Materials and Methods A detailed listing of mice and antibodies used are listed in the jajor resouce table in the Supplementary Material section.

RNA extraction and quantitative RT-PCR. RNA from spleen, aortic arch, and cultured cells was isolated using the RNeasy PowerLyzer Tissue & Cells Kit (Qiagen) and Direct-zol™ RNA Miniprep Plus (Zymo Research) for tissue and cells, respectively, according to the manufacturer's protocol. 200ng of RNA from each sample was reverse transcribed using Maxima First Strand cDNA Synthesis kit for qRT-PCR (Thermo Scientific) as previously described, and target genes were amplified using SYBR green (Thermo Scientific) and gene-specific primers, in triplicate, using an Eppendorf Realplex4 Mastercycler[6,9-12]. Ct values were quantitated by the Eppendorf software. Results were normalized using the housekeeping gene GAPDH or β-2 Microglobulin and relative gene expression was calculated and graphed as fold change ($2^{-\Delta\Delta Ct}$) from control. Primer pairs were purchased from Integrated DNA Technologies. The following primer pairs were used:
Arginase1: F- 5'AAGAATGGAAGAGTCAGTGTGG3', R- 5'GGGAGTGTTGATGTCAGTGTG3';
Arginase 2: F- 5'CAGAAGGTGATGGAACAGACA3', R- 5'GCCAGTTTAGGGTCAAATGC3';
β-2 Microglobulin: F- 5'ATGTGAGGCGGGTGGAACTG3', R- CTCGGTGACCCTGGTCTTTCTG3';
FOXP3: F- 5'AAGTACCACAATATGCGACCC3', R- 5'TCTGAAGTAGGCGAACATGC3';
GAPDH: F- 5'GCAAGGACACTGAGCAAGAG3', R- 5'GGGTCTGGGATGGAAATTGT3';
GATA3: F- 5'TACCACCTATCCGCCCTATG3', R- 5'CTCGACTTACATCCGAACCC3';
HuR: F- 5'GGGATAAAGTAGCAGGACACAG3', R- 5'TTGGGCGAGCATATGACAC3';
IL-1β: F- 5'CTAATAGGCTCATCTGGGATCC3', R- 5'GGTCCGTCAACTTCAAAGAAC3';
IL-10: F- 5'CTGTGTTTAAGCTGTTTCCATTGG3', R- 5'AGGAAGAACCCCTCCCATCAT3';
IL-12β: F- 5'GTGAAGCACCAAATTACTCCG3', R- 5'AGAGACGCCATTCCACATG3';
iNOS: F- 5'TTTGACGCTCGGAACTGTAG3', R- 5'GAGCCTGAAGTCATGTTTGC3';
MCP1: F- 5'TTAAAAACCTGGATCGGAACCAA3', R- 5'GCATTAGCTTCAGATTTACGGGT3';
PCNA: F- 5'GGGTGAAGTTTTCTGCAAGTG3', R- 5'GTACCTCAGAGCAAACGTTAGG3';
RORγ: F- 5'TTTCTGAGGATGAGATTGCCC3', R- 5'TTGTCGATGAGTCTTGCAGAG3';
T-Bet: F- 5'CCTGTTGTGGTCCAAGTTCAAC3', R- 5'CACAAACATCCTGTAATGGCTTGT3';
TNFα: F- 5'CTTCTGTCTACTGAACTTCGGG3', R- 5'CAGGCTTGTCACTCGAATTTTG3'
miR133a levels were detected using miScript II RT Kit, miScript SYBR Green PCR Kit, and miScript Primer Assay (Qiagen).

Western blotting. Protein extracts made as described were separated by SDS-PAGE, transferred to nitrocellulose membrane, incubated with a 1:3000 dilution of primary antibody HuR or TNFα (abcam, Santa Cruz Biotechnology), followed by a 1:4000 dilution of secondary antibody[4,9-12]. Equal loading of protein extracts on gels was verified by Ponceau S staining of the membrane, and blotting with the housekeeping protein anti-GAPDH or HSC70 (Cell Signaling Technology, Santa Cruz Biotechnology), and reactive proteins were visualized using enhanced chemiluminescence. The intensity of each band was quantitated using image analysis software (NIH Image J).

Immunohistochemistry. Aortic roots were frozen in OCT and 5 μm-thick serial sections were cut and placed on microscope slides. Immunoperoxidase staining (see below) was performed using CD68 antibody (Biolegend). Positively stained areas (brown) were quantified as a percentage of total lesion areas by quantitative morphometry, using 4 sections per aortic root, as described previously by us and others[9-12,37]. Aortas from *Ldlr*$^{-/-}$ mice on high fat diet for 14 weeks and from

C57BL/6 wild type mice on a normal diet were removed, formalin fixed and paraffin embedded (FFPE), and cut into 5 µm-thick sections. For immunoperoxidase staining for HuR, sections were deparaffinized and heat mediated antigen unmasking (Vector Labs) was performed. Sections were blocked with 5% goat serum (Vector) for 30 minutes, incubated with HuR (Abcam) primary antibody for 2 hours, washed, and incubated with secondary antibody conjugated to Biotin (Vector Labs) for 30 minutes. This was followed by Avitin-Biotin-Horseradish peroxidase complex and diaminobenzidine (DAB) substrate (brown stain) (Vector Labs Inc.) and counterstained with hematoxylin (blue stain). Immunofluorescent staining was performed on the same aortas (FFPE) mentioned above. Staining protocol is essentially identical to immunoperoxidase staining except that: tissues were blocked with 5% donkey serum (Jackson ImmunoResearch Labs, Inc.) for 30 mins., and the secondary antibodies are conjugated to fluorescent tags. HuR was visualized by using a donkey anti-rabbit secondary antibody conjugated to Alexafluor 568 (red), smooth muscle cell α actin, CD31, and CD68 were all visualized by using a secondary antibody conjugated to Alexafluor 488 (green) (Jackson ImmunoResearch Labs, Inc). Images were captured with an Olympus BX40 microscope and analyzed using Image J.

Intracellular Staining and Flow Cytometry. Flow cytometry analysis was performed on whole blood from mice to detect TNFα in peripheral blood lymphocytes. Briefly, red blood cells were lysed using lysing buffer (BD Pharm Lyse), leukocytes were cultured in RPMI 1640 medium supplemented with 10% FBS and stimulated with cell stimulation cocktail (eBioscience, Catalog #00-4975) for 5 hours. $1x10^6$ cells were harvested, washed in flow cytometry staining buffer (eBioscience, Catalog #00-4222), surface stained with Qdot605 conjugated anti-mouse CD4 (clone RM4-5) antibody, fixed and permeabilized using the Cytofix/Cytoperm Kit (BD Pharmingen) according to manufacturer's instructions. For intracellular staining, cells were incubated with either APC-conjugated anti-mouse TNFα antibody (clone MP6-XT22) or its isotype control Rat IgG1κ (eBRG1) (eBioscience). Acquisition was performed on LSR II flow cytometer with FACSDiva software (BD Biosciences), and data was analyzed with FlowJo software (Tree Star).

For identification of cell subsets within whole blood for complete blood counts, blood was collected retro-orbitally using heparinized capillary tubes, diluted with 3.8% sodium citrate, and analyzed using morphological flagging by Hemavet 950S analyzer (Drew Scientific).

Statistical analysis. Results are expressed as mean ± SEM. Differences between groups were evaluated with the use of ANOVA, with the Newman-Keuls method applied to evaluate differences between individual mean values or by unpaired Student's *t* test and a *p* value of <0.05 was considered indicative of a statistically significant result. D'Agostino's K^2 and F tests were performed to confirm data passed normality and equal variance for Student's *t* tests.

Major Resources Tables

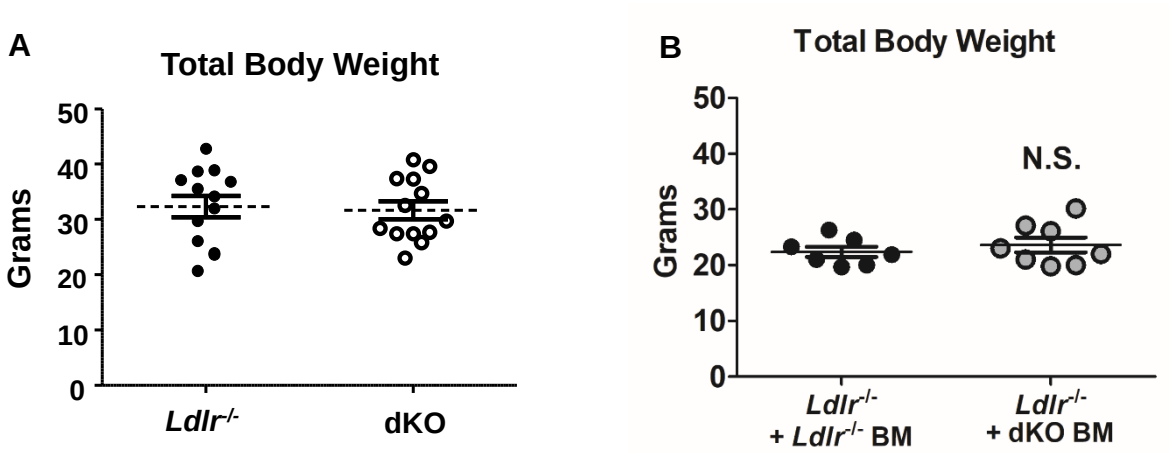
Animals

Species/Strain	Vendor or Source	Background Strain	Sex
Ldlr$^{-/-}$ mouse	Jackson Labs	C57BL/6	M, F
Il19$^{-/-}$ x *Ldlr*-/- mouse	generated in house	C57BL/6	M, F

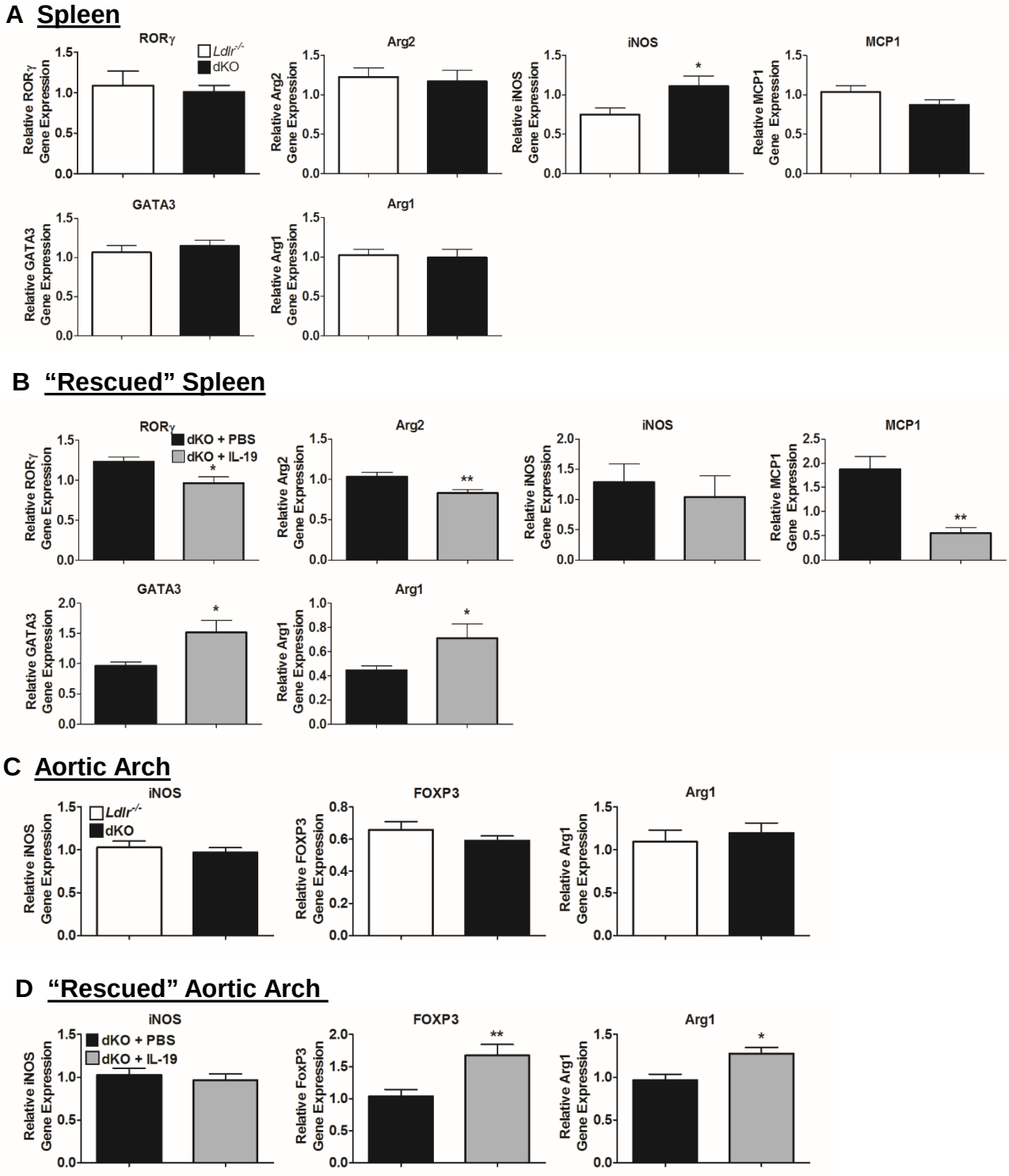
Antibodies

Target antigen	Vendor or Source	Catalog #	Working concentration	Lot # (preferred but not required)
HuR	abcam	200342	1:3000	
TNFα	Santa Cruz Biotechnology	SC-52746	1:3000	E0813
GAPDH	Cell Signaling Technology	14C10	1:3000	
HSC70	Santa Cruz Biotechnology	SC-7298	1:3000	I032

Supplement Material



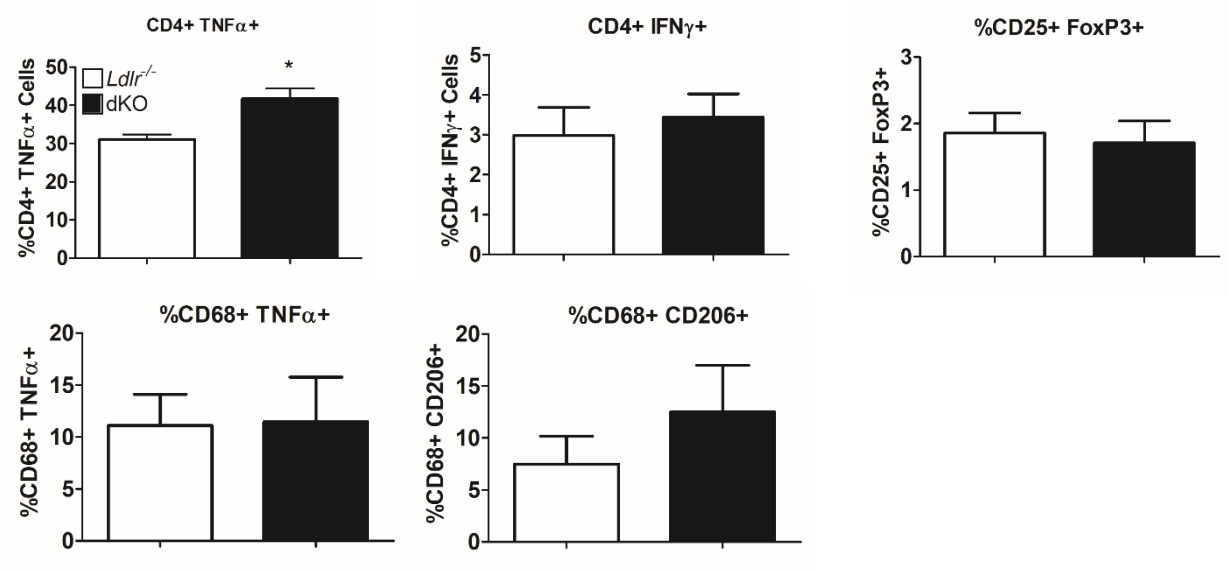
Supplemental Data Figure I. A All *Ldlr*$^{-/-}$ and dKO mice do not statistically differ in total weight after 14 weeks of HFD feeding; no differences were found across sex (32.21 ± 1.92g in *Ldlr*$^{-/-}$ vs 31.67 ± 1.56g in dKO; *n*=12 *Ldlr*$^{-/-}$ vs 13 dKO).
B *Ldlr*$^{-/-}$ mouse recipients of dKO bone marrow (BM) do not differ from recipients of *Ldlr*$^{-/-}$ BM in total body weight following 14 weeks of HFD; no differences were found across sex (22.39 ± 0.92g in *Ldlr*$^{-/-}$ recipients vs 23.65 ± 1.67g in dKO recipients; *n*=7 *Ldlr*$^{-/-}$ recipients vs 8 dKO recipients)**.**



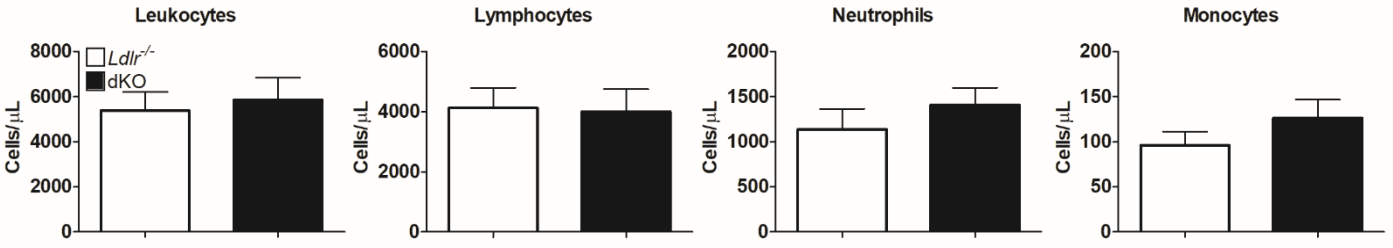
Supplemental Data Figure II.

Additional quantitative RT-PCR analysis of spleen and aortic arch harvested from *Ldlr*$^{-/-}$ and dKO mice after 14 weeks of HFD (**A**, **C**) and dKO mice simultaneously injected with IL-19 or PBS during HFD feeding (**B**, **D**). At the time of euthanasia. RNA was extracted, reverse transcribed, and amplified using primers for the genes shown. (*n*=8 spleen, aortic arch per group).

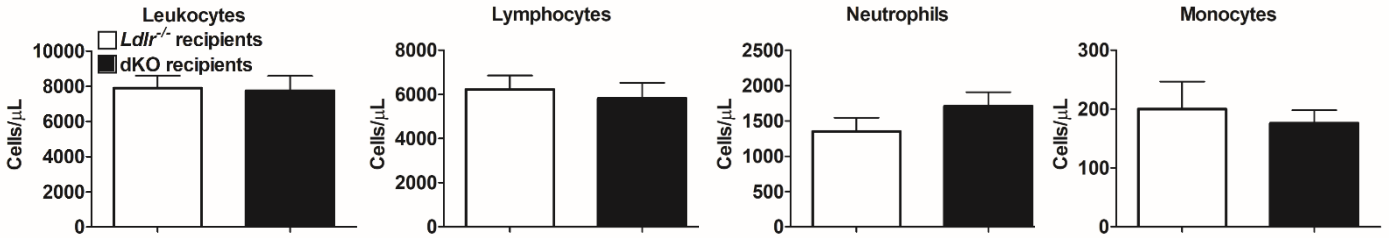
A Flow Cytometry



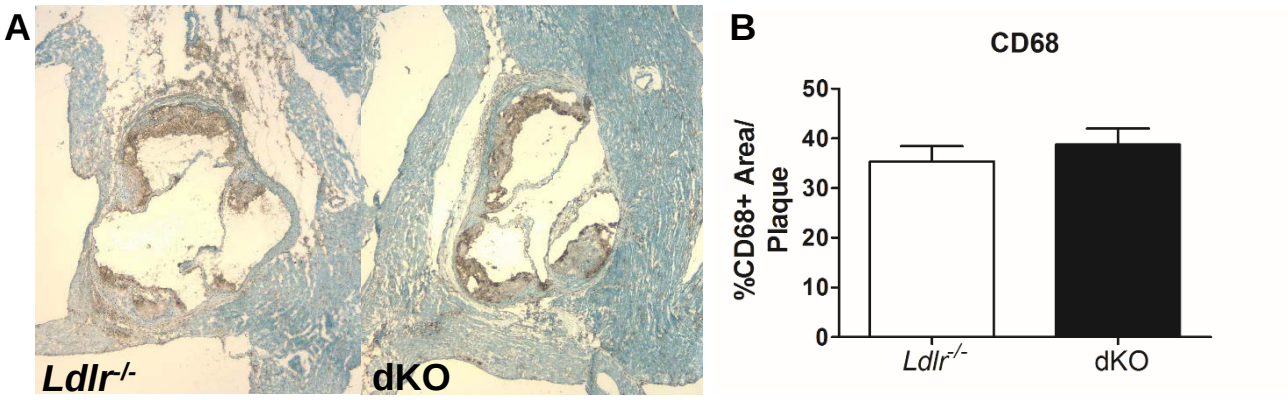
B Blood Count



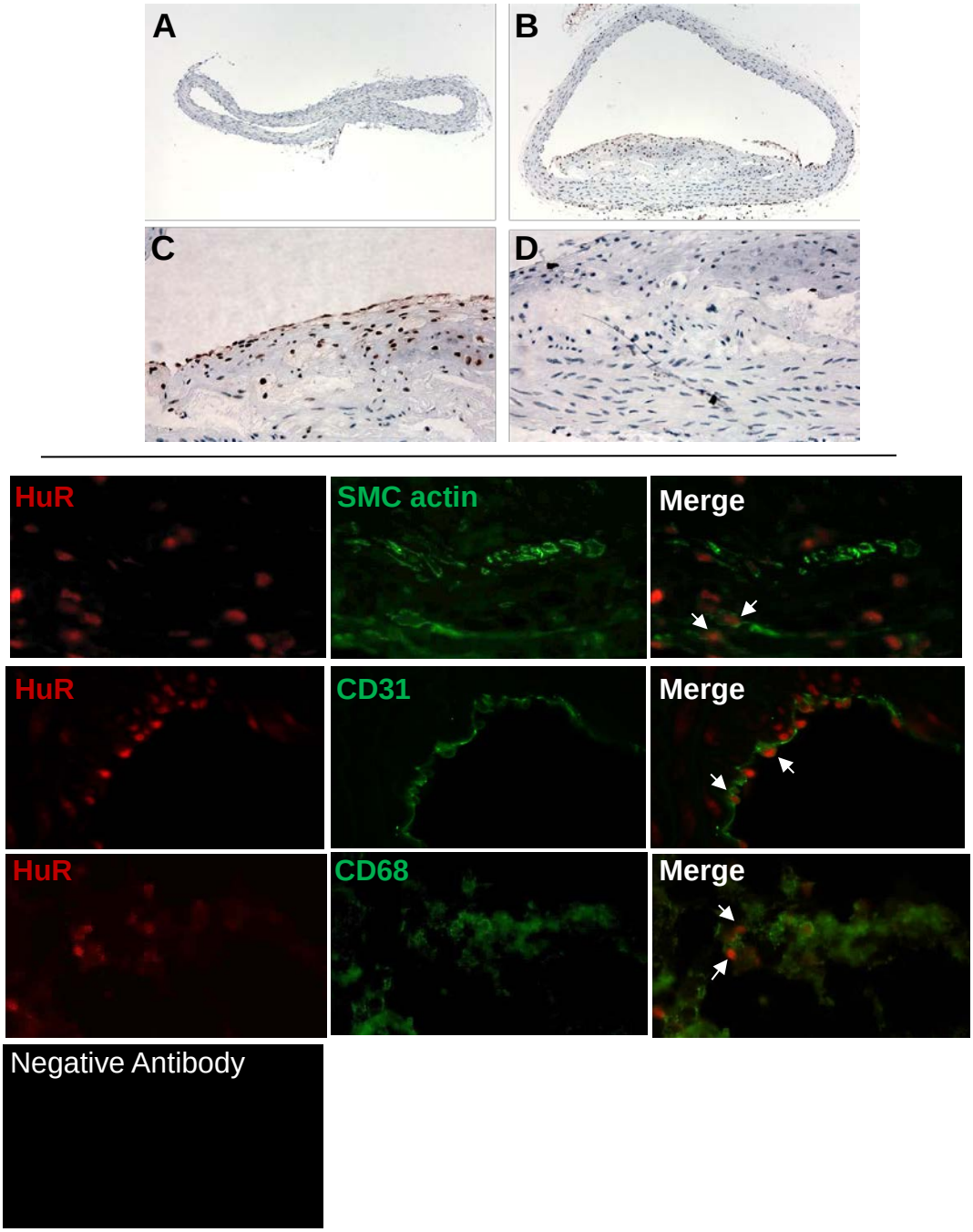
C Bone Marrow Transplant Blood Count



Supplemental Data Figure III Effects of deletion of IL-19 in circulating immune cells. Circulating cells were quantitated by flow cytometry (**A**) and complete blood count was analyzed by Hemavet (**B**) from peripheral blood obtained from *Ldlr*$^{-/-}$ and dKO mice after 14 weeks of HFD consumption, at the time of euthanasia. DKO mice had a significantly higher percentage of CD4+ TNFα+ T cells compared to control mice *(n*=4 per group).
C Complete blood counts from *Ldlr*$^{-/-}$ mice that were recipients of dKO BM did not differ from recipients of *Ldlr*$^{-/-}$ BM (*n*=7 *Ldlr*$^{-/-}$ recipients vs 8 dKO recipients)

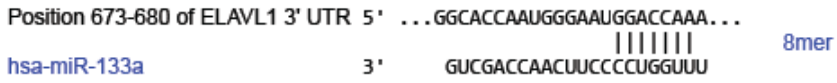


Supplemental Data Figure IV. Loss of IL-19 does not affect macrophage infiltrate in atherosclerotic lesions. **A** Aortic roots were harvested from *Ldlr*$^{-/-}$ and dKO mice after 14 weeks of HFD. Multiple serial sections of aortic root from the aortic sinus to the disappearance of valve cusps per root from were from sectioned and immunostained using anti-CD68 antibody. **B** Positively stained areas were quantified as a percentage of total lesion areas by quantitative morphometry. (35.38 ± 3.06% in *Ldlr*$^{-/-}$ vs 38.75 ± 3.27% in dKO, *n*=6 per group).

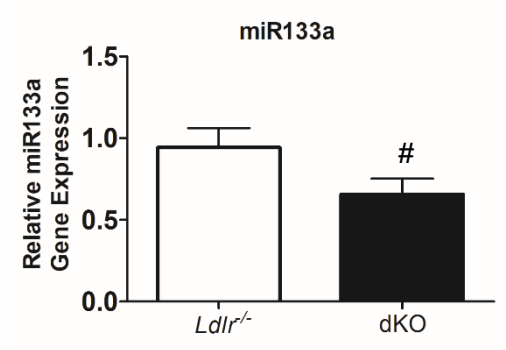


Supplemental Data Figure V. Expression of HuR in atherosclerotic plaque.
Top: Immunohistochemistry on mouse aortas. Expression of HuR is brown and hematoxylin counterstain in blue. **A** There is no expression of HuR in healthy C57BL/6 wild type aorta. **B** Expression of HuR is present in the atherosclerotic plaque of an aorta from an *Ldlr*$^{-/-}$ mouse fed high fat diet for 14 weeks; 400X shown in **C**. **D** Same tissue as B and C with negative control antibody.
Bottom: In the same atherosclerotic plaque of an aorta from a *Ldlr*$^{-/-}$ mouse fed high fat diet for 14 weeks, expression of HuR was seen in smooth muscle cells (SMCactin), endothelial cells (CD31) and macrophages (CD68) by immunofluorescent co-localization staining (arrows indicate co-localization). Isotype negative control antibodies were used for each type of antibody. Magnification 600X.

A



B **Aortic Arch**



Supplemental data Figure VI. **A** Predicted consequential pairing of target region (top) and miRNA133a (bottom). Targetscan analysis identifies seed regions of miR133a which target regions of HuR 3'UTR mRNA. The locations of the miR133a complementary sites on human HuR 3′UTR are shown.

B qRT-PCR analysis from aortic arch from *Ldlr*$^{-/-}$ and dKO mice after 14 weeks of HFD feeding shows insignificantly decreased levels of miR133a in dKO (# indicates p=0.074)

Spleen			
Gene	**Fold Change**		***p* value**
	Ldlr$^{-/-}$	**dKO**	
TNFα	1.160 ± 0.185	2.007 ± 0.203	<0.01
TBet	0.566 ± 0.136	2.527 ± 0.341	<0.001
IL-12β	1.909 ± 0.541	4.676 ± 0.889	<0.05
IL-1β	1.340 ± 0.330	3.205 ± 0.268	<0.001
FOXP3	1.188 ± 0.201	0.607 ± 0.073	<0.05
IL-10	1.049 ± 0.095	0.436 ± 0.120	<0.001
RORγ	1.090 ± 0.176	1.010 ± 0.082	N.S.
Arg2	1.228 ± 0.114	1.168 ± 0.143	N.S.
iNOS	0.749 ± 0.087	1.108 ± 0.087	<0.05
MCP1	1.034 ± 0.079	0.871 ± 0.064	N.S.
GATA3	1.065 ± 0.085	1.146 ± 0.074	N.S.
Arg1	1.022 ± 0.077	0.990 ± 0.108	N.S.
"Rescued" Spleen			
Gene	**Fold Change**		***p* value**
	dKO + PBS	**dKO + IL-19**	
TNFα	2.497 ± 0.169	0.988 ± 0.176	<0.001
TBet	3.234 ± 0.349	1.889 ± 0.286	<0.01
IL-12β	2.060 ± 0.523	0.685 ± 0.184	<0.05
IL-1β	2.469 ± 0.210	0.578 ± 0.139	<0.001
FOXP3	0.596 ± 0.069	1.277 ± 0.066	<0.001
IL-10	0.998 ± 0.246	4.119 ± 0.573	<0.001
RORγ	1.234 ± 0.058	0.966 ± 0.078	<0.05
Arg2	1.032 ± 0.054	0.830 ± 0.043	<0.01
iNOS	1.282 ± 0.303	1.041 ± 0.348	N.S.
MCP1	1.878 ± 0.267	0.554 ± 0.110	<0.01
GATA3	0.964 ± 0.061	1.520 ± 0.199	<0.05
Arg1	0.446 ± 0.037	0.710 ± 0.119	<0.05

Supplemental Table I. qRT-PCR fold change and *p* values.
Fold change ($2^{-\Delta\Delta CT}$) and *p* values for various genes from quantitative RT-PCR analysis of spleen harvested from *Ldlr$^{-/-}$* and dKO mice after 14 weeks of HFD and dKO mice simultaneously injected with IL-19 or PBS during HFD feeding.
Data shown graphically in Figures 2A, 2B and Supplemental Data Figures IIA, IIB.

Aortic Arch			
Gene	**Fold Change**		***p* value**
	Ldlr$^{-/-}$	**dKO**	
TNFα	1.006 ± 0.033	1.263 ± 0.033	<0.001
TBet	0.243 ± 0.109	0.756 ± 0.054	<0.001
Arg2	1.846 ± 0.348	2.926 ± 0.273	<0.001
IL-12β	1.375 ± 0.382	3.088 ± 0.552	<0.05
IL-1β	0.879 ± 0.219	1.645 ± 0.244	<0.05
MCP1	0.802 ± 0.070	1.030 ± 0.076	<0.001
RORγ	1.147 ± 0.197	2.608 ± 0.265	<0.001
GATA3	0.375 ± 0.058	0.181 ± 0.017	<0.01
IL-10	0.767 ± 0.047	0.589 ± 0.046	<0.01
iNOS	1.028 ± 0.073	0.967 ± 0.073	N.S.
FOXP3	0.657 ± 0.052	0.591 ± 0.028	N.S.
Arg1	1.022 ± 0.077	0.990 ± 0.108	N.S.
"Rescued" Aortic Arch			
Gene	**Fold Change**		***p* value**
	dKO + PBS	**dKO + IL-19**	
TNFα	1.115 ± 0.038	0.861 ± 0.012	<0.001
TBet	2.327 ± 0.500	0.880 ± 0.163	<0.01
Arg2	1.184 ± 0.038	0.794 ± 0.141	<0.05
IL-12β	1.392 ± 0.101	0.967 ± 0.073	<0.01
IL-1β	1.479 ± 0.062	0.863 ± 0.030	<0.001
MCP1	1.376 ± 0.319	0.566 ± 0.095	<0.05
RORγ	1.216 ± 0.258	0.616 ± 0.080	<0.05
GATA3	1.216 ± 0.258	0.616 ± 0.080	<0.05
IL-10	1.017 ± 0.065	1.376 ± 0.059	<0.001
iNOS	1.027 ± 0.082	0.966 ± 0.073	N.S.
FOXP3	1.033 ± 0.110	1.668 ± 0.171	<0.01
Arg1	0.963 ± 0.072	1.272 ± 0.076	<0.05

Supplemental Table II. qRT-PCR fold change and *p* values. Fold change ($2^{-\Delta\Delta CT}$) and *p* values for various genes from quantitative RT-PCR analysis of aortic arch harvested from *Ldlr*$^{-/-}$ and dKO mice after 14 weeks of HFD and dKO mice simultaneously injected with IL-19 or PBS during HFD feeding. Data shown graphically in Figures 2A, 2B and Supplemental Data Figures IIA, IIB.