Supplemental Figure Legends

Supplemental Fig. 1. Generation of CB2 receptor-deficient Ldlr$^{-/-}$ mice. (A) Genomic DNA isolated from tail biopsies was subjected to PCR amplification using CB2 receptor and Ldlr specific primers to confirm the CB2$^{-/-}$Ldlr$^{-/-}$ and CB2$^{+/+}$Ldlr$^{-/-}$genotypes. The expected sizes of CB2 wild-type, CB2-null, Ldlr wild-type and Ldlr-null PCR amplification products are as indicated in the figure. Control DNA= genomic DNA isolated from C57BL/J6 mice. (B) Immunoblotting with anti-CB1 and anti-CB2 antibodies demonstrates the presence of CB2 (45 kDa) and CB1 (61 kDa) expression in macrophages isolated from wild type mice (+/+) and the absence of CB2 expression in macrophages isolated from CB2$^{-/-}$Ldlr$^{-/-}$ mice (-/-).

Supplemental Fig. 2. Lack of CB2 receptor does not alter systemic parameters of Ldlr$^{-/-}$ mice. (A) Body weights of male CB2$^{-/-}$ Ldlr$^{-/-}$ and CB2$^{+/+}$Ldlr$^{-/-}$ (control) mice after 8 and 12 weeks on an atherogenic diet (AD) or a standard chow diet. Values are the mean ± SD, n for each group is as indicated. (B-E) After 4, 8, and 12 weeks of an atherogenic or a standard chow diet, blood samples from CB2$^{-/-}$ Ldlr$^{-/-}$ and control mice were collected following an overnight fast and assayed for (B) total plasma cholesterol and (C) triglyceride levels using colorimetric reagent kits from Pointe Scientific Inc. (Canton, MI). After 8 weeks of atherogenic diet intervention, plasma samples from randomly selected CB2$^{-/-}$ Ldlr$^{-/-}$ mice (n=6) and control mice (n=6) were pooled and the lipoprotein profiles obtained by fast protein liquid chromatography (FPLC). (D) Total cholesterol and (E) triglyceride levels in plasma fractions separated by FPLC are shown. The experiment was repeated twice, and similar results were obtained, although some variability in triglyceride content was observed.

Supplemental Fig. 3. Lack of CB2 receptor does not alter the extent of atherosclerosis observed in *en face* prepared aortas of hyperlipidemic Ldlr$^{-/-}$ mice. After 8 weeks of atherogenic

diet the mice were sacrificed and the aortas were processed by *en face* using Sudan IV staining to visualize lesions. (A) Representative images showing the extent of surface lesions in *en face* aortic preparations of $CB2^{-/-}$ $Ldlr^{-/-}$ and control mice after 8 weeks of an atherogenic diet. (B) Digital quantification of the total aortic surface area occupied by lesions in *en face* prepared aortas from $CB2^{-/-}$ $Ldlr^{-/-}$ and control mice. Values are the means ± SD. (n=8 for each group)

Supplemental Fig. 4. TUNEL-positive nuclei are present in macrophage-enriched regions of atherosclerotic lesions of Ldlr-null mice. Representative photomicrographs are shown adjacent cryosections of an aortic root lesion from Ldlr-/- mice fed an atherogenic diet for 12 weeks subjected to *in situ* TUNEL analysis using fluorescein isothiocyanate-labeled dUTP (left panel) or immunostaining with anti-MOMA2 (middle panel). The panel on the right shows the results on merging the images in the left and middle panels. Fluorescent green stain indicates TUNEL-positive nuclei; brown stain indicates MOMA-2 immunoreactive cells.