Supplemental Table 1. Circulating inflammatory mediators in the experimental groups (mean±SEM, n=7 each).

Mediator (ng/ml)	Sham	HT	CAS	CAS+HT	*P* value
GM-CSF	0.06±0.02	0.02±0.01	0.04±0.01	0.04±0.02	0.48
IL-1α	0.025±0.003	0.028±0.004	0.026±0.005	0.030±0.004	0.84
IL-1β	0.20±0.03	0.2±0.05	0.22±0.03	0.24±0.04	0.85
IL-1ra	0.21±0.03	0.25±0.04	0.41±0.21	0.31±0.09	0.70
IL-2	0.05±0.02	0.06±0.03	0.05±0.02	0.04±0.01	0.83
IL-4	0.37±0.06	0.81±0.24	0.40±0.06	0.39±0.06	0.07
IL-6	0.02±0.01	0.02±0.01	0.03±0.01	0.01±0.01	0.65
IL-8	0.032±0.014	0.017±0.008	0.016±0.004	0.030±0.014	0.54
IL-10	0.15±0.03	0.14±0.02	0.15±0.02	0.13±0.03	0.87
IL-12	0.40±0.04	0.41±0.09	0.30±0.03	0.31±0.05	0.40
IL-18	0.67±0.08	0.72±0.11	0.75±0.11	0.61±0.04	0.77
TNFα	0.05±0.02	0.06±0.02	0.05±0.01	0.08±0.02	0.62

GM-CSF, granulocyte-macrophage colony-stimulating factor; HT, hypertension; CAS, coronary artery stenosis; IL, interleukin; TNF, tumor necrosis factor.

Supplemental Table 2. Systemic characteristics, kidney hemodynamics and function in Sham and femoral artery stenosis (FAS) pigs (mean±SEM).

	Sham	FAS
Degree of FAS, %	0	82.5±7.5
Body weight, kg	48.0±2.8	54.0±3.0
MAP, mmHg	96.7±2.8	92.2±11.4
GFR, $ml \cdot min^{-1}$	71.6±15.9	72.0±2.8
RBF, $ml \cdot min^{-1}$		
Basal	469.0±63.1	475.8±8.6
Ach	677.4±32.5	873.2±41.4
Perfusion $ml \cdot min^{-1} \cdot ml^{-1}$		
Cortex: *baseline*	4.10±0.47	3.90±0.23
Ach	6.21±0.29	7.23±0.15
Medulla: *baseline*	2.84±0.44	4.00±0.76
Ach	3.77±0.55	6.18±0.95
RVR, $mmHg \cdot min^{-1} \cdot ml^{-1}$	0.18±0.02	0.19±0.02
Creatinine, $mg \cdot dL^{-1}$	1.17±0.31	1.23±0.14
Urine protein, $\mu g \cdot ml^{-1}$	16.9±2.5	11.5±0.5

MAP, mean arterial pressure; GFR, glomerular filtration rate; RBF, renal blood flow; Ach, acetylcholine; RVR, renal vascular resistance.

Supplemental Table 3. Systemic characteristics, kidney hemodynamics and function in Sham, coronary artery stenosis (CAS) and CAS+Bendavia pigs (mean±SEM).

	Sham	CAS	CAS+Bendavia
Degree of CAS, %	0	77.3±8.9*	80.0±5.0*
Myocardial perfusion	1.02±0.07	0.70±0.09*	0.56±0.02*
Body weight, kg	48.0±2.8	51.6±4.6	55.0±3.0
MAP, mmHg	96.7±2.8	101.3±5.6	104.9±1.5
GFR, ml·min^{-1}	71.6±15.9	83.4±36.4	73.2±2.0
RBF, ml·min^{-1}			
Basal	469.0±63.1	422.3±82.5	412.4±32.7
Ach	677.4±32.5†	590.6±111.0†	581.6±47.8†
Perfusion ml·min^{-1}·ml^{-1}			
Cortex: *baseline*	4.10±0.47	3.80±0.46	3.70±0.15
Ach	6.21±0.29†	4.94±0.60†	5.38±0.66†
Medulla: *baseline*	2.84±0.44	1.98±0.35	3.50±0.19
Ach	3.77±0.55†	3.82±0.47†	4.30±0.77
RVR, mmHg·min^{-1}·ml^{-1}	0.18±0.02	0.27±0.04*	0.26±0.02*

Creatinine, $mg \cdot dL^{-1}$	1.17±0.31	1.62±0.32*	1.08±0.31#
Urine protein, $\mu g \cdot ml^{-1}$	16.9±2.5	18.4±6.1	13.5±10.2

MAP, mean arterial pressure; GFR, glomerular filtration rate; RBF, renal blood flow; Ach, acetylcholine; RVR, renal vascular resistance.

* $P<0.05$ vs. Sham; # $P<0.05$ vs. CAS; ŧ $P<0.05$ vs. baseline.

Supplemental Figure legends:

Figure 1s. Full blots showing **r**enal expression of inflammatory and oxidative factors. Tumor necrosis-factor (TNF)-α, monocyte chemoattractant protein (MCP)-1, GP91-phox and nitrotyrosine (NT). Inflammatory and oxidative markers were elevated in coronary artery stenosis (CAS), and further augmented in CAS+Hypertension (HT).

Figure 2s. Full blots showing **r**enal expression of growth factors. Hypoxia-inducible factor (HIF)-1α, vascular endothelial growth-factor (VEGF), transforming growth-factor (TGF)-β1, tissue inhibitor of metalloproteinase (TIMP)-1 and endothelial nitric-oxide synthase (eNOS). Hypoxia and fibrotic markers increased in CAS+HT, whereas eNOS decreased; VEGF expression decreased in HT and further fell in CAS+HT (D).

Figure 3s. Evaluation of pigs with femoral artery stenosis (FAS). Representative femoral artery angiography shows the femoral artery stent location (A). Kidney fibrosis (Trichrome, ×20), DHE staining (normalized to DAPI-positive nuclei, ×20), renal microvascular media-to-lumen ratio (α-SMA, ×20) and tubular injury score (PAS staining, ×20) (B-F) did not increase in FAS pigs compared with Sham.

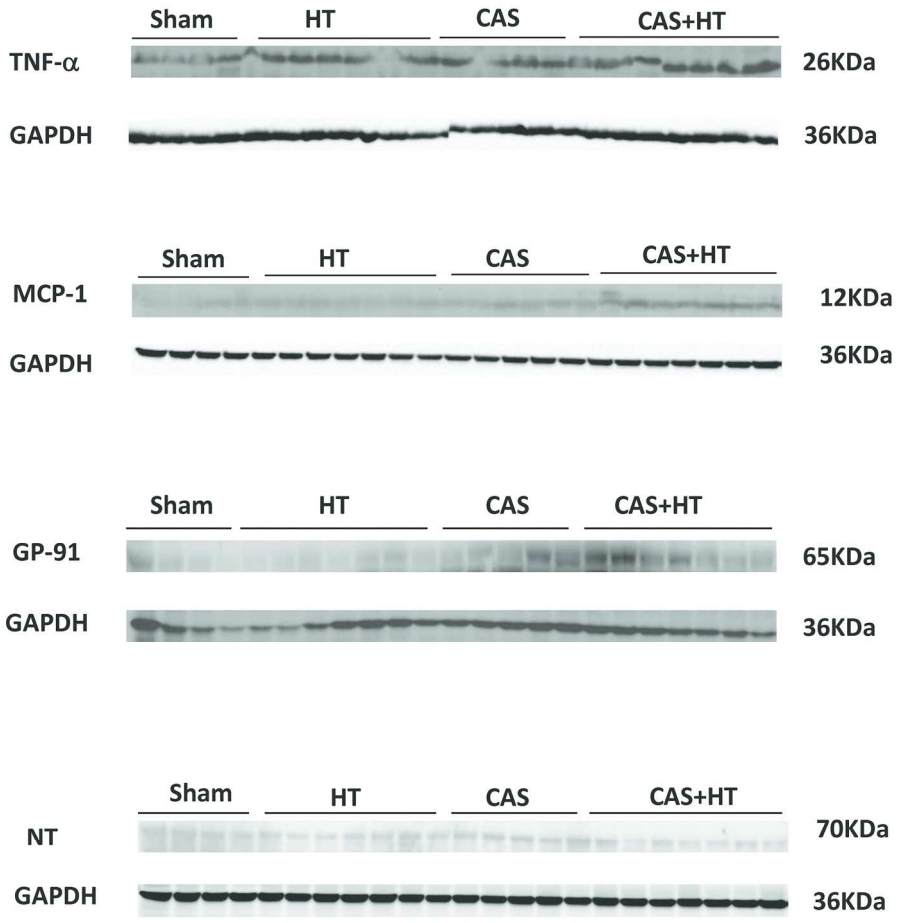
Figure 4s. Renal tissue remodeling in pigs with coronary artery stenosis (CAS) treated by the mitochondria-targeted peptide Bendavia. A. Representative renal trichrome (×20), dihydroethidium (DHE) (×20), α-SMA (×20) and PAS staining (×20). Kidney fibrosis increased in CAS compared with Sham, and decreased after treatment by Bendavia (B). DHE staining (normalized to DAPI-positive nuclei) increased in CAS compared with Sham, and decreased after treatment by Bendavia (C). Renal microvascular media-to-lumen ratio (α-SMA) increased in CAS

compared with Sham, and decreased after treatment by Bendavia (D). Tubular injury score (PAS staining) increased in CAS, and decreased after treatment by Bendavia (E). $^{*}P<0.05$ vs. Sham.

Figure 5s. Renal expression of inflammatory, oxidative, and growth factors in CAS+Bendavia pigs. Representative (2 bands shown per group) immunoblotting of (A): tumor necrosis-factor (TNF)-α, p67-phox, GP91-phox, transforming growth factor (TGF)-β1, endothelial nitric-oxide synthase (eNOS). Inflammatory and oxidative markers were elevated in coronary artery stenosis (CAS), and decreased after treatment by Bendavia (B-D). TGF-β1 increased in CAS, and eNOS decreased in CAS. After Bendavia treatment, TGF-β1 decreased in CAS, whereas eNOS did not increase. $^{*}P<0.05$ vs. Sham.

Figure 6s. Proposed mechanisms of the cardio-renal interaction in the study. Experimental coronary artery stenosis increases systemic oxidative stress, which leads to renal inflammation, oxidative stress, and endothelial dysfunction. Hypertension induces renal microvascular loss and glomerular hyperfiltration, which also lead to renal damage, and their interaction is synergistic.

Supplemental Figure 1



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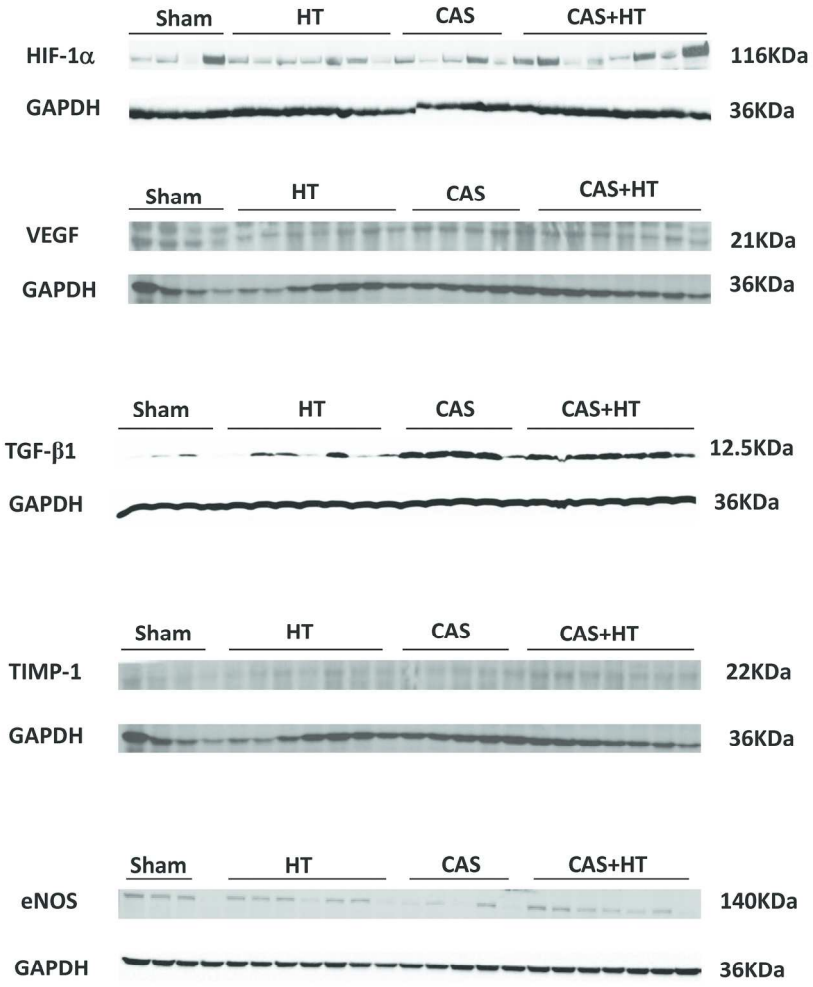
Supplemental Figure 2



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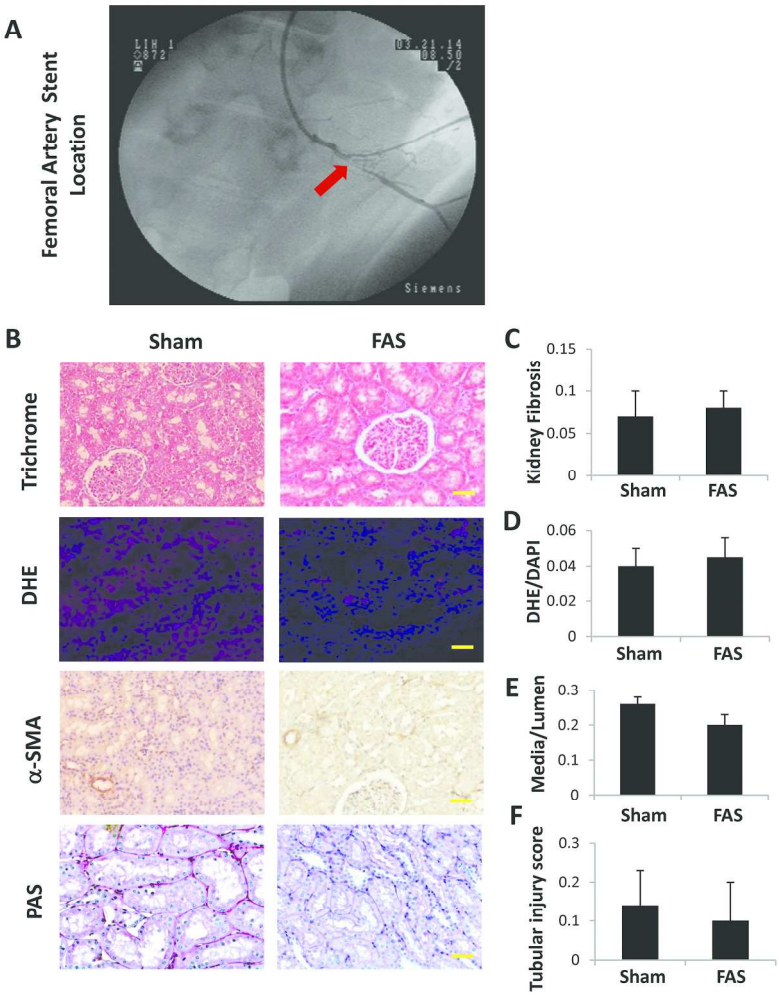

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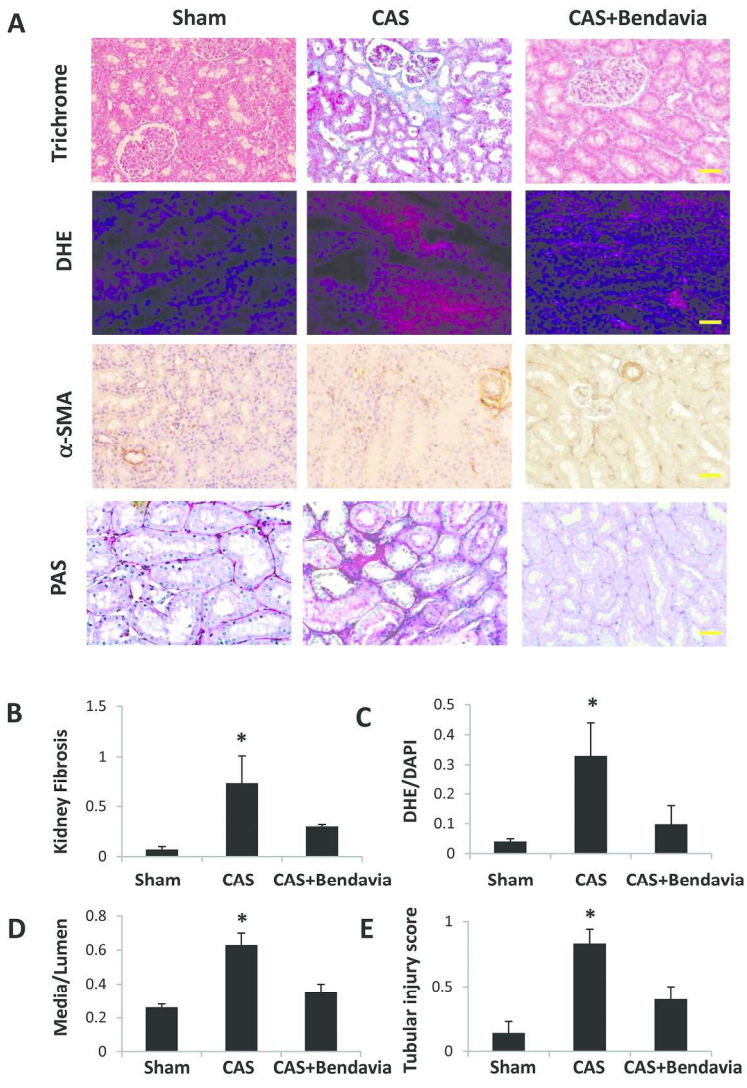

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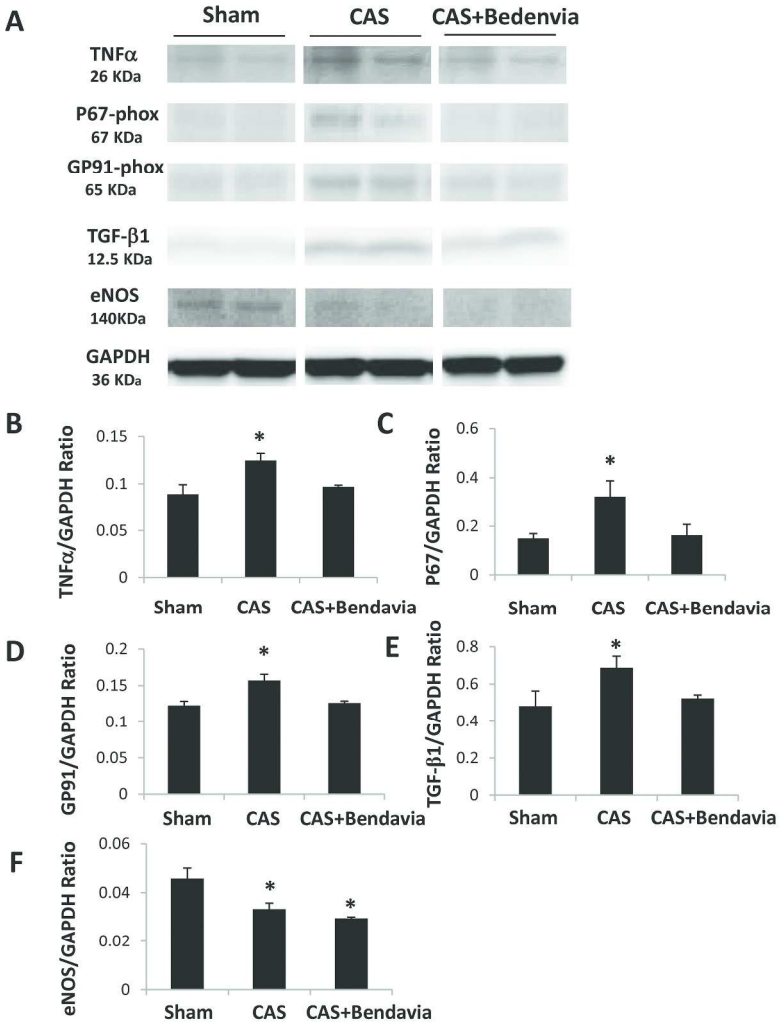
Supplemental Figure 5



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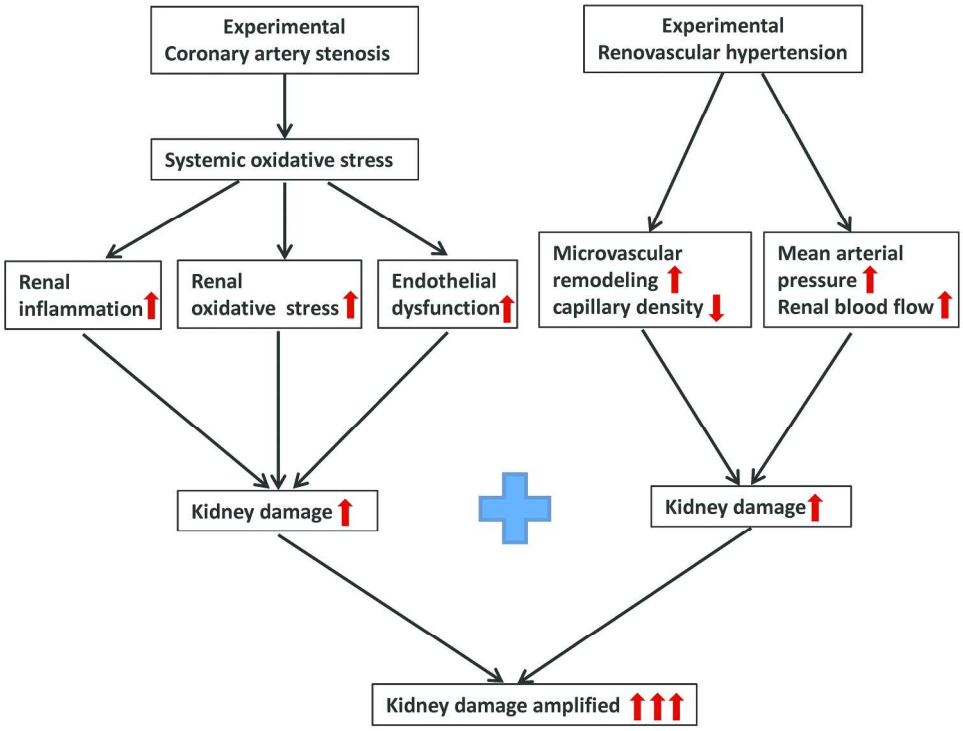
Supplemental Figure 6



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