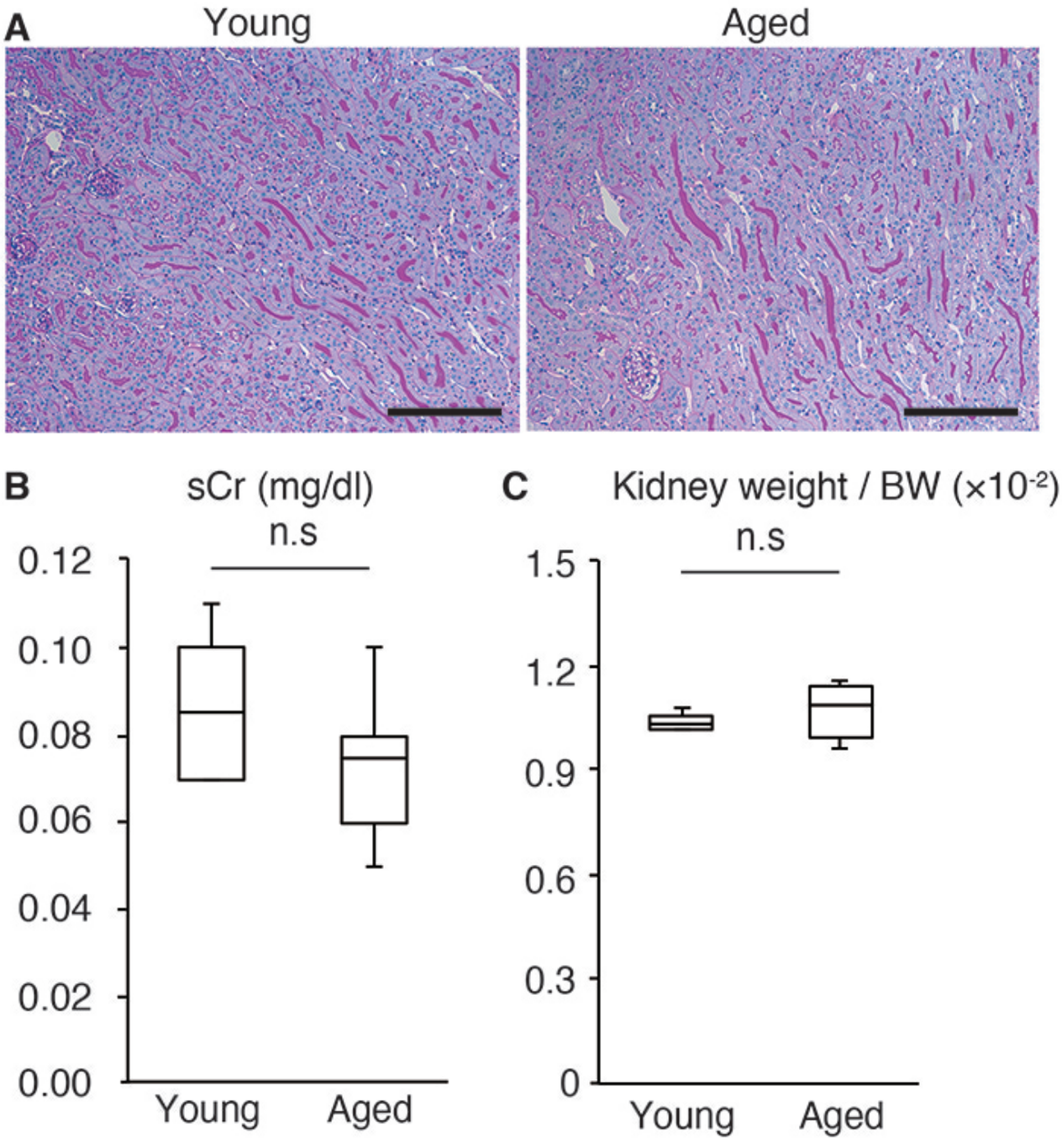

Figure S1. No difference in renal function or morphology is detected between young and aged mice at baseline.

(**A**) Histological analysis of young and aged mouse kidneys. PAS staining did not show tubular injury or fibrosis in the young and aged mouse kidneys. (**B**) Renal function, assessed by serum creatinine (sCr), and (**C**) weight were comparable in both groups ($n = 8$ per group). Scale bars: (**A**) 200 μm. BW: Body Weight. n.s.= not significant, p values were calculated using a 2-tailed Student's t-test. The box corresponded to the first quartile, median (horizontal bar in the box), and third quartile, and the whiskers extended from minimun to maximum values.

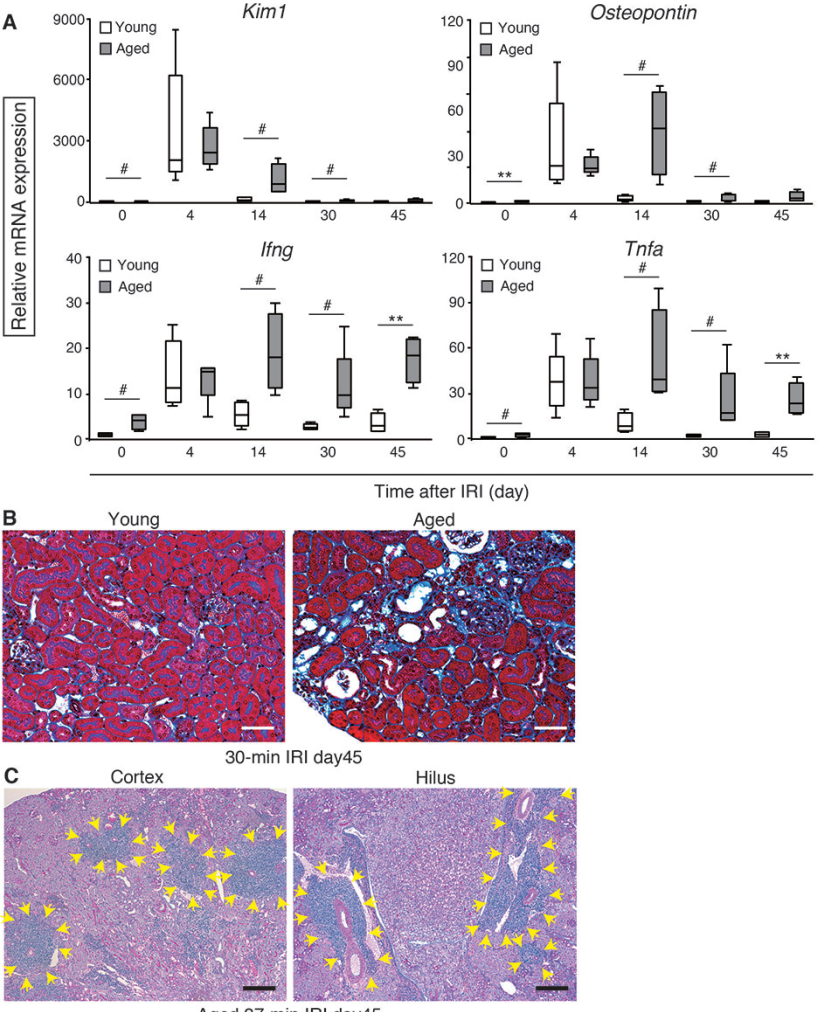

Figure S2. Aged mice develop renal tertiary lymphoid tissues (TLTs), inflammation and fibrosis after ischemic reperfusion injury (IRI). (**A**) Renal mRNA expression of kidney injury markers (*Kim1* and *Osteopontin*) and pro-inflammatory cytokines (*Ifng* and *Tnfa*) at various times after 30-min IRI in young and aged mice (n = 4-5 per group). The expression levels were normalized to those of *Gapdh* and expressed relative to those of young mouse kidney at day 0 (IRI). **: $p < 0.01$, #: $p < 0.05$ versus control, calculated by a 2-tailed Student's t-test.The box corresponded to the first quartile, median (horizontal bar in the box), and third quartile, and the whiskers extended from minimun to maximum values. (**B**) Masson trichrome (MTC) staining showed interstitial fibrosis in the renal cortex of the aged kidney 45 days after 30-min IRI.(**C**) Periodic acid-Schiff (PAS) staining showed inflammatory cell aggregates in the cortex and along the hilus of the aged kidney 45 days after 37-min IRI. Scale bars: (**B**) 50 μm, (**C**) 200 μm.

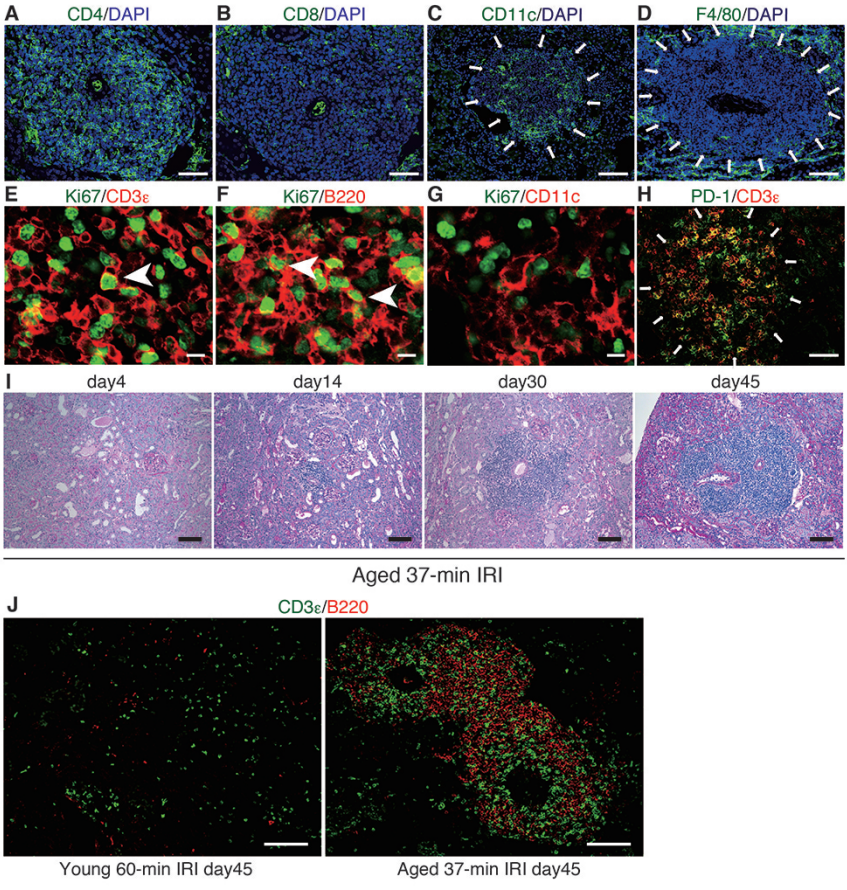

Figure S3. Characteristics of renal tertiary lymphoid tissues (TLTs).
Immunohistological analysis of inflammatory cell aggregates in aged kidneys at day 45 after 37-min ischemic reperfusion injury (IRI). Immunofluorescence (IF) of (**A**) CD4; (**B**) CD8; (**C**) CD11c; (**D**) F4/80; (**E**) Ki67 and CD3ε; (**F**) Ki67 and B220; (**G**) Ki67 and CD11c; and (**H**) programmed cell death protein (PD-1) and CD3ε. Arrows in (**C, D, H**) indicate aggregates. T cells were mainly $CD4^+$ with a smaller $CD8^+$ population. Some dendritic cells were identified as the third populations, whereas $F4/80^+$ cells were almost undetectable within the aggregates. Some T and B cells were $Ki67^+$ (arrowheads); dendritic cells were $Ki67^-$. Some T cells in the aggregates expressed PD-1. (**I**) TLTs over time after IRI. Periodic acid-Schiff (PAS) staining detected the small TLTs 14 days after 37-min IRI; the TLTs expanded at day 30 and day 45. (**J**) IF of CD3ε and B220 in young and aged kidneys 45 days after IRI. Scale bars: (**A, B, H**) 50 μm, (**C, D, I, J**)100 μm, (**E-G**) 10 μm.

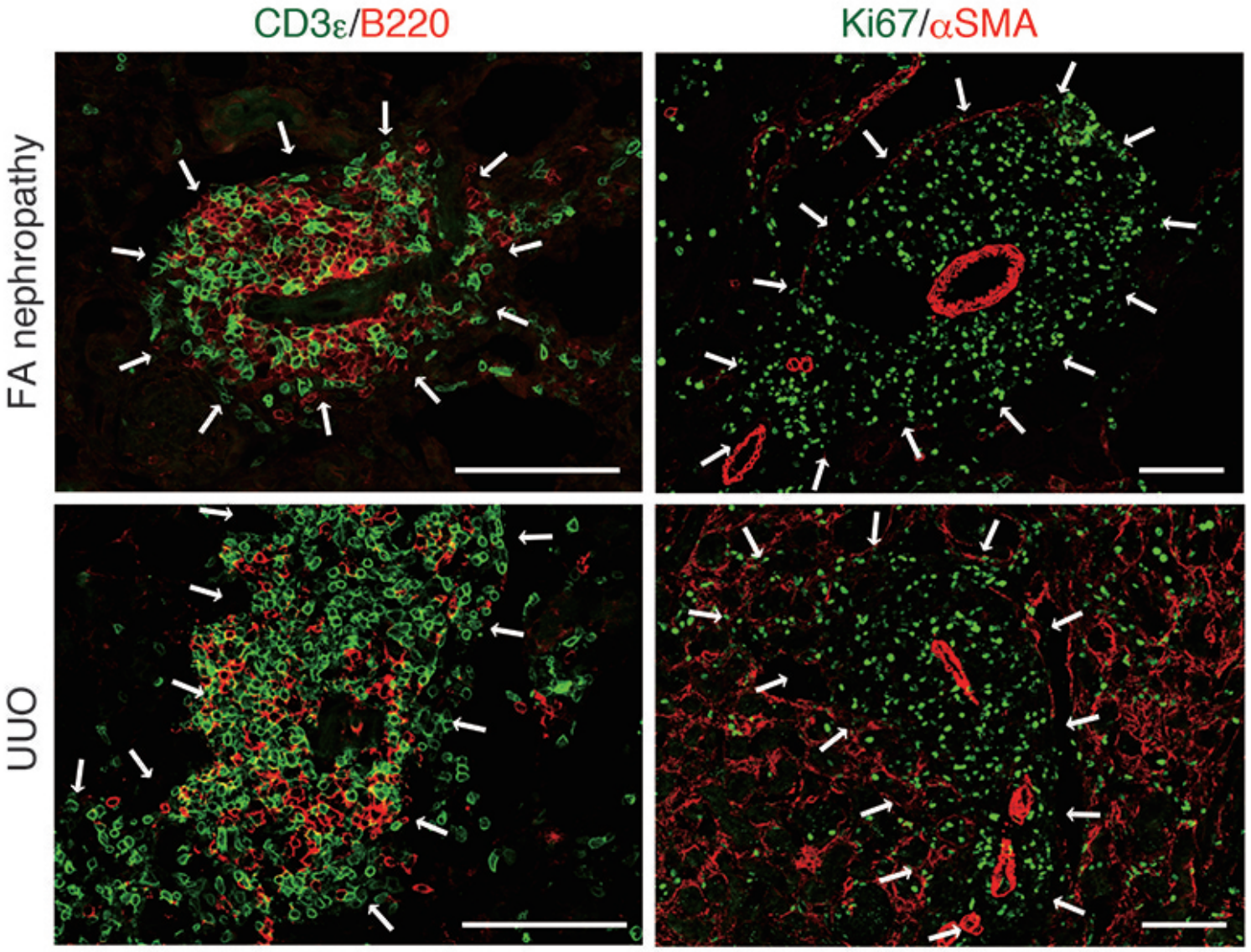

Figure S4. Aged mice develop renal tertiary lymphoid tissues (TLTs) in folic acid (FA) nephropathy model and unilateral ureteral obstruction (UUO) model.
Immunofluorescence of CD3ε and B220; Ki67 and α-smooth muscle actin (αSMA) in TLTs of aged mouse kidney (FA nephropathy at day 21 and UUO at day14). Arrows indicate TLT localization. Scale bars: 100 μm.

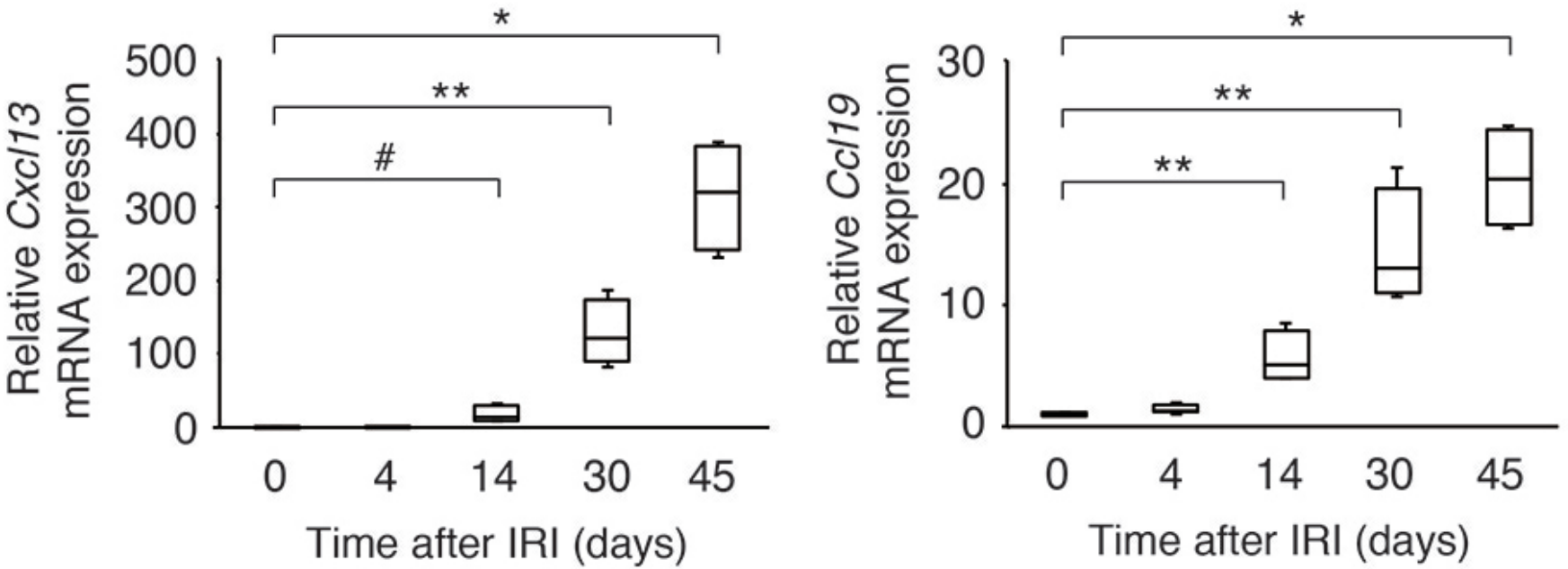

Figure S5. *Cxcl13* and *Ccl19* mRNA levels increase as tertiary lymphoid tissues (TLTs) form.

Cxcl13 and *Ccl19* mRNA expression in aged kidneys began gradually increasing 14 days after ischemic reperfusion injury (IRI), coinciding with TLT formation. The expression levels were normalized to those of *Gapdh* and expressed relative to those in aged mice without IRI (n = 4-5 per time point). *: $p < 0.001$, **: $p < 0.01$, #: $p < 0.05$ versus day 0 after IRI. p values were calculated using a 2-tailed Student's t-test. The box corresponded to the first quartile, median (horizontal bar in the box), and third quartile, and the whiskers extended from minimun to maximum values.

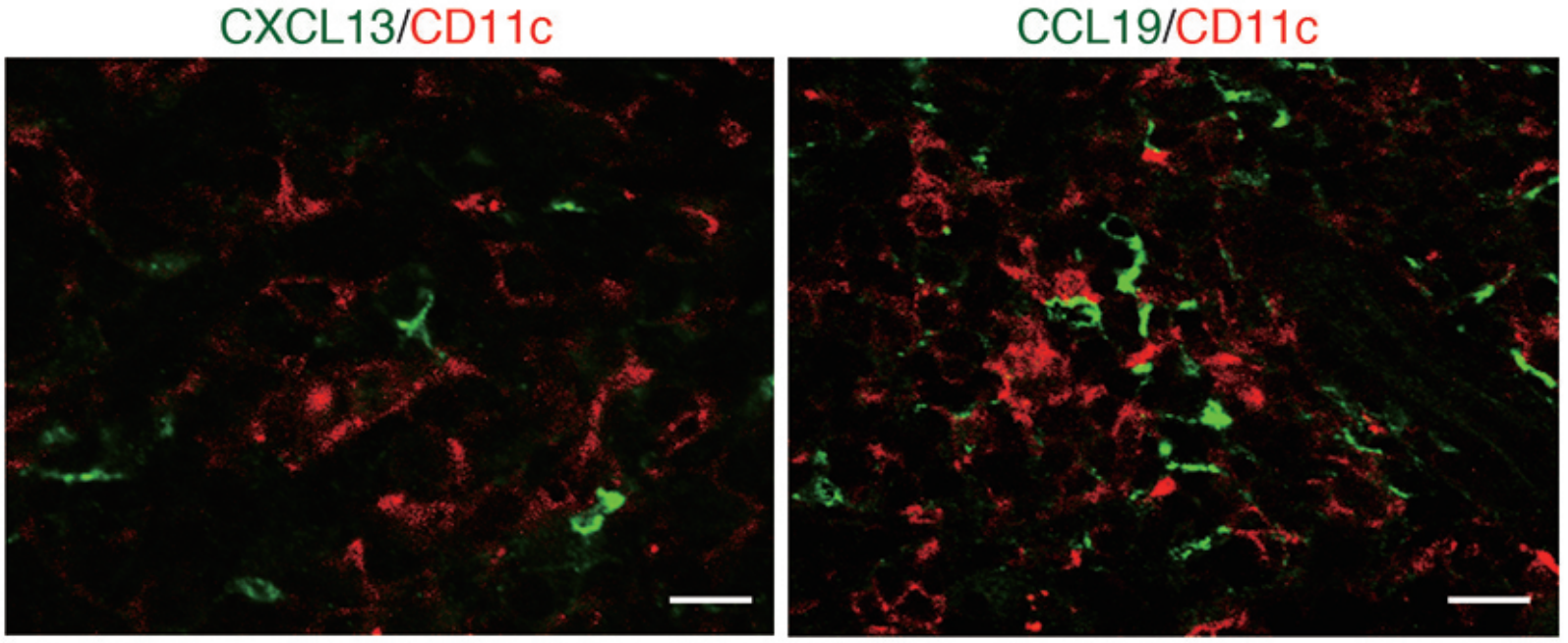

Figure S6. CD11c$^+$ dendritic cells in aged ischemic reperfusion injury (IRI) kidneys do not express CXCL13 or CCL19.
Immunohistological analysis of aged mouse kidneys 45 days after 37-min IRI. Immunofluorescence analysis of CD11c, CXCL13, and CCL19 showed that dendritic cells were not the major producer of CXCL13 or CCL19 in aged IRI kidneys. Scale bar: 10 μm.

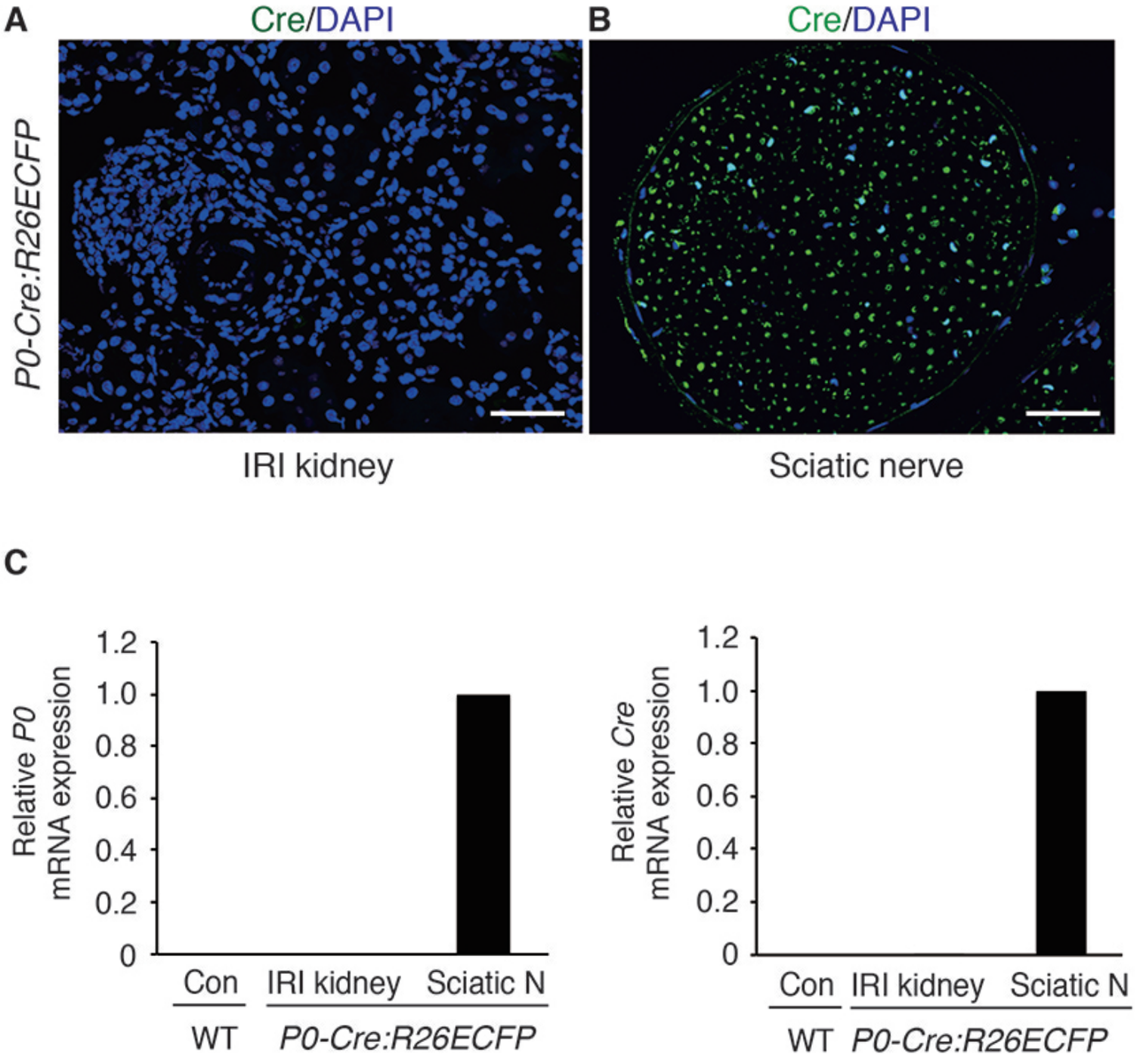

Figure S7. No Cre protein or *Myelin protein zero (P0)* or *Cre* mRNA is detected in aged ischemic reperfusion injury (IRI) kidneys.

(**A**) Cre protein was undetectable in the aged IRI kidneys from *P0-Cre:R26ECFP* mice, whereas (**B**) Cre protein was highly expressed in the sciatic nerve of the same mice, providing a positive control for Cre protein immunofluorescence. Scale bars: (**A, B**) 50 μm. (**C**) The expression of *P0* and *Cre* mRNAs were undetected in the aged IRI kidneys of *P0-Cre:R26ECFP* mice; The expression levels were normalized to those of *Gapdh* and expressed relative to that in the sciatic nerve (Sciatic N). Aged mice were analyzed 30 days after 60-min IRI ($n = 4$).

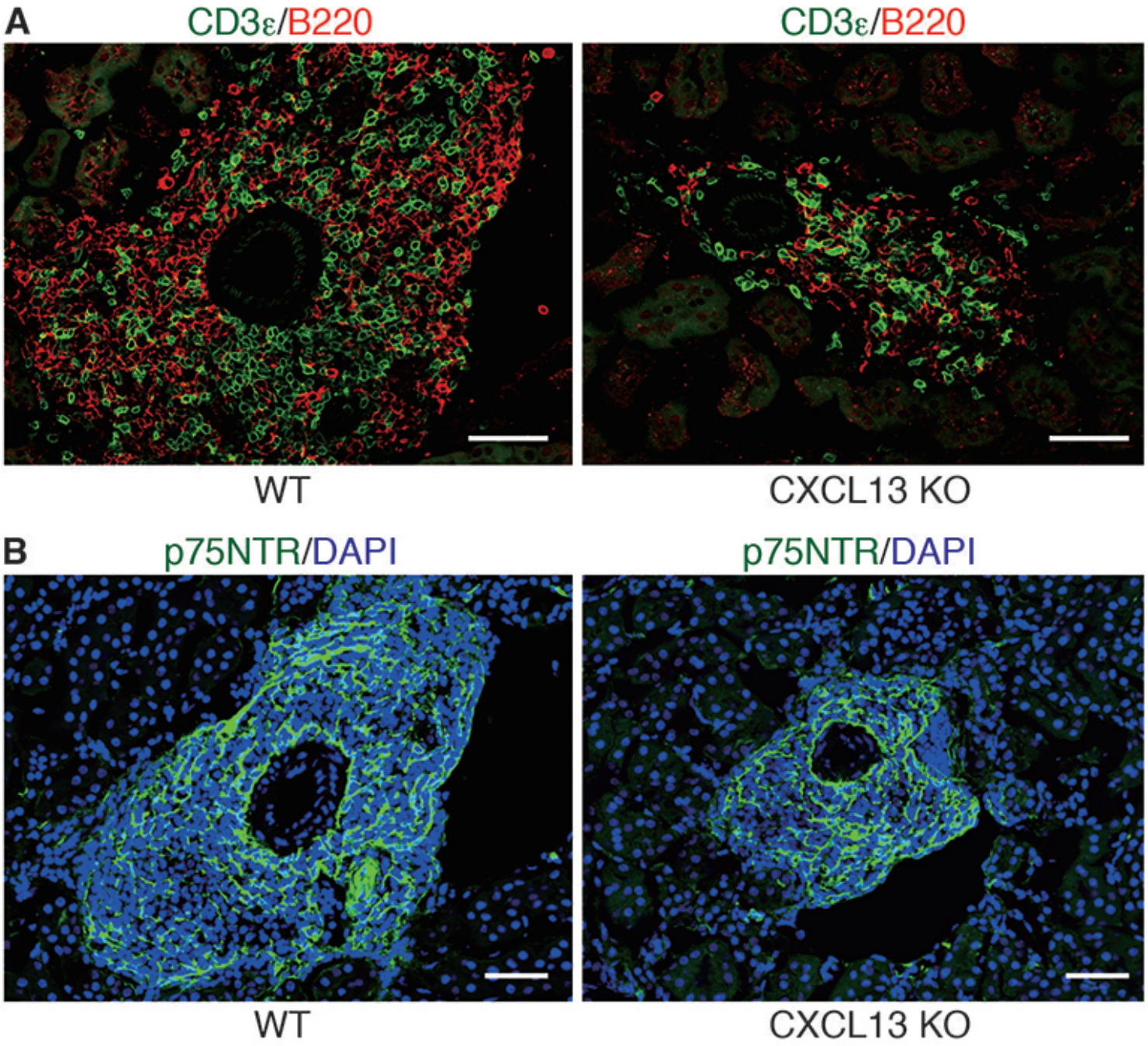

Figure S8. Renal tertiary lymphoid tissues (TLTs) in aged *CXCL13*-deficient mice and their wild-type littermates are phenotypically equivalent.
Immunohistological analysis of 9-month-old *CXCL13*-deficient mice (CXCL13 KO) and wild-type littermates (WT) 45 days after 37-min IRI. The immunofluorescence of (**A**) CD3ε and B220; and (**B**) p75 neurotrophin receptor (p75NTR). Scale bars: (**A, B**) 50 μm.

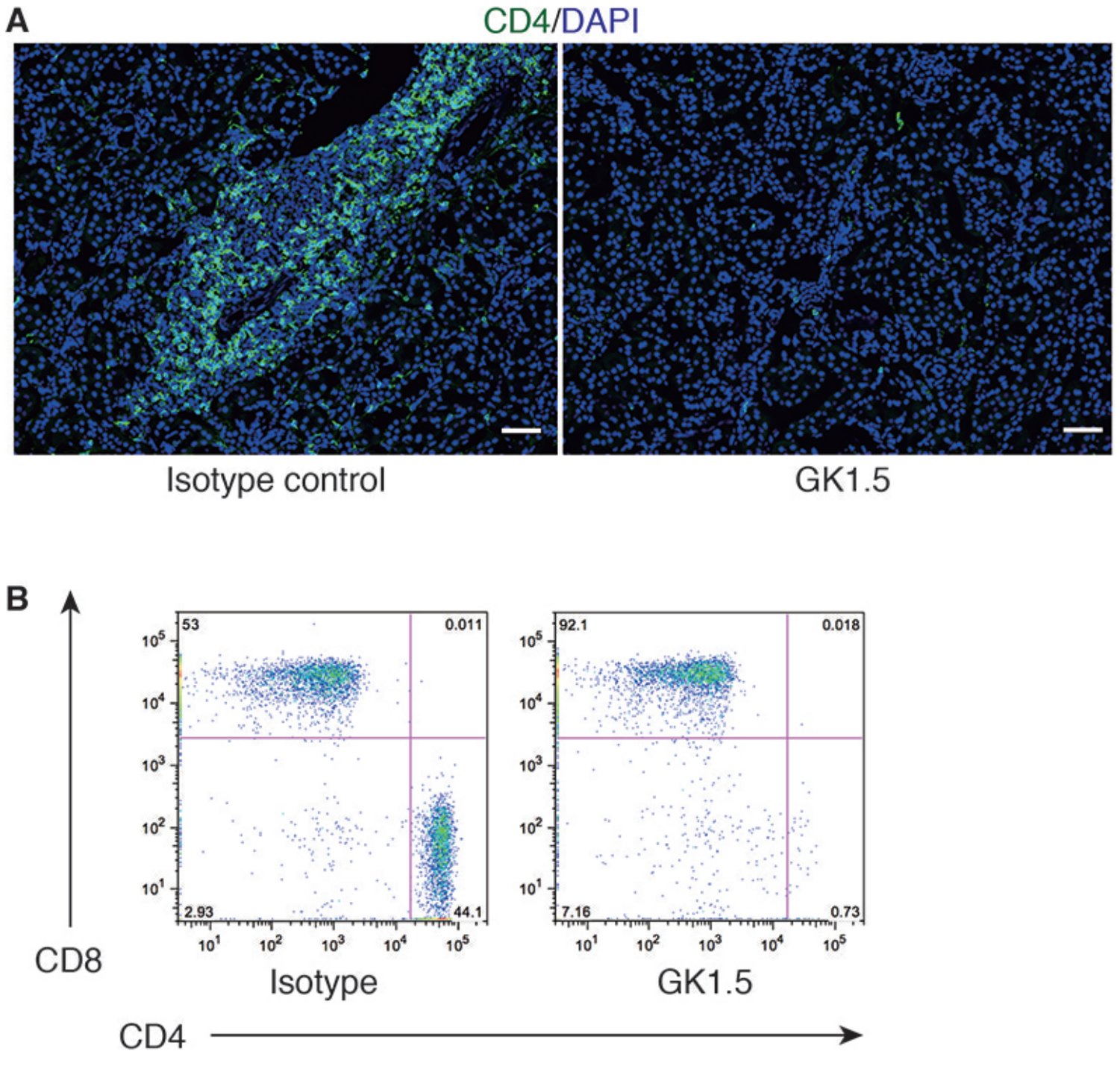

Figure S9. GK1.5 treatment depletes CD4⁺ cells in the kidney and peripheral blood after ischemic reperfusion injury (IRI).

(**A**) CD4⁺ cells were aggregated in renal tertiary lymphoid tissues (TLTs) in mice treated with isotype control antibody, whereas CD4⁺ cells were almost undetectable in the kidneys from GK1.5-treated mice. Scale bar: 50 μm. (**B**) CD3ε⁺ TCRβ⁺ T cells in the peripheral blood 45 days after IRI. CD4⁺ T cells in peripheral blood were dramatically reduced in the GK1.5-treated mice. Data shown are representative of five independent experiments.

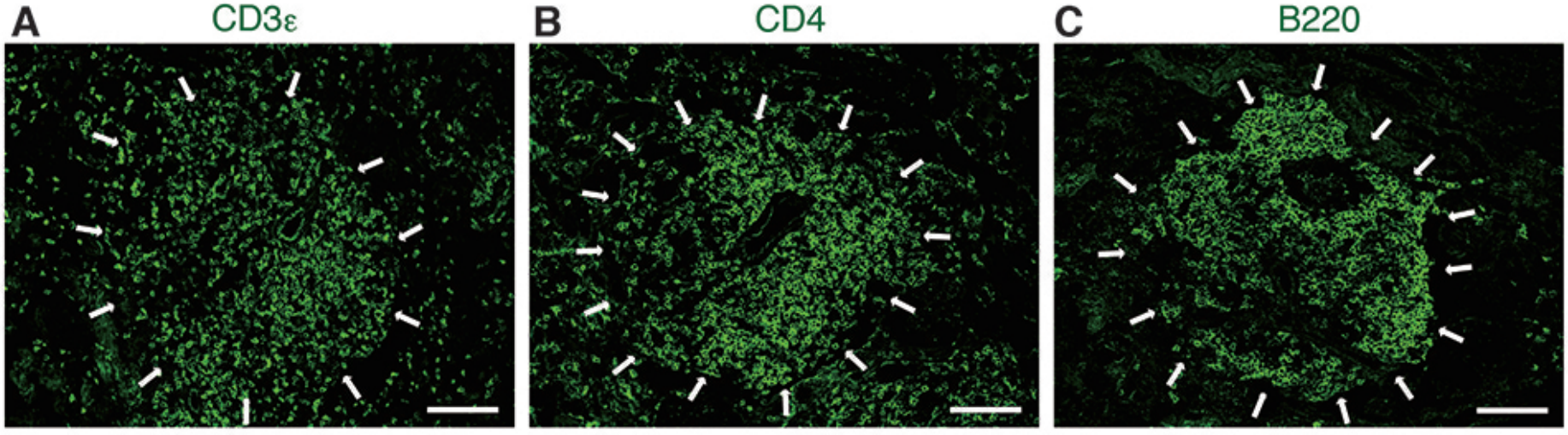

Figure S10. T cells, especially CD4⁺ T cells, spread outward from renal tertiary lymphoid tissues (TLTs).
Immunohistological analysis of aged kidneys 45 days after 45-min ischemic reperfusion injury (IRI). Immunofluorescence analysis of (**A**) CD3ε; (**B**) CD4; (**C**) B220. Arrows indicate the localization of TLTs. Scale bars: 50 μm.

Supplementary Table 1. Clinical characteristics of the patients.

	Young (< 40 yr old)	Aged (> 60 yr old)
Patients (*n*)	13	43
Age (yr) mean +/- SD	35.7 +/- 4.6	70.2 +/- 6.4 (*)
TLT + (%)	0 (0%)	12 (28%) (#)
Male (%)	7 (54%)	20 (47%) (n.s.)
Female (%)	6 (46%)	23 (53%) (n.s.)
DM + (%)	1 (8%)	8 (19%) (n.s.)
HTN + (%)	2 (15%)	29 (67%) (*)
eGFR mean +/- SD (a)	75.9 +/- 30.3	56.7 +/- 29.3 (#)
Serum Cr mean (mg/dl)	1.01 +/- 0.59	1.89 +/- 3.18 (n.s.)

n.s.: not significant, DM: diabetes mellitus, HTN: hypertention,

eGFR: estimated glomerular filtration rate.

a: eGFR was calculated using the formula below:

$$eGFR\ (\text{mL/min per } 1.73\ m^2) = 194 \times Cr^{-1.094} \times Age^{-0.287}\ (\text{in case of female, } \times 0.739)$$

*: $p < 0.001$, #: $p < 0.05$ versus young patients. *p* values were calculated using Pearson's χ^2 test.

Supplementary Table 2. Primer sequences used for real-time PCR.

Gene	Sequence(5'-3')	
	Forward	Reverse
Gapdh	ACGGCAAATTCAACGGCACAGTCA	TGGGGGCATCGGCAGAAGG
Kim1	TCTATGTTGGCATCTGCATCG	GAAGGCAACCACGCTTAGAGA
Osteopontin	TTTGCCTGTTTGGCATTGC	TCAGGCACCAGCCATGTG
Ifng	CTCATGGCTGTTTCTGGCTGTTAC	TTTCTTCCACATCTATGCCACTTG
Tnfa	CCTCCCTCTCATCAGTTCTATGG	CGTGGGCTACAGGCTTGTC
Cxcl13	CGTGCCAAATGGTTACAAAGATT	GTGGCTTCAGGCAGCTCTTC
Ccl19	CCTGGGAACATCGTGAAAGC	TGGAGGTGCACAGAGCTGATA
Ccl21	AAGGCAGTGATGGAGGGG	CGGGGTAAGAACAGGATTG
Aid	CCAAGGGACGGCATGAGA	GCCAGACTTGTTGCGAAGGT
p75ntr	GGAGAGAAACTGCACAGCGACA	TCACCATTGAGCAGCAGCTTCTCG
collagen1a1	GTTTGGAGAGAGCATGACCGA	TGGACATTAGGCGCAGGAA
fibronectin	CCTTTCACCCTTAAGCCTTTTG	TCCCTATTGATCCCAGACCAA
Cre	CTCGACCAGTTTAGTTACCC	ACGACCAAGTGACAGCAATG
Myelin protein 0	CAAAAACCCACCGGACATAGTG	CGAAGATTTGTGAAATCTCCCC