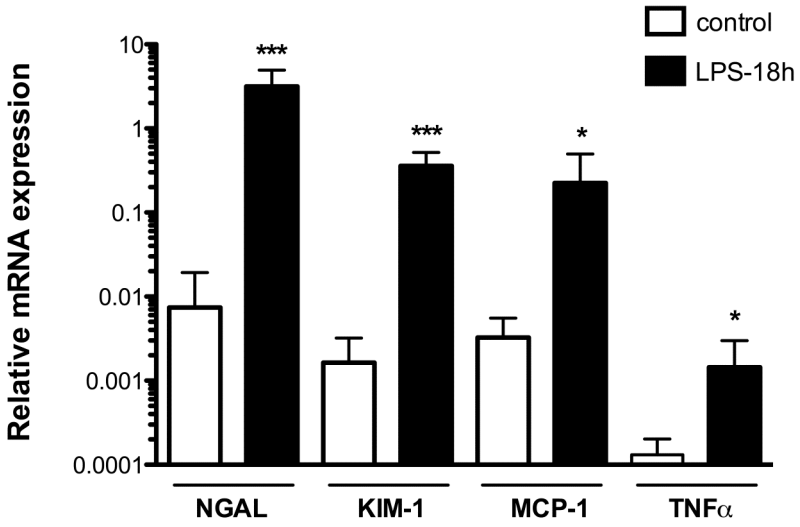
SUPPLEMENTAL FIGURES

Supplemental Figure 1: Further characterization of the endotoxemia model. **(A)** real-time PCR for markers of renal injury on kidney RNA taken 18 h after vehicle control (n = 9) or LPS (n = 13-15) treatment. Results normalized to β-actin and presented on log10 scale *p < 0.05, ***p < 0.0001. **(B)** Hypoxia inducible factor-1α (HIF-1α) protein measured by commercial ELISA (standard curve depicted in upper panel) in whole kidneys homogenates prepared 18 h after vehicle or LPS treatment (n = 5 per condition).

A.



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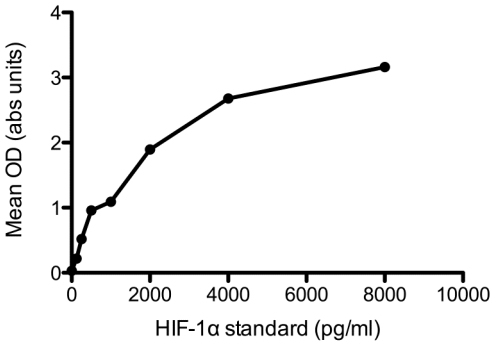
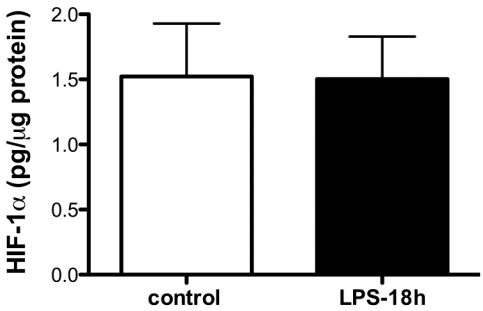
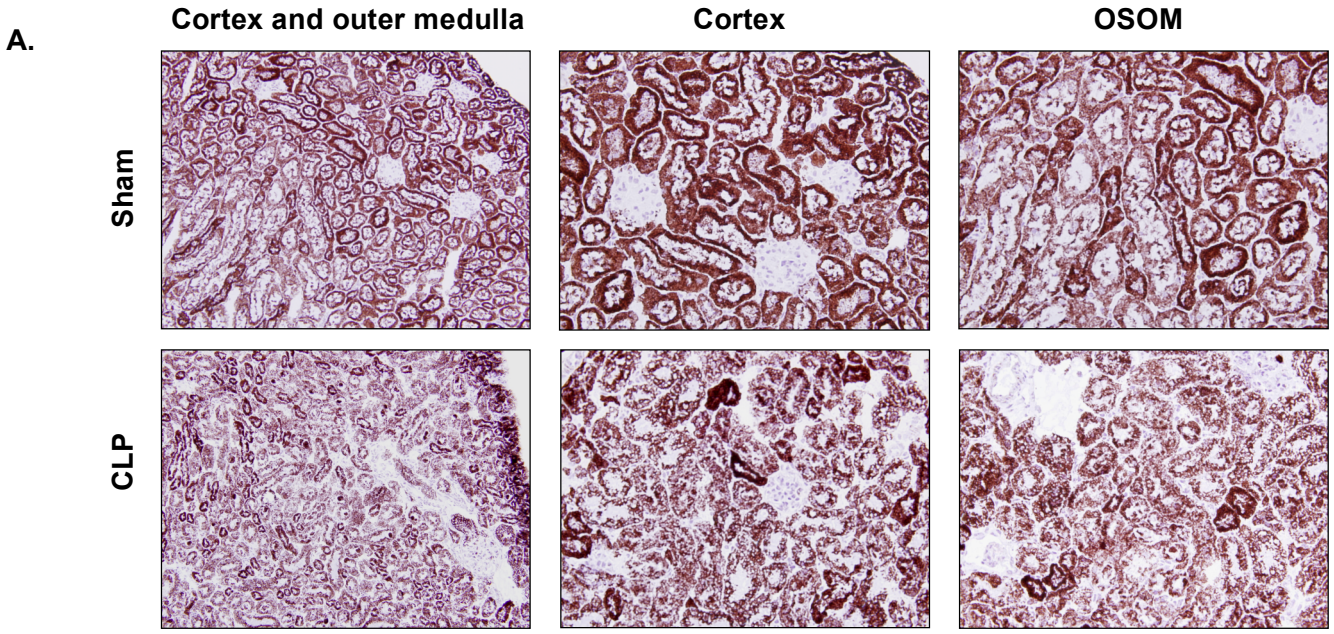
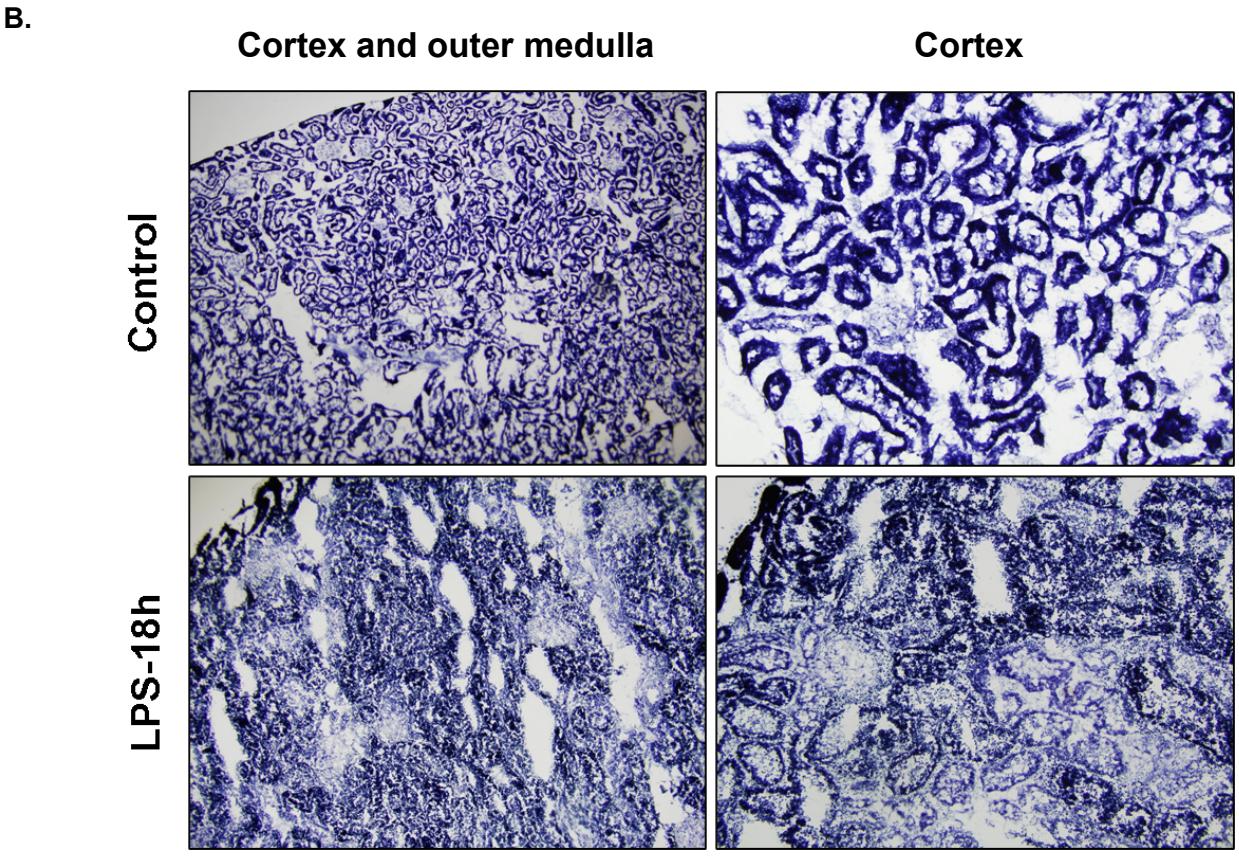


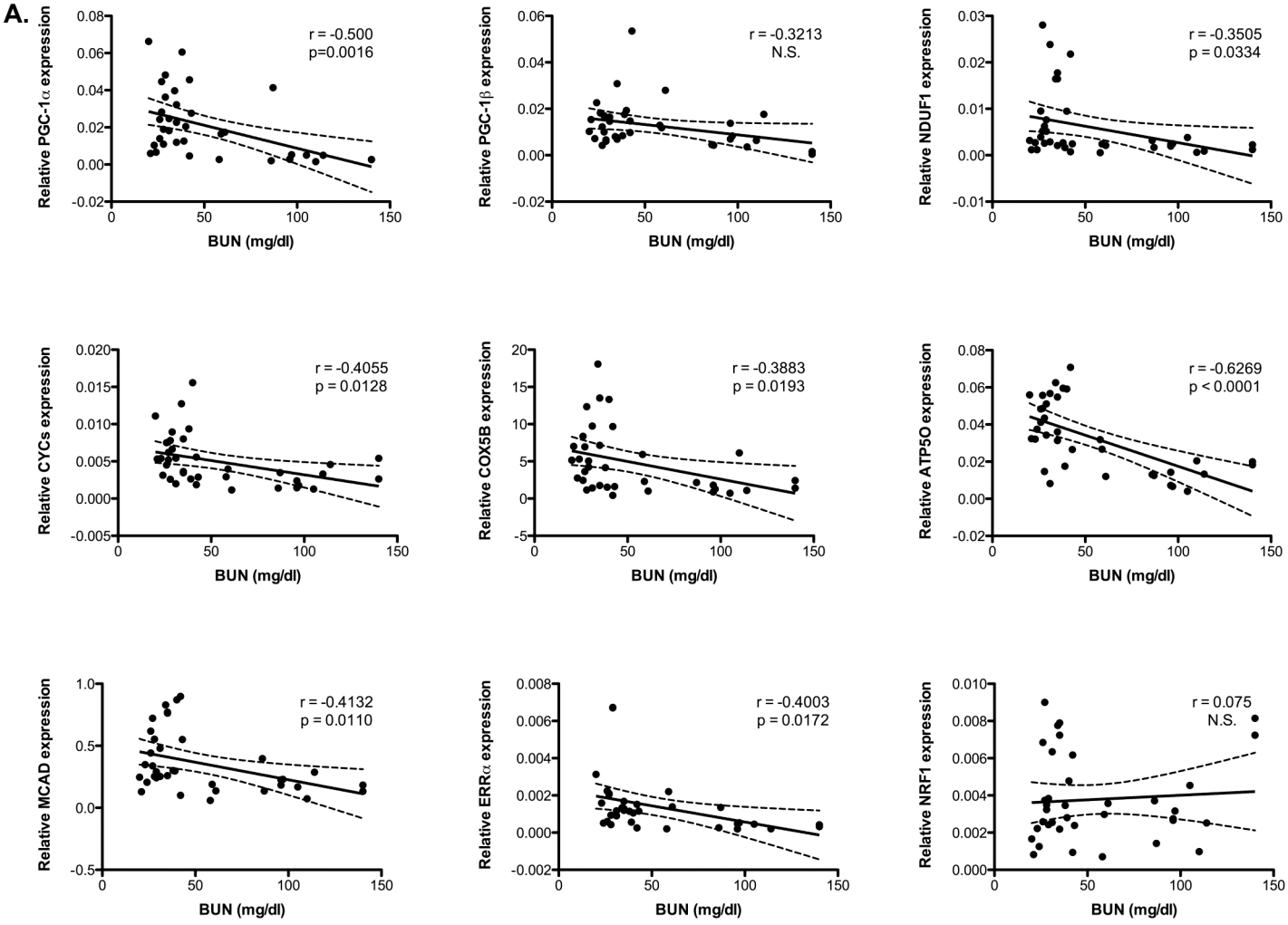


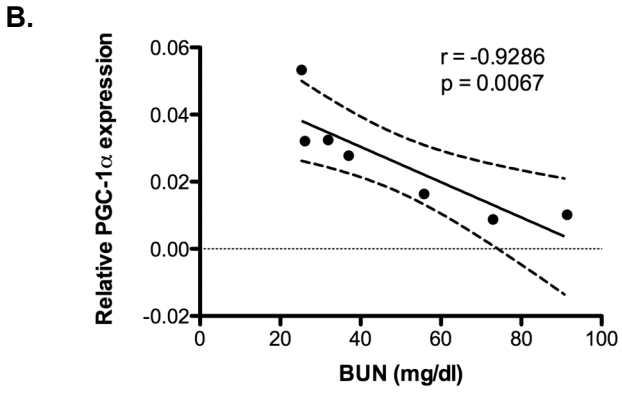
Supplemental Figure 2: In situ enzyme chemistry. **(A)** Cytochrome c oxidase enzyme activity of kidneys 24 h after sham operation or CLP (OSOM for outer stripe of outer medulla, representative of n = 3 per condition). Original magnification: x10 (cortex and outer medulla); x20 (cortex, OSOM). **(B)** NADH dehydrogenase enzyme activity 18 h after vehicle or LPS exposure. Representative of n = 4 per condition. Original magnification: x10 (cortex and outer medulla); x20 (cortex).





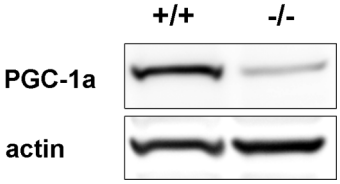
Supplemental Figure 3: Suppression of PGC-1α and downstream gene expression in proportion to the degree of renal functional impairment. **(A)** Transcript abundance relative to β-actin was measured by real-time PCR for the indicated genes in n = 35-37 kidney RNAs prepared at 0, 18, or 42 h in the resuscitated LPS model (LPS 10 mg/kg at t = 0 h followed by 10 ml/kg saline at t = 18 h). These data demonstrate that, regardless of heterogeneity within any given time point, gene expression is strongly associated with the degree of functional impairment as measured by BUN. Note that PGC-1β expression does not significantly correlate to the degree of impairment. **(B)** 18 h after cecal ligation and perforation, mice were sacrificed for measurement of renal function and renal PGC-1α expression (n = 7, p = 0.0067). Correlation coefficient (r) and p-values for (**A**) and (**B**) calculated by Spearman method.





Supplemental Figure 4: Validation of renal PGC-1α suppression in endotoxemia by Western analysis. **(A)** Confirmation of the specificity of the anti-PGC-1α antibody. **(B)** Measurement of PGC-1α in whole kidney homogenates prepared 18 h after vehicle or LPS.

A.



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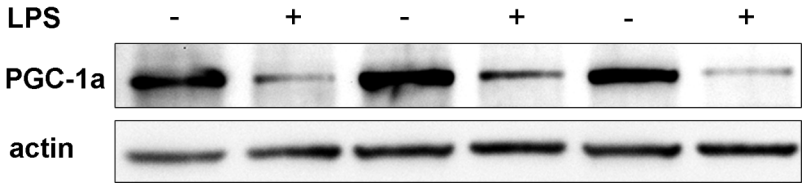
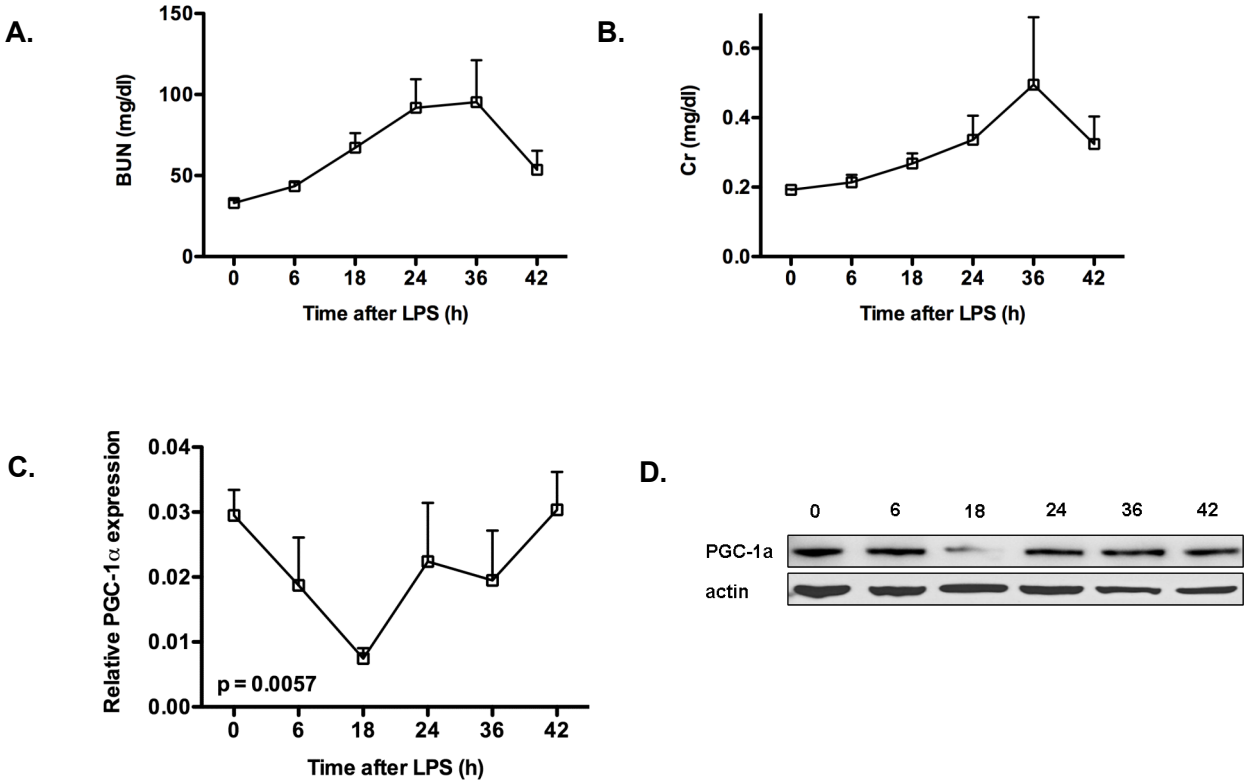
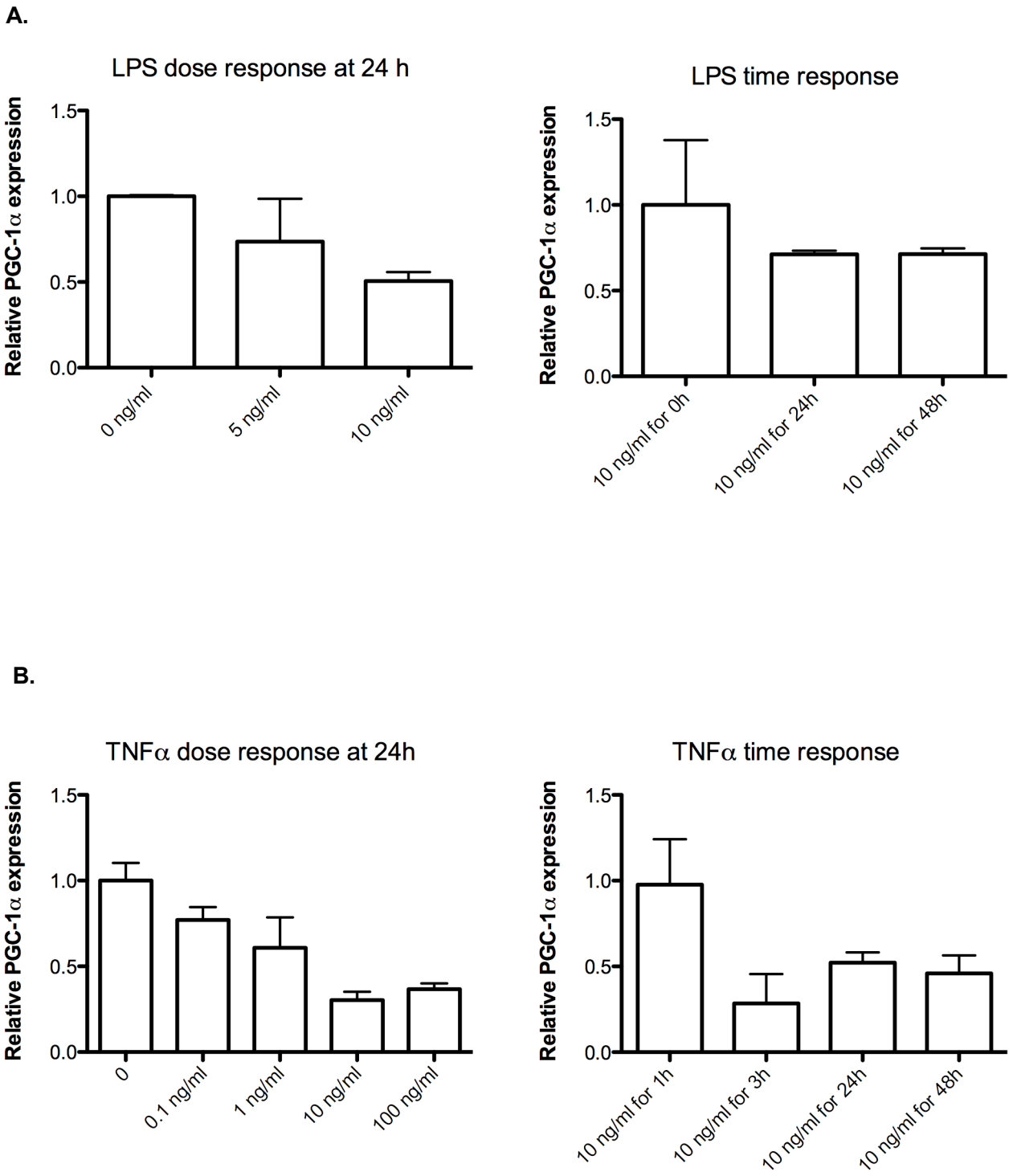


Supplemental Figure 5: Time-course of renal function and PGC-1α changes in the resuscitated LPS model. **(A, B)** BUN and creatinine changes in following LPS. 10 ml/kg saline was injected intraperitoneally at 18 h after LPS to resuscitate animals (n ≥ 4 per time point). **(C)** Expression of PGC-1α in renal homogenates collected from animals in (A, B) above showing an inverse pattern to BUN or creatinine and revealing the nadir of expression to occur near 18 h after LPS. **(D)** Western analysis of renal lysates from representative animals in (A, B) above.



Supplemental Figure 6: Dose and time-dependent suppression of PGC-1α by TNFα in a second in vitro human proximal tubule model, the HK-2 cell line. **(A)** Abundance of PGC-1α transcript relative to β-actin in HK-2 cells treated with LPS at the indicated doses and durations (n = 3-5 per condition). Note: LPS was supplemented with LPS-binding protein and CD14. **(B)** Abundance of PGC-1α transcript relative to β-actin in HK-2 cells treated with TNFα at the indicated doses and durations (n = 3-5 per condition).



Supplemental Figure 7: Baseline renal parameters of PGC-1α global and proximal-tubule specific knockout mice. **(A)** (left) BUN and Cr of knockout male mice at 8 weeks of age and wild-type littermates. (right) Giemsa-stained semi-thin section of cortex (upper row; original magnification: x40), transmission EM of basement membranes showing intact foot processes (middle row; original magnification: x3200), and high-power transmission EM of proximal tubule mitochondria (lower row; original magnification: x18,000). Arrow points to one mitochondrion with reduced density of cristae. **(B)** BUN and Cr of 8-week old tubule-specific male knockout mice (Cre/+ fl/fl) and genotype controls (fl/fl).