Figure Legends

Supplemental Figure 1: *Expression of AR increases with lesion progression in the aortic sinus of apo E-null mice.* Cross sections of aortic sinus obtained from 10-, 22- and 52-week old apoE-null mice, maintained on normal chow, were stained with anti-AR antibody. Digital images of the lesions were acquired at 10x magnification.

Supplemental Figure 2: *Inhibition of AR does not affect advanced atherosclerotic lesions.* ApoE-null mice (24-week old) were fed either sorbinil (0.2 g/L in 0.5% ethanol in drinking water; *Protocol IIB*) or vehicle II (0.5% ethanol in drinking water; *Protocol IIA*) for 12 weeks. Plasma cholesterol and triglycerides levels in sorbinil-fed mice were comparable with controls (see Supplemental Table 1). Lesion formation was examined in the aortic sinus (**A**) and in the aorta (**B**). Lipids were stained with Oil-Red O in the aortic sinus and Sudan IV in the aorta (*en face*).

Supplemental Figure 3: *Genetic ablation of AR does not affect cytokine production.* (**A**) Pro-inflammatory cytokines were measured in the spleen of 8-week old female $AR^{+/+}/apoE^{-/-}$ and $AR^{-/-}/apoE^{-/-}$ mice fed high-fat diet for 12 weeks (Protocol IV). All primers were validated to yield single specific band with conventional RT-PCR. Values obtained were normalized to GAPDH to calculate $\Delta C(T)$ values. (**B**) Plasma IL-6 levels in $AR^{+/+}/apoE^{-/-}$ and $AR^{-/-}/apoE^{-/-}$ mice.

Supplemental Figure 4: *Effect of genetic ablation of AR on MDA accumulation.* Eight week old female $AR^{-/-}$/$apoE^{-/-}$ and $AR^{+/+}$/$apoE^{-/-}$ mice were maintained on high-fat diet for 12 weeks (*Protocol IV*). Plasma MDA levels were measured by GC-MS as described under *Materials and Methods*. Panel **A** shows the representative chromatogram of MDA in the plasma of $AR^{+/+}$/$apoE^{-/-}$ (**i**) and $AR^{-/-}$/$apoE^{-/-}$ mice (**ii**) by select ion monitoring. Panel **B** shows the spectrum of select ions monitored for the quantification of MDA (**ii** and **iv**). Benzaldehyde ring D_5 (**i** and **iii**) was used as an internal standard for MDA quantification. Following ions were monitored for the indicated aldehyde: benzaldehyde ring D_5 - m/z 256 and 286 [M^+-HFNO and M^+-HF and MDA m/z 204 and 415 [M^+- $C_7H_2F_5$-HFNO-C_2H_3 and M^+- NO_2]. Panel **C** shows group data of plasma aldehyde. Values are mean ± SEM. *P<0.01 versus controls. Panel D shows the photomicrographs of sections of the innominate arteries stained with polyclonal anti-protein-MDA antibody. Sections treated with non-immune mouse IgG served as negative controls for staining.

Supplemental Figure 5: AR protects against atherogenesis in diabetic mice. Diabetes was induced in mice by streptozotocin as described under *Methods*. (**A**) Inhibition by sorbinil (**i**) or genetic ablation of AR (**ii**) exacerbated lesion formation in the aortic arch after 6 weeks of diabetes. (**B**) After 12 weeks of diabetes, lesion formation was significantly increased in the aortic arch (**i**) and the abdominal aorta (**ii**) of $AR^{-/-}$/$apoE^{-/-}$ when compared with $AR^{+/+}$/$apoE^{-/-}$ mice. Lipids were

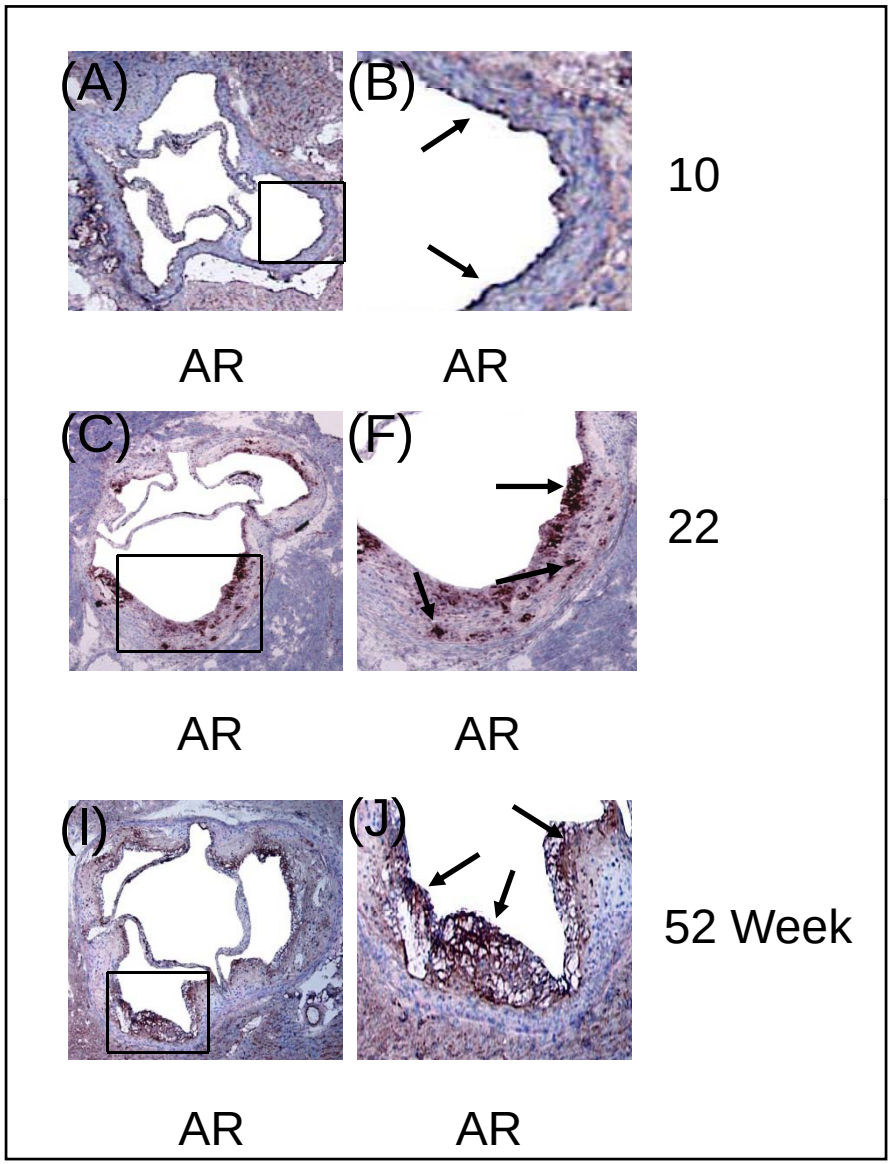
visualized by Sudan IV staining (*en face*). Values are mean ± SEM. $^{*}P<0.01$ and $^{\#}P<0.02$ versus controls.

Supplemental Table 1*: Parameters measured in non-diabetic and diabetic mice*.

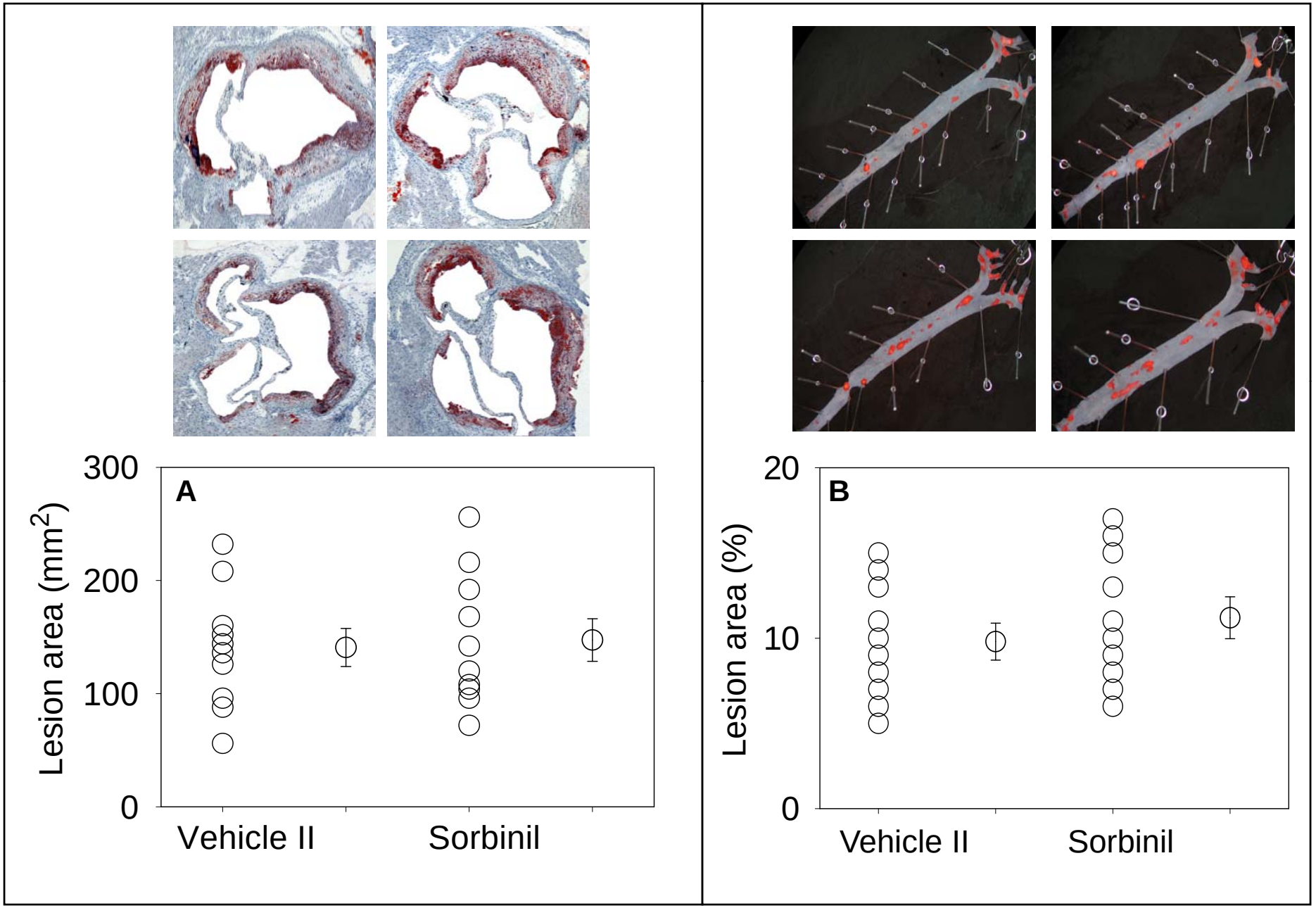
Protocol No.	Genotype	Sex	Treatment	Diet	Study period (weeks)	Sorbitol (nmol/mg protein)	Cholesterol (mg/dl)	Triglycerides (mg/dl)	Blood Glucose (mg/dl)
Non-diabetic									
1A	apoE$^{-/-}$	Male	Vehicle I	HF	8-12	47±4	888±78	102±9	ND
IB	apoE$^{-/-}$	Male	+Tolrestat	HF	8-12	14±1*	828±36	93±9	ND
IC	apoE$^{-/-}$	Male	Vehicle II	HF	8-12	42±3	853±33	115±24	ND
ID	apoE$^{-/-}$	Male	+Sorbinil	HF	8-12	9±1*	854±28	87±16	ND
IIA	apoE$^{-/-}$	Male	Vehicle II	NC	24-36	ND	635±54	125±17	ND
IIB	apoE$^{-/-}$	Male	+Sorbinil	NC	24-36	ND	618±28	114±17	ND
IIIA	AR$^{+/+}$/apoE$^{-/-}$	Male	-	HF	8-12	ND	806±59	109±11	ND
IIIB	AR$^{-/-}$/apoE$^{-/-}$	Male	-	HF	8-12	ND	791±33	95±12	ND
IVA	AR$^{+/+}$/apoE$^{-/-}$	Male	-	HF	8-20	ND	1350±101	151±15	ND
IVB	AR$^{-/-}$/apoE$^{-/-}$	Male	-	HF	8-20	ND	1501±171	160±40	ND
IVC	AR$^{+/+}$/apoE$^{-/-}$	Female	-	HF	8-20	ND	1576±53	138±10	ND
IVD	AR$^{-/-}$/apoE$^{-/-}$	Female	-	HF	8-20	ND	1536±62	150±11	ND
Diabetic									
VA	apoE$^{-/-}$	Male	Vehicle II	NC	6-14	125±9	1409±95	101±10	444±8
VB	apoE$^{-/-}$	Male	+Sorbinil	NC	6-14	40±3*	1203±107	117±18	460±16
VC	AR$^{+/+}$/apoE$^{-/-}$	Male	-	NC	6-14	ND	1504±120	89±9	526±31
VD	AR$^{-/-}$/apoE$^{-/-}$	Male	-	NC	6-14	ND	1491±160	89±15	514±45
VA	AR$^{+/+}$/apoE$^{-/-}$	Male	-	NC	6-20	ND	1260±76	102±9	552±22
VB	AR$^{-/-}$/apoE$^{-/-}$	Male	-	NC	6-20	ND	1315±132	110±15	539±30

Diabetes was induced by streptozotocin. Values are mean ± SEM. *P<0.01 Protocols IB vs IA, ID vs IC and VB vs VA. HF-High fat; NC-Normal chow; ND-Not determined.

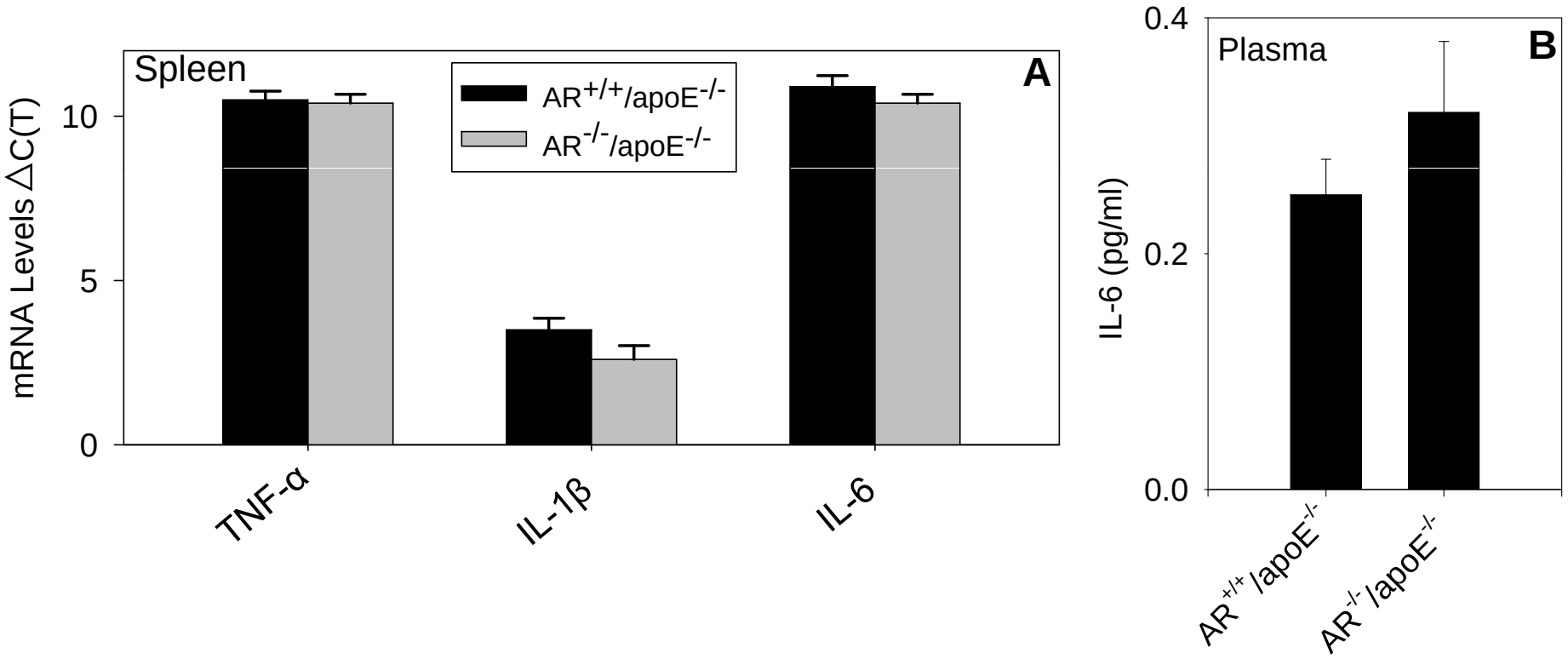
Supplemental Figure 1



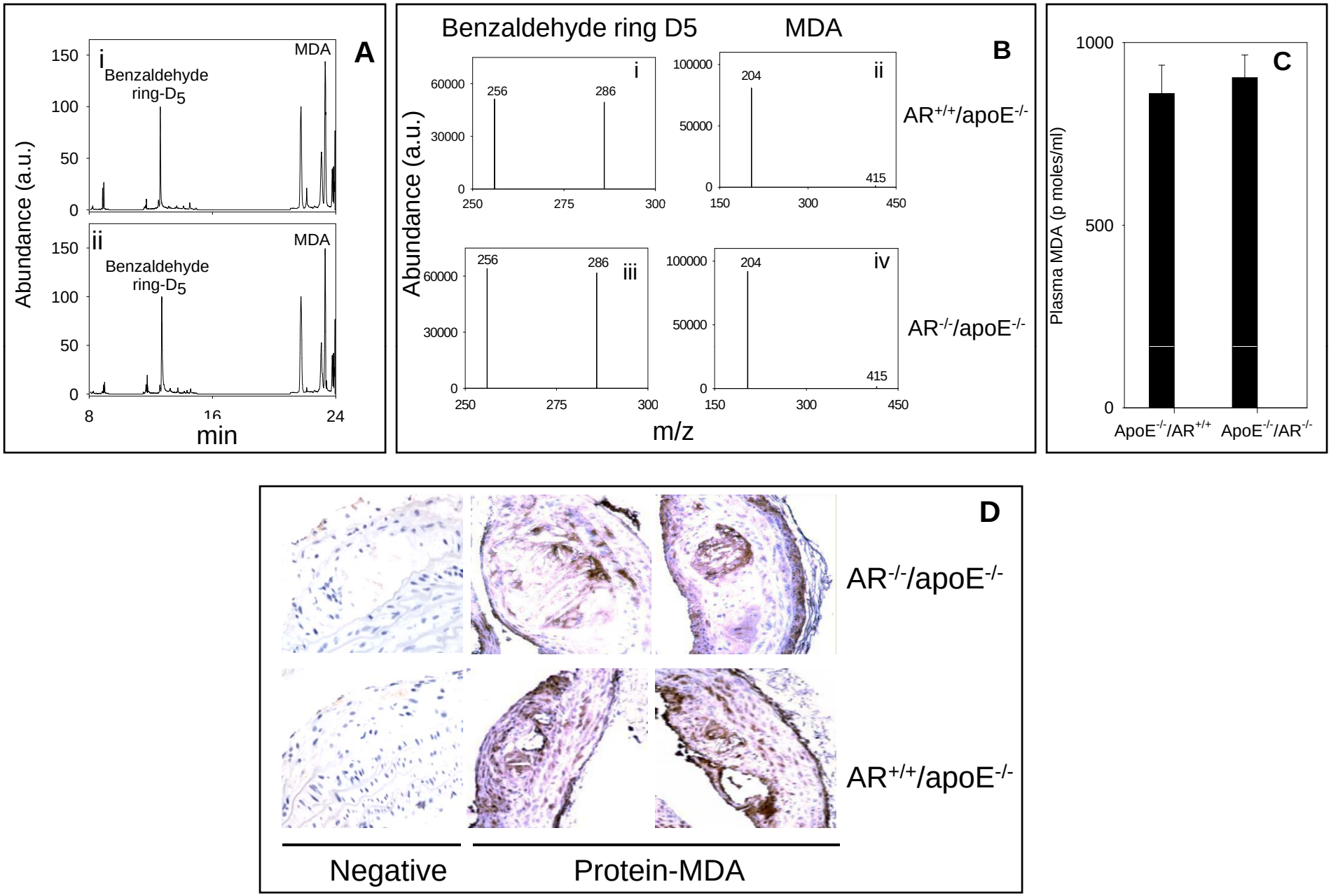
Supplemental Figure 2



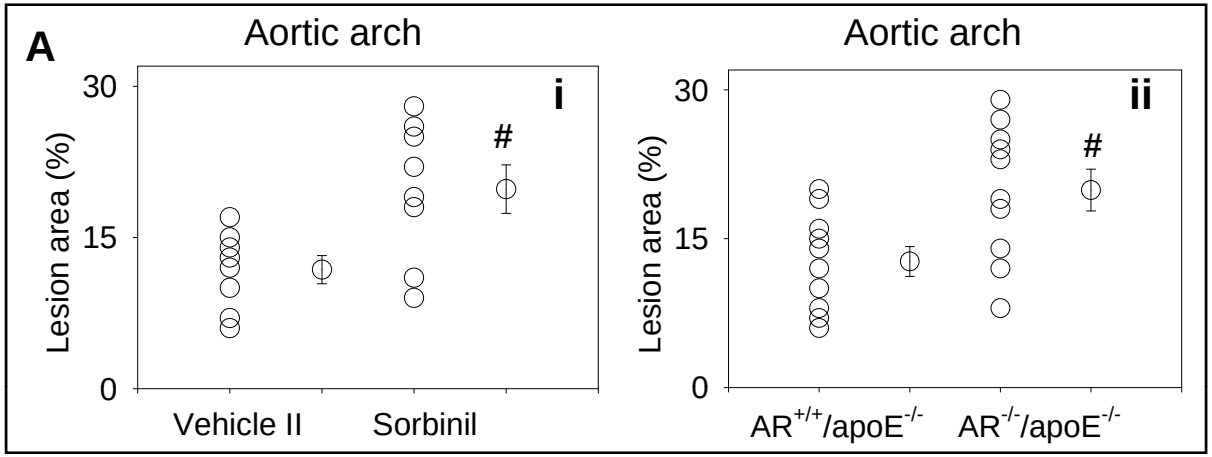
Supplemental Figure 3



Supplemental Figure 4



6 Weeks



12 Weeks