

SUPPLEMENTARY DATA

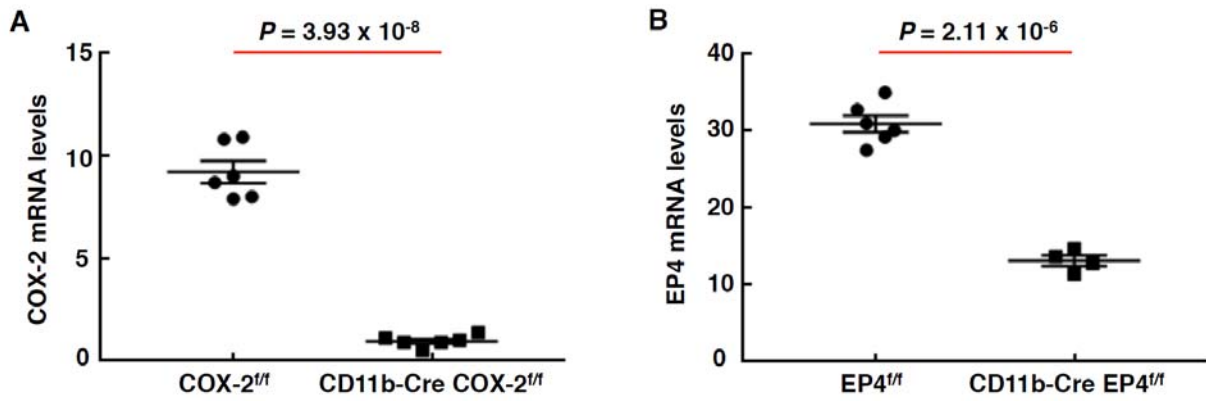
**Supplementary Table 1.** Effect of COX-2 or EP4 deletion in macrophages on development of diabetic nephropathy in STZ-induced diabetic mice (C57/BL6)

<b>A</b>	<b>Parameter</b>	<b>Genotype</b>	<b>Baseline</b>	<b>24 weeks after STZ</b>
	BW (gram)	WT	27.6 ± 0.7 (n=10)	26.4 ± 1.2 (n=8)
		COX-2 KO	27.7 ± 1.2 (n=10)	27.2 ± 1.2 (n=8)
	BG (mg/dl)	WT	126.5 ± 4.3 (n=10)	434.4 ± 20.8 (n=8)
		COX-2 KO	119.9 ± 5.7 (n=10)	402.8 ± 15.8 (n=8)
	ACR (μg/mg)	WT	9.7 ± 1.0 (n=10)	37.7 ± 4.8 (n=8)
		COX-2 KO	11.1 ± 2.5 (n= 10)	67.7 ± 7.0 (n=8)**
<b>B</b>	<b>Parameter</b>	<b>Genotype</b>	<b>Baseline</b>	<b>24 weeks after STZ</b>
	BW (gram)	WT	25.6 ± 0.7 (n=8)	26.1 ± 0.6 (n= 8)
		EP4 KO	25.3 ± 1.0 (n=8)	25.4 ± 1.0 (n=8)
	BG (mg/dl)	WT	129.8 ± 7.7 (n=8)	448.6 ± 10.5 (n=8)
		EP4 KO	128.6 ± 6.4 (n=8)	476.8 ± 18.6 (n=8)
	ACR (μg/mg)	WT	9.9 ± 1.1 (n=8)	34.3 ± 5.9 (n=8)
		EP4 KO	10.2 ± 1.2 (n= 8)	64.1 ± 5.5 (n=8)**

COX-2 KO mice: CD11b-Cre; COX-2<sup>fl/fl</sup> mice; EP4 KO: CD11b-Cre; EP4<sup>fl/fl</sup> mice.  
 COX-2<sup>fl/fl</sup> and EP4<sup>fl/fl</sup> mice were used as WT for COX-2 KO and EP4 KO, respectively. \*\*: P < 0.01 vs. corresponding WT mice.

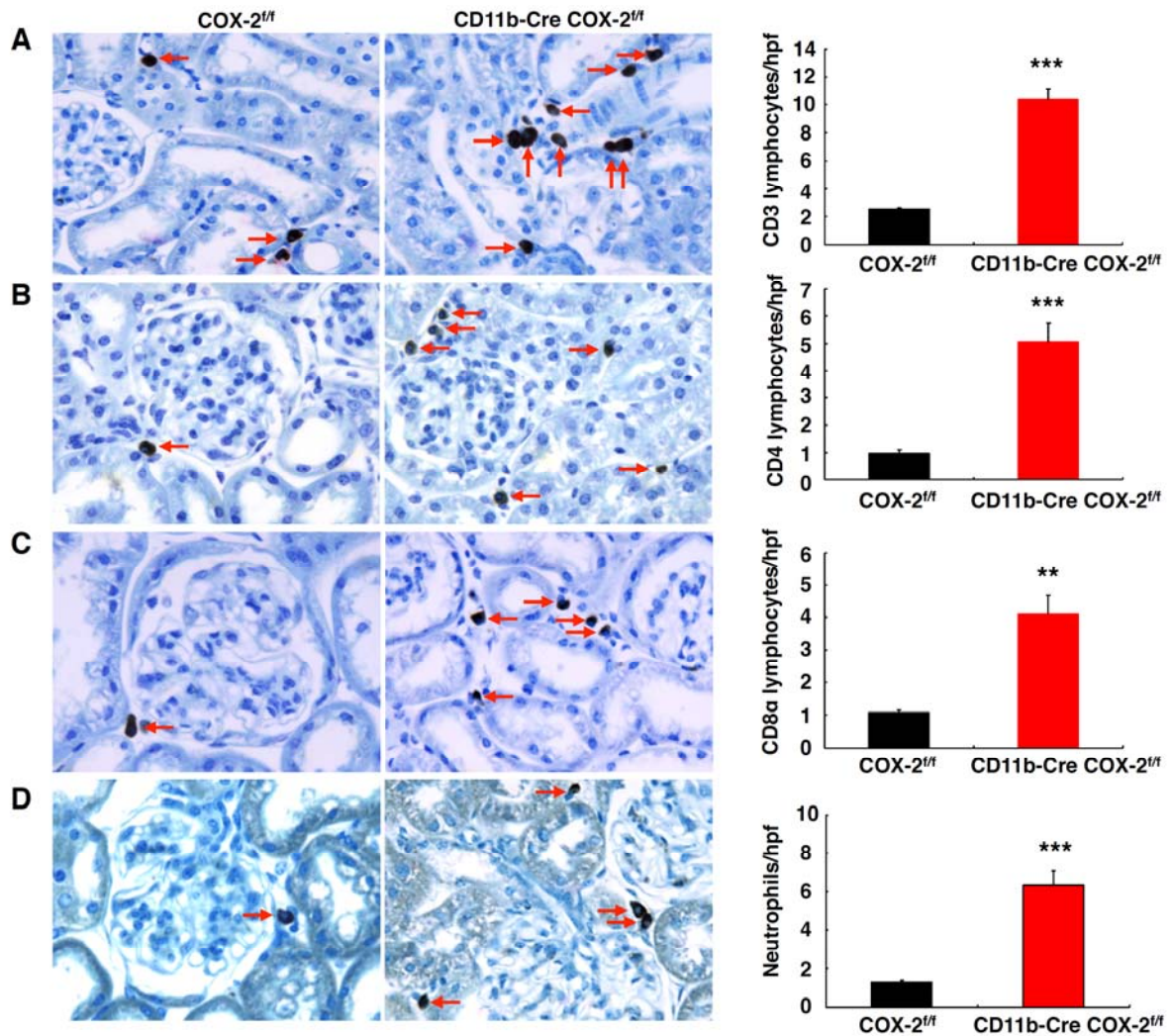
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**Supplementary Figure 1.** Renal macrophages were isolated using CD11b magnetic beads were used for qPCR. **A:** Renal macrophage COX-2 mRNA levels were dramatically reduced in CD11b-Cre COX-2<sup>fl/fl</sup> mice compared to COX-2<sup>fl/fl</sup> mice (wild type). **B:** Renal macrophage EP4 mRNA levels were markedly lower in CD11b-Cre EP4<sup>fl/fl</sup> mice than EP4<sup>fl/fl</sup> mice (wild type).



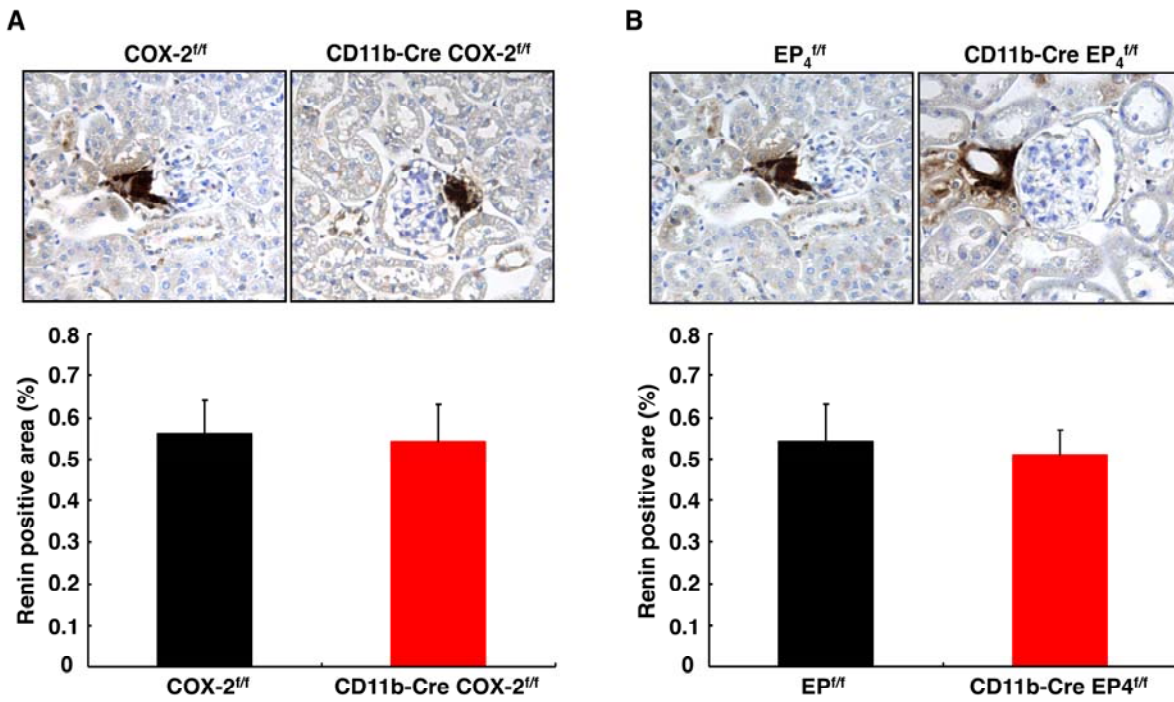
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**Supplementary Figure 2.** COX-2 deletion in macrophages led to increases in renal lymphocyte and neutrophil infiltration in diabetic mice. Total T lymphocytes (CD3) (A), CD4 lymphocytes (B), CD8 lymphocytes (C), and neutrophil (Gr-1) (D) were all increased in diabetic CD11b-Cre COX2<sup>f/f</sup> kidneys. \*\*  $P < 0.01$ , \*\*\*  $P < 0.001$ ;  $n = 4$ . Original magnification: x 400.



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**Supplementary Figure 3.** COX-2 deletion or EP4 deletion in macrophages had minimal effect on renal renin expression. Renin immunostaining showed comparable renal renin expression levels between diabetic COX-2<sup>f/f</sup> mice and diabetic CD11b-Cre COX-2<sup>f/f</sup> mice (A) and between diabetic EP4<sup>f/f</sup> mice and diabetic CD11b-Cre EP4<sup>f/f</sup> mice. N = 3 in each group.



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**Supplementary Figure 4.** COX-2 deletion had minimal effect on expression of components of the renal renin angiotensin system (RAS). Renal mRNA levels of the component of RAS including renin, angiotensinogen (AGT), ACE, ACE2, AT1a, AT1b, AT2 and Mas, were comparable between diabetic COX-2<sup>f/f</sup> mice and diabetic CD11b-Cre COX-2<sup>f/f</sup> mice. N = 6 in each group.

