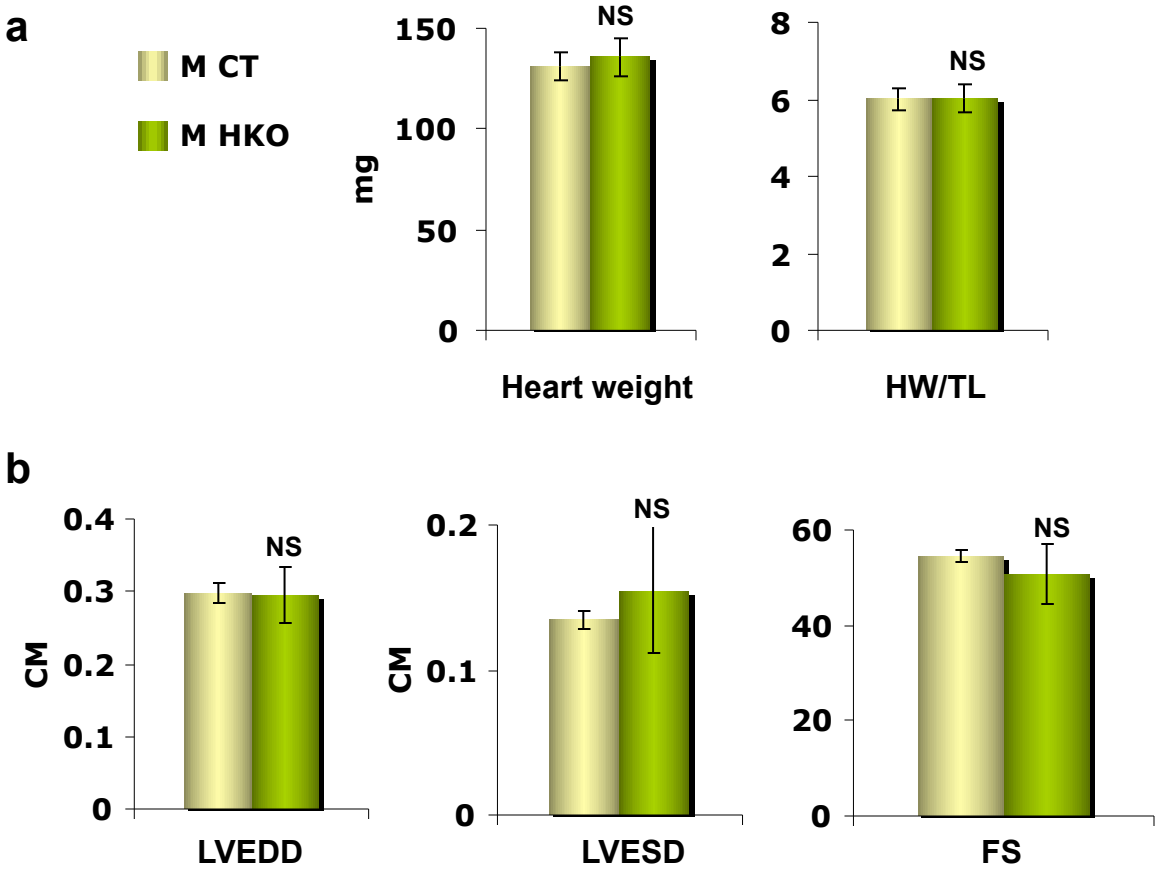
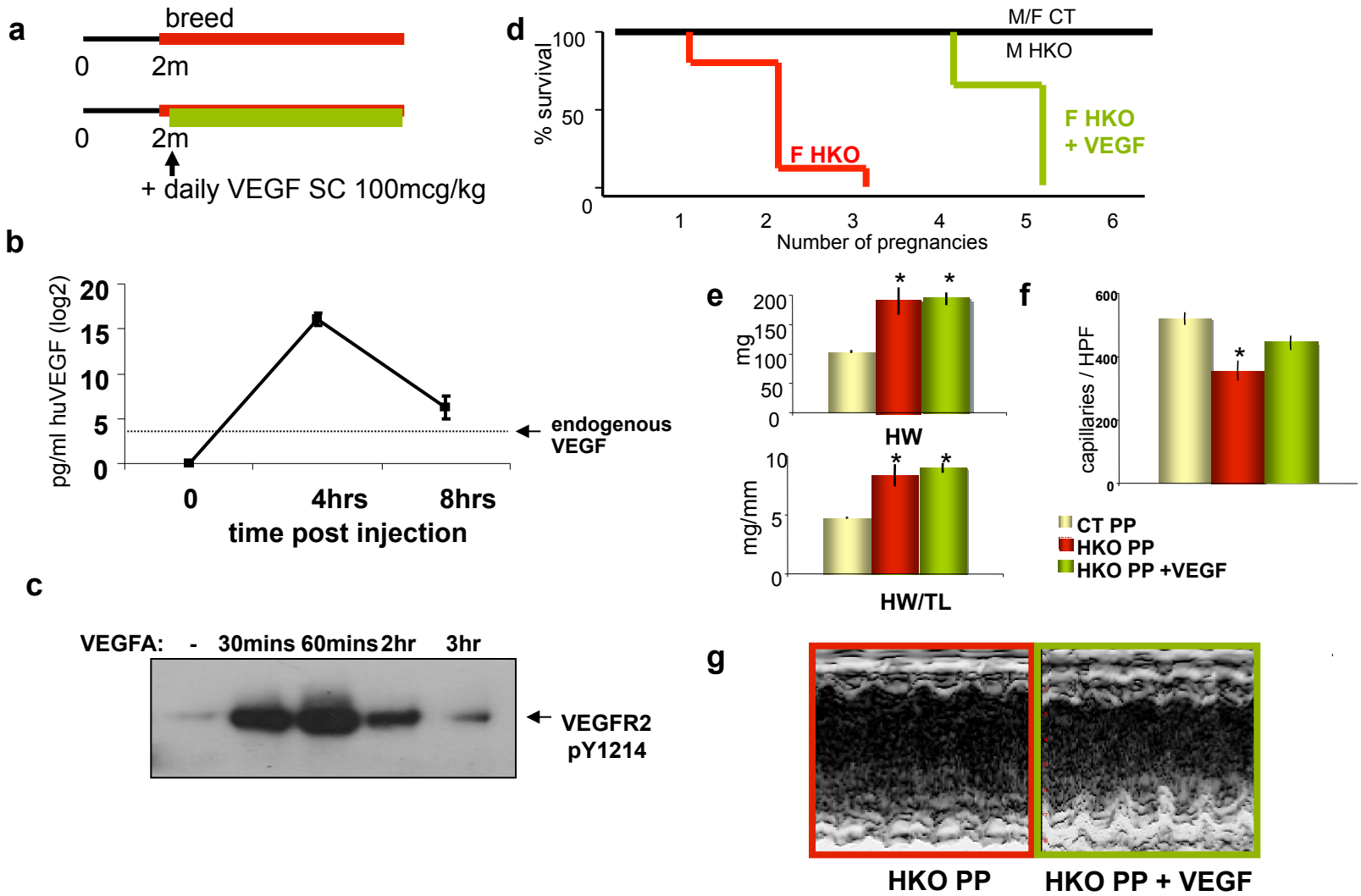
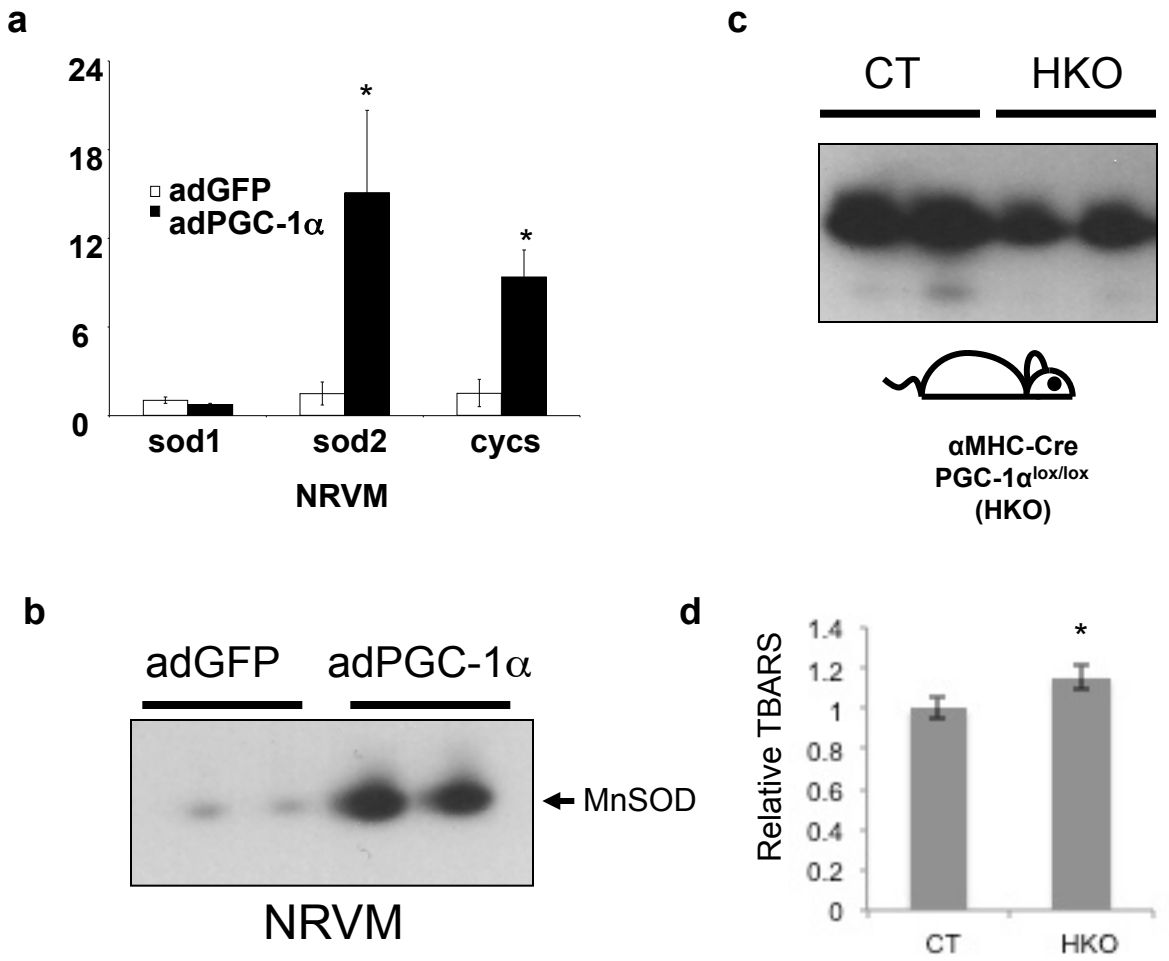


Supplementary Figure S1

Normal cardiac size and function of male PGC-1α cardiac knockout mice. **a**, Heart weight (HW) and heart weight/tibial length (HW/TL) ratios. **b,** Measured LV end-diastolic (LVEDD) and end-systolic (LVESD) dimensions, and fractional shortening (%FS). NS: non-significant.

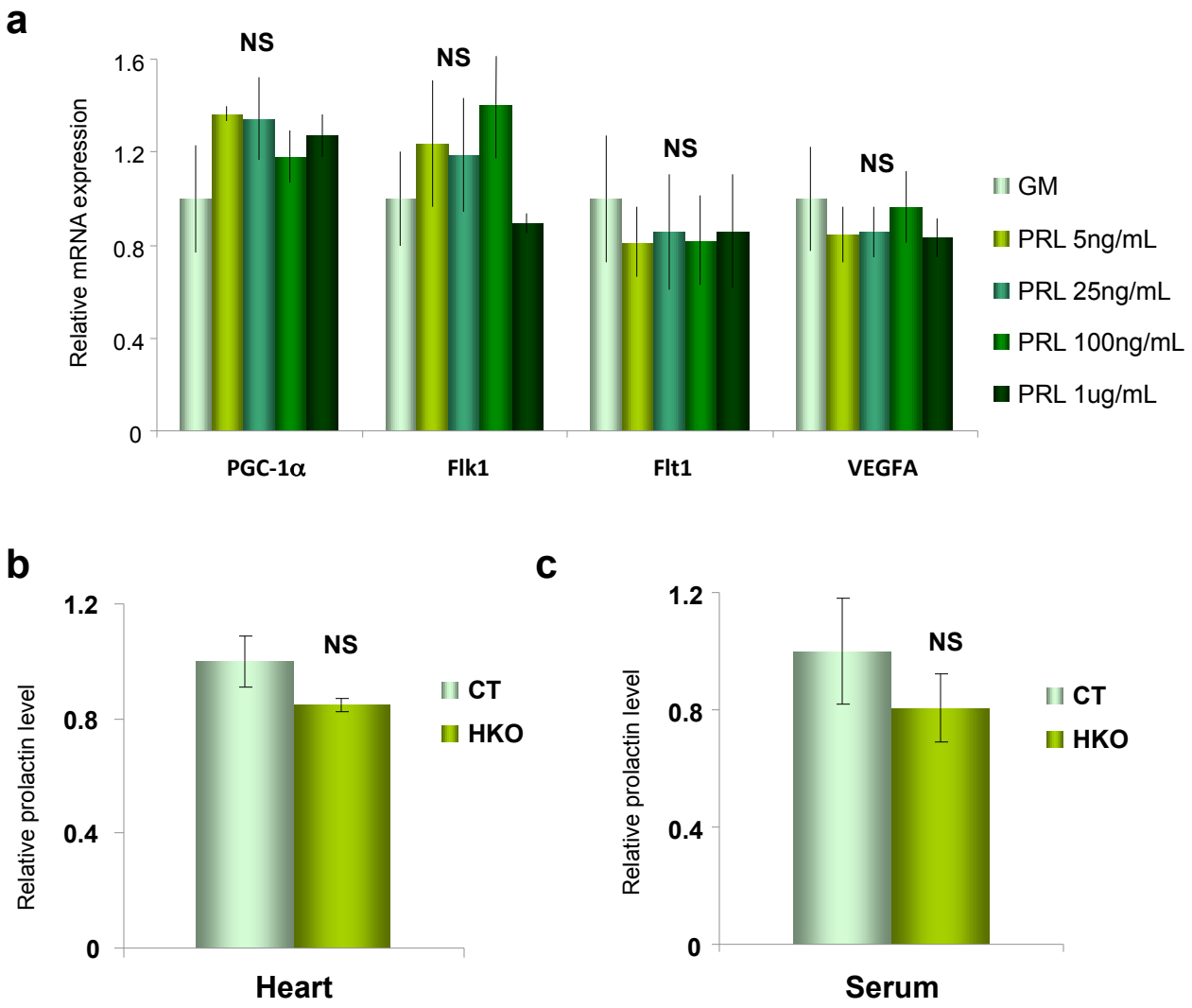


Supplementary Figure S2. Partial rescue of capillary density and lethality in post-partum PGC-1α cardiac knockout mice by daily treatment with VEGF. **a,** Experimental outline. Mice were bred starting at the age of 8 wks while daily subcutaneous injections of 100mcg/kg of recombinant human VEGF-121. **b,** VEGF concentration in serum of mice at the indicated times after injection of VEGF-121. **c,** Activation of VEGFR2 in hearts of mice, as determined by immuno-precipation of total VEGFR2 followed by Western blotting with VEGFR2 pY1214 of hearts harvested at the indicated times after injection of VEGF-121. **d,** Kaplan-Meier survival curve as a function of number of pregnancies in female HKO mice receiving VEGF (F HKO + VEGF), versus females of the same genotype receiving saline control (F HKO), HKO males, or either male or female CT animals. **e,** Heart weight (HW) and heart weight/tibial length (HW/TL) ratios of post-partum control floxed-only mice, HKO mice, and HKO mice treated with VEGF. **f,** Vascular density in hearts from post-partum CT and HKO treated with VEGF or saline control, as determined by staining for CD31 (PECAM). **g,** Sample M-mode echocardiograms from the LV of post-partum HKO mice treated with VEGF or saline control. Error bars are +/- SE. *p<.05 versus CT PP.



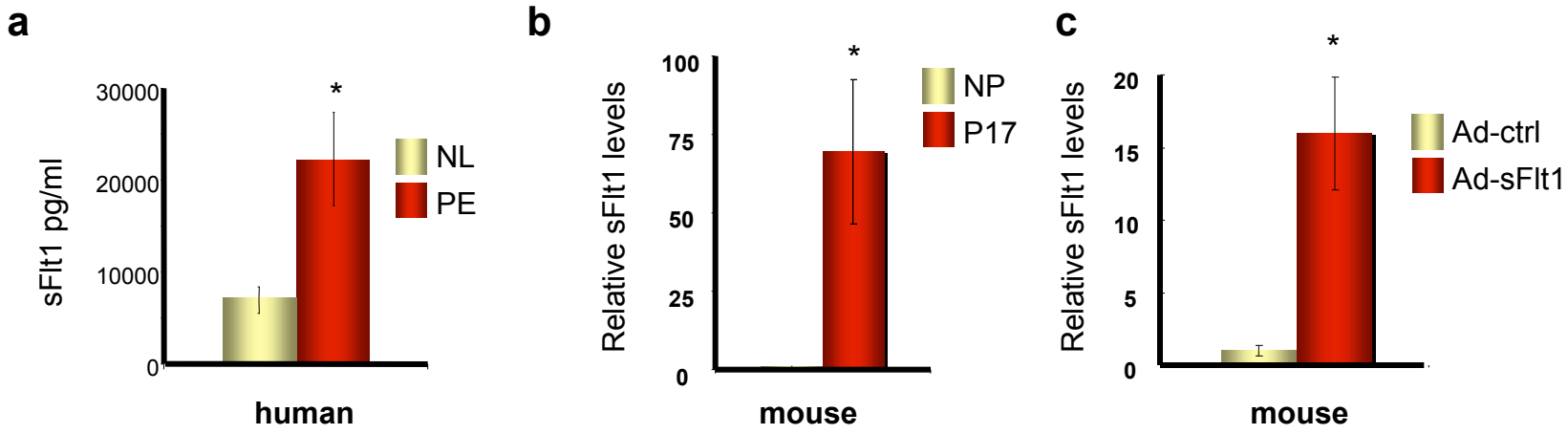
Supplementary figure S3

PGC-1α regulates superoxide dismutase 2 in cardiomyocytes. **a,** Expression of mitochondrial gene (cycs), sod1, and sod2 48 hours after infecting neonatal rat ventricular myocytes (NRVMs) with adenovirus expressing either PGC-1α or GFP as control. **b,** Sod2 (MnSOD) protein expression in NRVMs treated as in (**a**). **c,** Sod2 (MnSOD) protein expression in hearts from HKO mice, versus floxed only controls. (d) Relative thiobarbituic acid reactive substances (TBARS) in hearts from HKO mice, versus floxed only controls. Error bars are +/- SE. *p<.05 versus control.



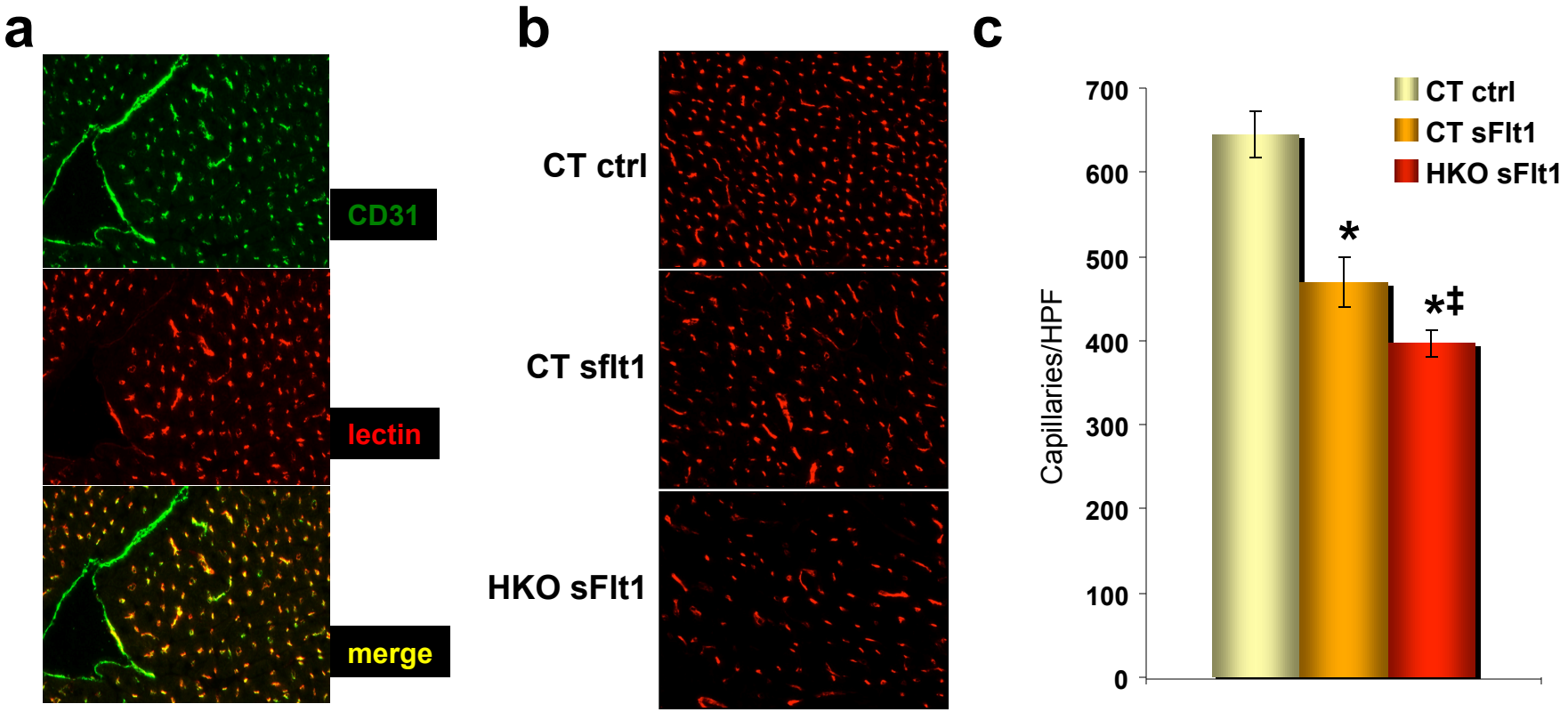
Supplementary Figure S4

Levels of prolactin are not altered in HKO animals, and prolactin has no direct effect on cardiac cells. **a,** Expression of the indicated genes in neonatal rat ventricular myocytes (NRVMs) 24hrs after treatment with purified prolactin at the indicated concentrations. **b,** Prolactin levels in serum (left) and heart (right) of CT and HKO animals. Error bars are +/- SE. NS nonsignificant.



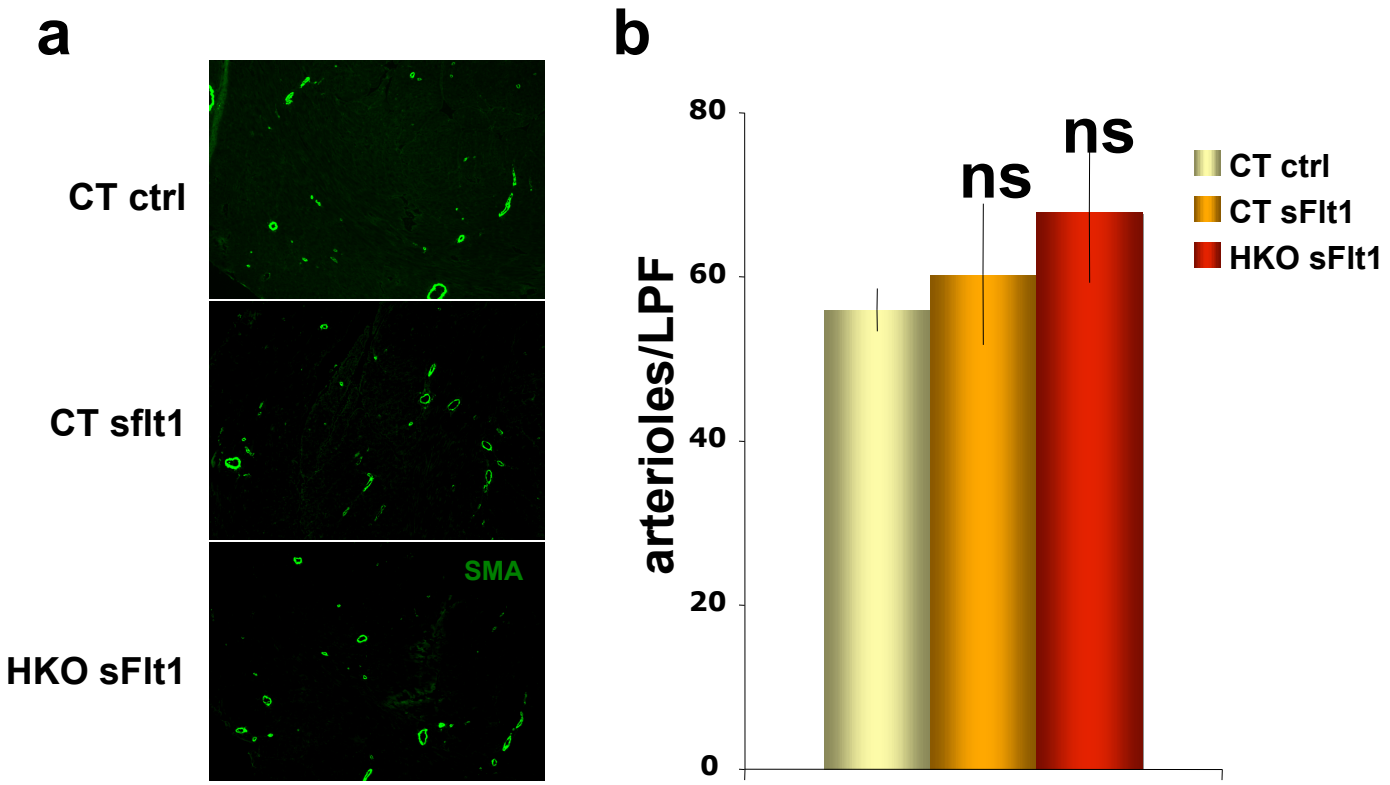
Supplementary Figure S5

sFlt1 levels in (**a**) normal (NL) versus pre-eclamptic (PE) human pregnancies (p=.005), (**b**) non-pregnant (NP) versus pregnant (gestational day 17, P17) mice (p=.009), and (**c**) pregnant mice with or without additional adenovirus-sFlt1 (p=.0008). Note: murine and human levels are not directly comparable to each other, because the ELISAs have not been standardized to each other. Mouse values are normalized to the control group. Error bars are +/- SE. *p<.05 versus control.



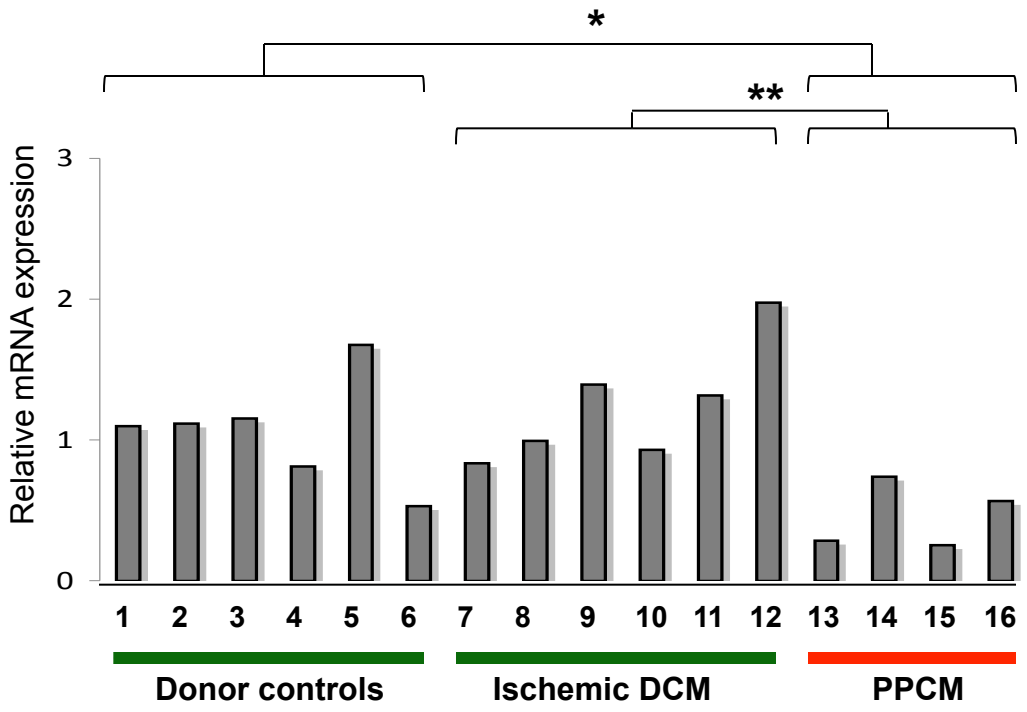
Supplementary Figure S6

Decreased cardiac capillary density 21 days after injection with adenovirus expressing sFlt1. **a,** Staining of capillaries by immuno-staining with anti-CD31 antibody versus isolectin B4. Note that isolectin B4 is specific to small vessels, and that within the microvasculature there is little difference between CD31 and isolectin B4 staining. **b,** Samples images of isolectin B4 stains from control animals (CT), animals injected with adeno-sFlt1 (CT sFlt1), or HKO animals injected with virus (HKO sFlt1). **c,** quantification of vascular density, as in b. n=6 or more per group. Error bars are +/- SE. *p<.05 versus CT. ‡p<.05 versus CT sFlt1.



Supplementary figure S7

Arteriolar density is not altered in WT or HKO mice injected with adeno-sFlt1. **a,** Samples images of smooth muscle actin (SMA) stains from control animals (CT), animals injected with adeno-sFlt1 (CT sFlt1), or HKO animals injected with virus (HKO sFlt1). **b,** quantification of arteriolar density, as in a. n=6 or more per group. Error bars are +/- SE. ns: non-significant.



Supplementary Figure S8

mRNA expression of PGC-1α in donor hearts (left 6 columns), hearts from patients with idiopathic dilated cardiomyopathy (middle 6 columns), and hearts from women with PPCM (right 4 columns). *p=.038 by Mann-Whitney, .024 by Student's t-test. **p=.010 by Mann-Whitney, .010 by Student's t-test.