cells (HKC-8) were transfected with either empty vector (pCDNA3.0) or Wnts expression vectors. Conditioned media were collected after incubation for 48 hours. Western blotting revealed the presence of Wnt1 protein in the conditioned medium. (B) Tubular cell conditioned medium (CM) promoted fibronectin and α -SMA expression in HKC-8 cells. HKC-8 cells were incubated with conditioned medium enriched in Wnt1 for 48 hours, and cell lysates were analyzed by Western blotting using antibodies against fibronectin, α -SMA and α -tubulin, respectively.



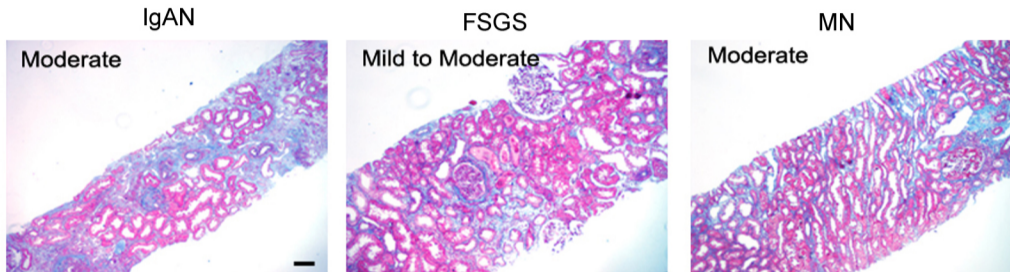
Supplementary Figure 2. Tubule-specific deletion of Wls represses renal inflammation. Representative immunofluorescence micrographs show CD45-positive cells in the control and Ksp-Wls^{-/-} kidneys at 7 days after UUO. Arrow indicates positive cells. Scale bar, 50 μ m.



Supplementary Figure 3. Fibroblast-specific deletion of Wls exhibits little effects on kidney fibrosis after IRI. (A) Serum creatinine level in control and FC-Wls^{-/-} mice at 10 days after UIRI (n = 5). (B) qRT-PCR analyses show renal α -SMA mRNA expression in control and FC-Wls^{-/-} mice at 10 days after UIRI (n = 5). N.S., not significant. (C) Western blot analyses demonstrate that renal α -SMA protein levels in control and FC-Wls^{-/-} mice at 10 days after UIRI. (D) Quantitative data of renal α -SMA protein in control and FC-Wls^{-/-} mice at 10 days after UIRI. N.S., not significant



Supplementary Figure 4. Wnt ligands promote fibroblast activation and matrix production *in vitro*. (A, B) Western blot analyses demonstrate that recombinant Wnt3a, Wnt4 and Wnt5a induced PDGFR- β and PCNA (A) as well as fibronectin (B) expression in NRK-49F fibroblasts after incubation for 48 hours. (C) Representative micrographs show that Wnt3a, Wnt4 and Wnt5a induced fibronectin expression and deposition. NRK-49F cells were incubated with different Wnts for 48 hours, and fibronectin expression was assessed by immunofluorescence staining.



Supplementary Figure 5. Representative micrographs of human kidney biopsy specimens from IgAN, FSGS and MN patients. Masson trichrome staining revealed renal interstitial fibrosis in varying degree in these patients. Scale bar, 50 μm. IgAN, IgA nephropathy; FSGS, focal and segmental glomerulosclerosis; MN, membranous nephropathy.

Supplementary Table 1. Demographic Characteristics of the Participants Included in the Wnts staining

IgA Nephropathy										
ID No.	Sex	Age (years)	BUN (mmol/l)	Scr (μmol/l)	24h UPro (g)	ALB (g/l)	Hb (g/l)	Pathologic description		Final diagnosis
								Glomeruli	Tubule-Interstitium	
2015337	M	48	7.0	123.8	1.2	-	159	10 gloms (8 global sclerosis)	Moderate to severe tubule atrophy and interstitial fibrosis	Hass V
2015338	M	24	9.42	167.0	-	42.7	140	54 gloms (18 global, 5 segmental sclerosis, 5 fibrotic-cellular crescents)	Moderate to severe tubule atrophy and interstitial fibrosis	Hass III
2015344	F	66	8.3	85.0	0.96	41.8	119	11 gloms (5 global sclerosis)	Mild to moderate tubule atrophy and interstitial fibrosis	Hass III
2015345	F	47	5.31	113.9	3.18	37.1	113.7	9 gloms (1 global sclerosis, 4 fibrotic crescents)	Moderate tubule atrophy and interstitial fibrosis	Hass IV
2015586	M	38	4.72	64.0	++	38.8	161	27 gloms (2 global sclerosis, 2 fibrotic crescents)	Mild to moderate tubule atrophy and interstitial fibrosis	Hass III
Membranous Nephropathy										
2015381	M	55	4.18	77.0	+++	26	138	28 gloms (5 global sclerosis)	Moderate tubule atrophy and interstitial fibrosis	MN
2015383	F	55	14.7	90.0	4.098	20	123	62 gloms (2 global sclerosis)	Mild tubule atrophy and interstitial fibrosis	MN
2015395	M	52	6.9	87.0	2.827	22	136	10 gloms (mild glomerular basement membrane thickening)	Mild interstitial fibrosis	MN
2015411	M	39	-	-	7.236	13	-	12 gloms (mild glomerular basement membrane thickening)	Mild interstitial fibrosis	MN
2015584	F	58	3.1	61.0	3.668	-	114	7 gloms (mild glomerular basement membrane thickening)	Mild interstitial fibrosis	MN

Focal segmental glomerulosclerosis (FSGS)										
2015450	M	19	5.99	105.0	1.872	43.2	128	10 gloms (2 global, 2 segmental sclerosis, 2 fibrotic crescents)	Mild to moderate tubule atrophy and interstitial fibrosis	Perihilar Variant
2015516	M	68	6.89	100.0	1.55	38.7	138	40 gloms (2 global, 2 segmental sclerosis and hyalinization)	Mild to moderate tubule atrophy and interstitial fibrosis	Perihilar Variant
2015531	M	51	5.58	82.0	3.02	41.5	150	13 gloms (3 global, 3 segmental sclerosis and 1 fibrotic crescent)	Moderate tubule atrophy and interstitial fibrosis	Perihilar Variant
2015572	M	22	6.33	103.0	4.28	20.3	165	13 gloms (Intra-capillary stenosis in 2 gloms urinary pole, endothelium and podocytes segmentally proliferated)	Mild interstitial fibrosis	Tip Variant
2015590	F	57	8.61	117.0	8.86	33.2	115	17 gloms (9 global, 2 segmental sclerosis)	Moderate tubule atrophy and interstitial fibrosis	Not Otherwise Specified

Abbreviations: BUN: blood urea nitrogen, Scr: serum creatinine, 24h UPro: 24 hours urinary protein, ALB: albumin, Hb: hemoglobin.

Supplementary Table 2. Nucleotide sequences of the primers used for RT-PCR

Mouse	Primer Sequence 5' to 3'	
	Forward	Reverse
MMP7	TAGGCGGATGCTCACTTTT	TTCTGAATGCCTGCAATGTC
Collagen I	ATCTCCTGGTGCTGATGGAC	ACCTTGTTTGCCAGGTTTAC
Collagen III	AGGCAACAGTGGTTCTCCTG	GAACCTCGTGCTCCAGTTAGC
α -SMA	GAGGCACCACTGAACCCTAA	CATCTCCAGAGTCCAGCACA
FN	CGAGGTGACAGAGACCACAA	CTGGAGTCAAGCCAGACACA
FSP-1	AGCTACTGACCAGGGAGCTG	TCATTGTCCCTGTTGCTGTC
PAI-1	TGGAAAGAGCCAGATTTATCAT	GAAGTAGAGGGCATTACCAG
β -actin	CAGCTGAGAGGGAAATCGTG	CGTTGCCAATAGTGATGACC