Supplemental Figure 1. Experimental design for in vivo vascular disease models. ApoE-KO mice were employed in studies designed to investigate: **a)** aortic vascular disease burden and aneurysm formation, and **b)** vascular remodeling in a vein graft model characterized by the development of neointimal hyperplasia.

Supplemental Figure 2. Apelin inhibits native atherosclerosis in the ApoE null model. Apelin (2mg/kg/day) and AngII (1.4mg/kg/day) were administered by osmotic minipumps to ApoE-KO mice on a high fat diet. Relative area of vascular disease in the aortic root was significantly reduced in apelin treated mice (*$P<0.05$ compared to saline). Black bar represents 200μm.

Supplemental Figure 3. Apelin suppresses disease-related $O_2^{\bullet-}$ production in vein grafts. Cellular $O_2^{\bullet-}$ production in vein grafts, measured by 2-hydroxyethidium (DHE) fluorescent nuclear staining in ApoE-KO mice was assessed in the endothelial and neointimal layers of the vessel wall. There was no difference in $O_2^{\bullet-}$ production in the endothelium among the different conditions. $O_2^{\bullet-}$ production was attenuated in the neointima in apelin treated mice even when co-administered with AngII (54%, *$P<0.05$, apelin vs. saline; and 48%, †$P<0.05$, AngII+apelin vs. AngII alone). Vein graft vessel wall exhibits green autofluorescence. White arrows denote DHE staining, white arrowheads denote neointima, white bar represents 5 μm.
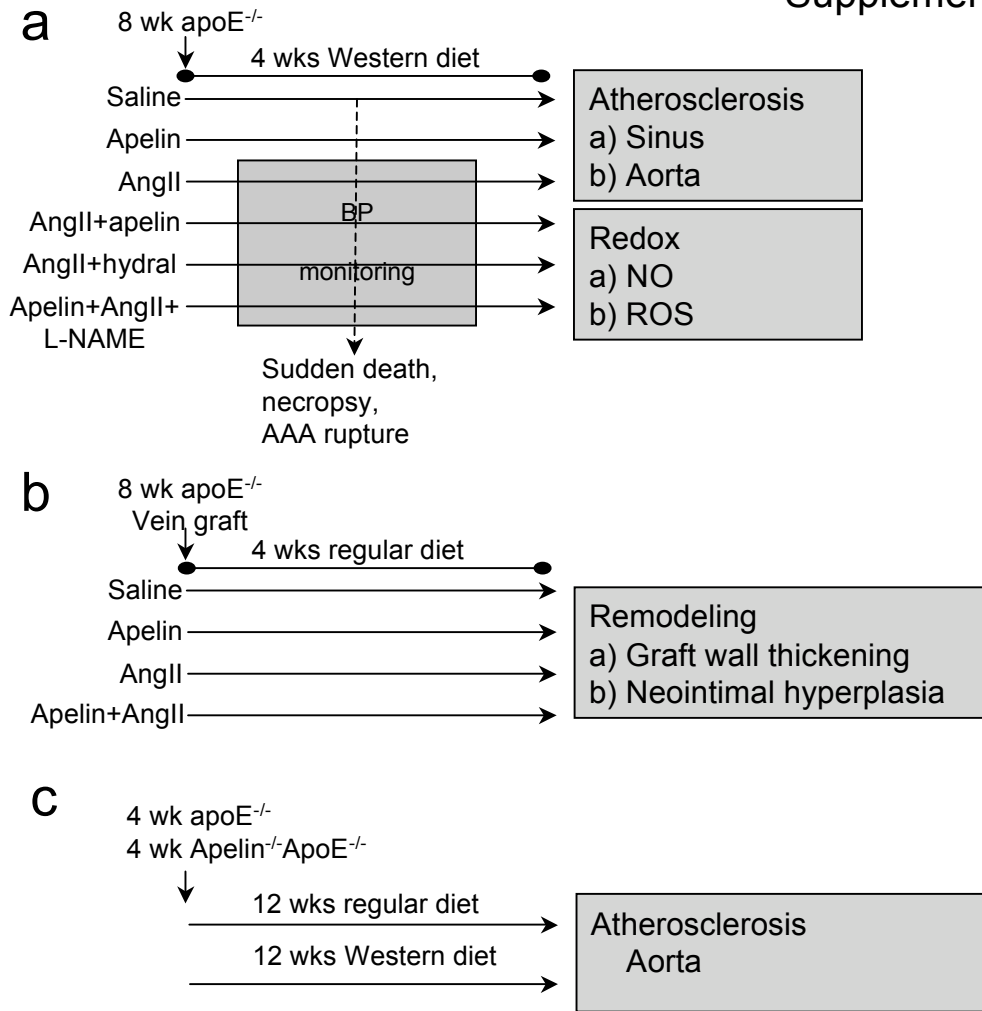
Supplemental Figure 4. Apelin does not compete with AngII for binding to the primary AngII receptor AT1R. a) FAM-labeled

AngII (10 nM) binds to cells transfected with AT1R (blue curve) but

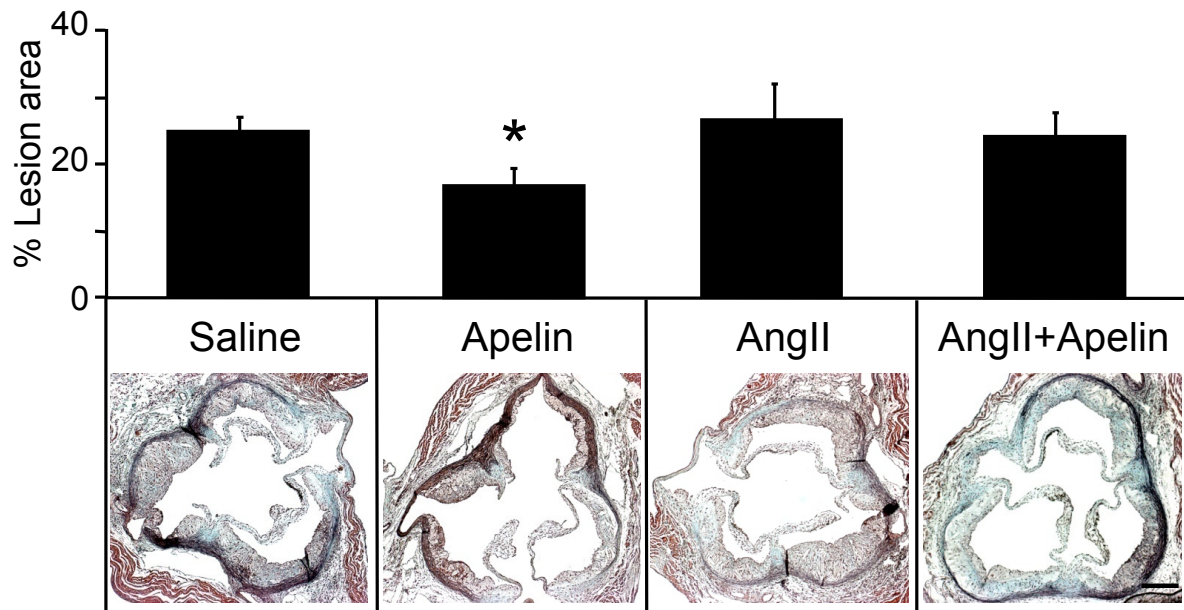not to cells with control vector transfection (red curve).

b) Unlabeled AngII (100 nM) inhibits binding of FAM-AngII (10 nM) to

AT1R (blue curve), compared to FAM-AngII (10 nM) in the absence of

unlabeled AngII (red curve).

c) Unlabeled apelin (100 nM) does not compete with FAM-AngII for
binding to AT1R (blue curve) and shows no difference to FAM-AngII
(10 nM) binding in the absence of apelin (red curve). The x-axis
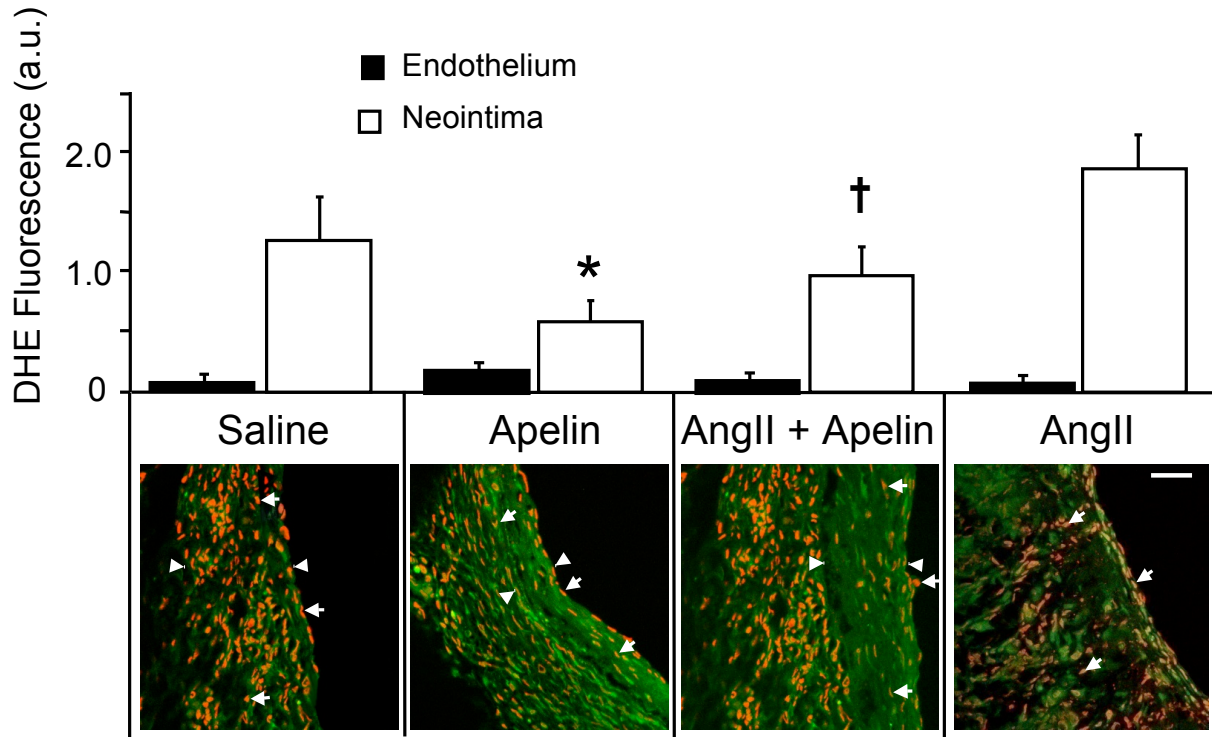represents fluorescence intensity.

a

8 wk apoE⁻/⁻

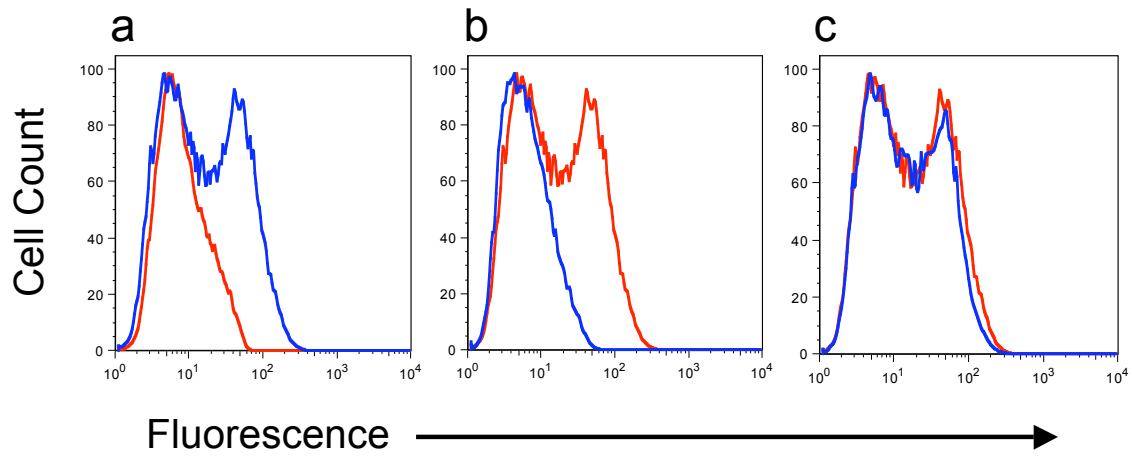4 wks Western diet

Saline → Atherosclerosis
a) Sinus
b) Aorta

Apelin →

AngII →

AngII+apelin → | BP monitoring

AngII+hydral →

Apelin+AngII+ L-NAME →

Redox
a) NO
b) ROS

Sudden death, necropsy, AAA rupture

b

8 wk apoE⁻/⁻
Vein graft

4 wks regular diet

Saline →

Apelin →

AngII →

Apelin+AngII →

Remodeling
a) Graft wall thickening
b) Neointimal hyperplasia

c

4 wk apoE⁻/⁻
4 wk Apelin⁻/⁻ApoE⁻/⁻

12 wks regular diet →

12 wks Western diet →

Atherosclerosis
Aorta

| Saline | Apelin | AngII | AngII+Apelin |

	Saline	Apelin	Ang+apelin	AngII
Total Cholesterol	1201$\pm$167	1095$\pm$93	1236$\pm$146	1111$\pm$121
HDL-Cholesterol	105$\pm$12	86$\pm$8	99$\pm$9	108$\pm$11
Triglycerides	223$\pm$112	211$\pm$102	191$\pm$97	209$\pm$126
Body Weights	27$\pm$2.4	24$\pm$3.0	23$\pm$4.6	27$\pm$2.9

Supplemental Table 1. - Lipid Profiles and Body Weights of Experimental Animals.

Serum lipid values are expressed in mg/dl, and body weights in grams (statistical analysis with ANOVA).