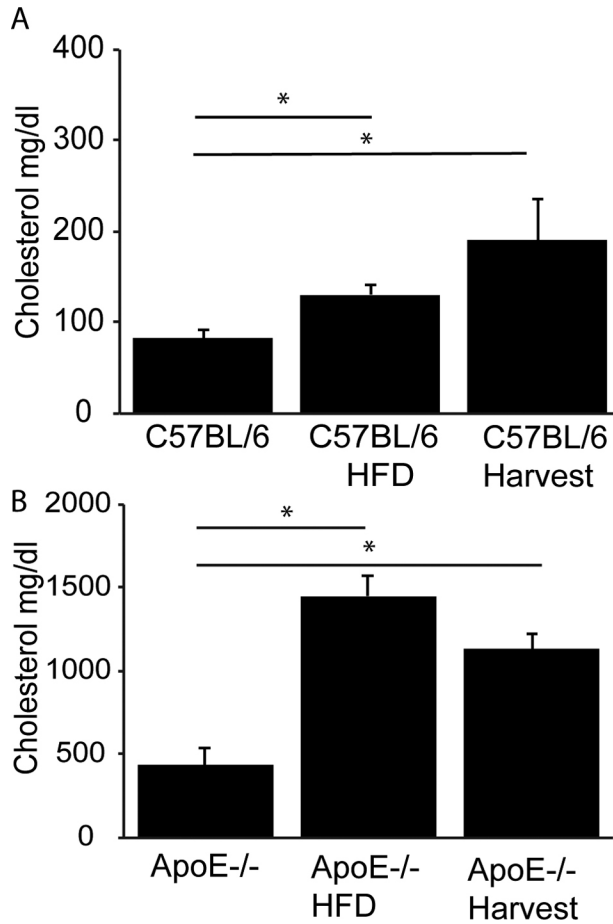


## Supplemental Figures:

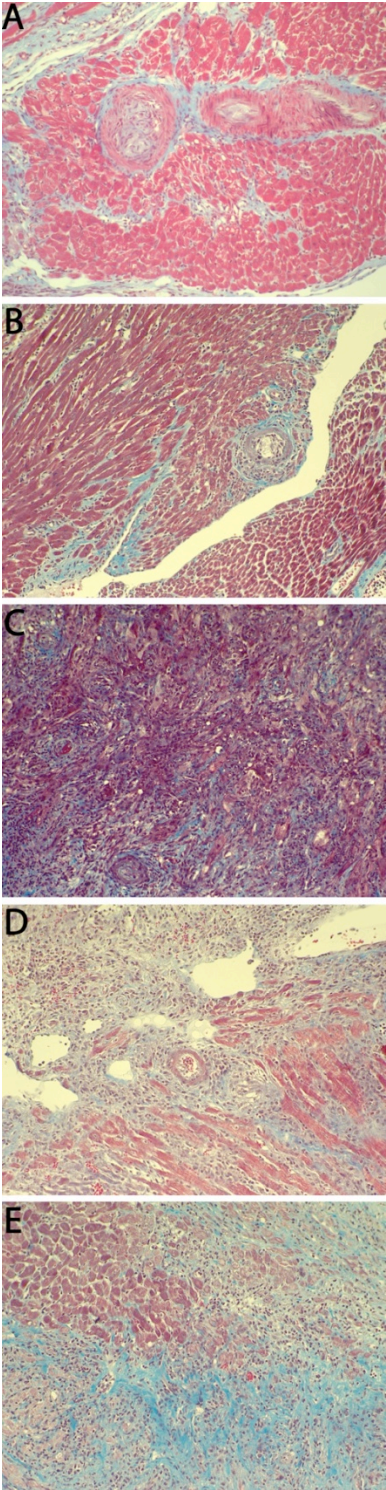
### Figure S1



Serum cholesterol levels in mice fed a high-fat diet. Shown are levels of cholesterol in C57BL/6 mice (top panel) or ApoE<sup>-/-</sup> mice (bottom panel) prior to starting them on a high-fat diet, after being fed a high fed for 4-weeks on the day of transplant (HFD), or at the time the mice were sacrificed and hearts harvested (Harvest).  $n=5-6$  mice per group. Asterisk indicates  $P < 0.05$ . A full discussion of the plasma cholesterol levels in ApoE<sup>-/-</sup> and C57BL/6 mice fed normal chow or high fat diet can be found in (47). For reference, transplant patients are considered hyperlipidemic when they have plasma

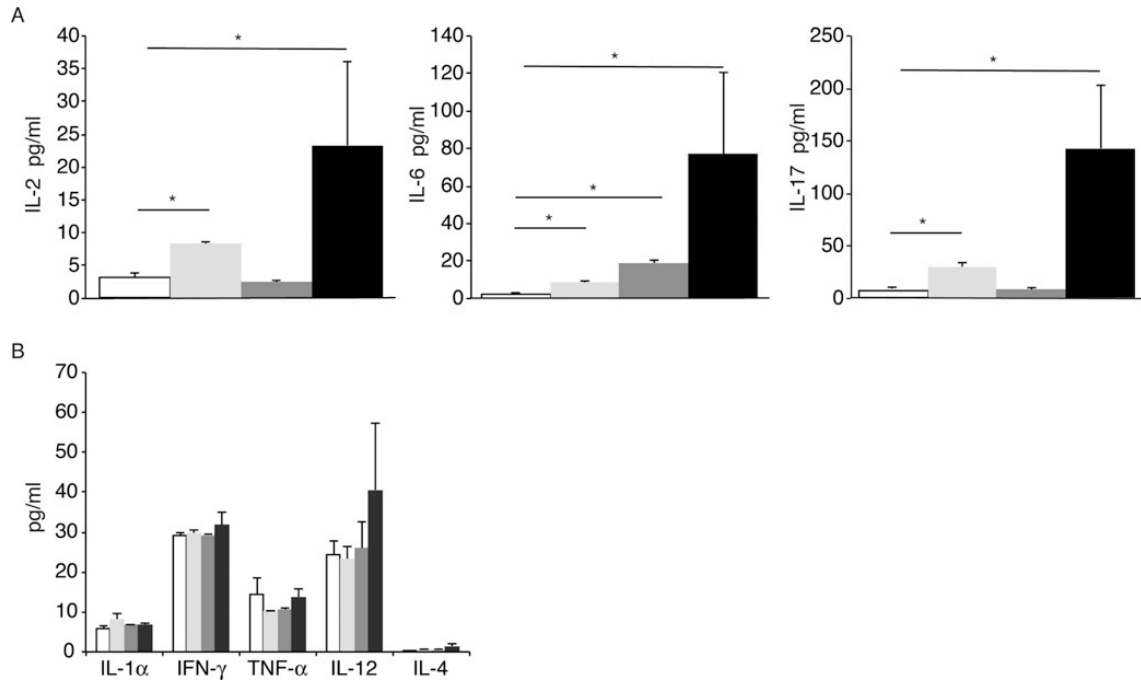
cholesterol levels greater than 200 mg/dl. A retrospective study of lipid control in transplant patients in a single center identified a range of from 91 mg/dl to 1665 mg/dl among patients tested (48). It is important to note that wild-type mice have a different plasma cholesterol composition, with high high density lipoprotein (HDL), and low low density lipoprotein (LDL) levels compared with humans. While the goal for human transplant patients is less than 100mg/dl LDL, C57BL/6 mice fed normal diet have an LDL of 7mg/dl. In ApoE<sup>-/-</sup> mice, in contrast to wild-type mice, low density LDL and VLDL particles are enriched, similar to what is observed in hyperlipidemic humans.

Figure S2



Trichrome staining of tissue sections from a transplanted bm12 heart harvested after 100 days from C57B/6 control mice fed normal chow (A); a syngeneic heart harvested after 100 days from an ApoE<sup>-/-</sup> mouse fed a high-fat diet (B); a bm12 heart harvested at the time of rejection from a C57BL/6 mouse fed a high-fat diet (C, day 60); a bm12 heart harvested at the time of rejection from an ApoE<sup>-/-</sup> mouse fed a high-fat diet (D, day 21); a bm12 heart harvested at the time of rejection from an ApoE<sup>-/-</sup> mouse fed a normal diet (E, day 60). Representative tissue sections are shown. 20x magnification is shown.

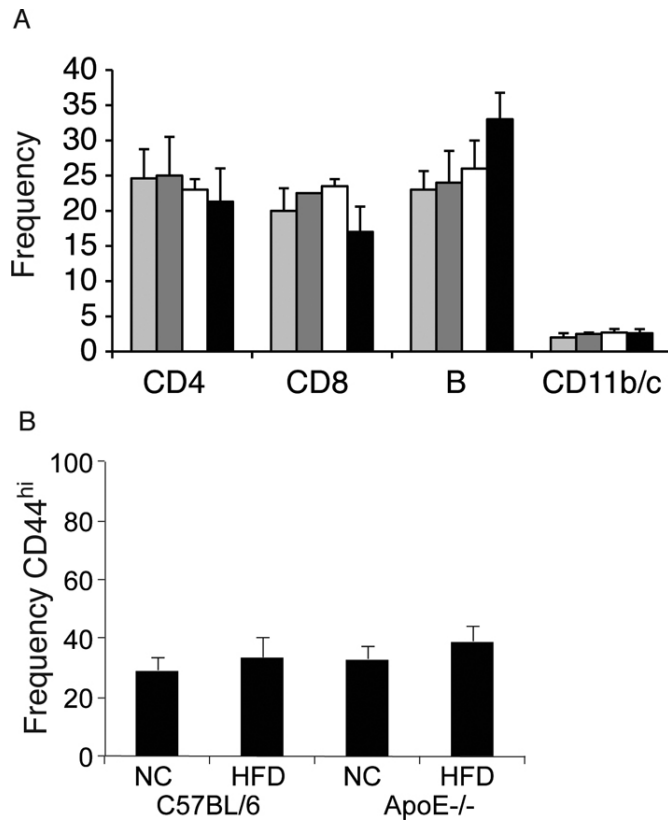
**Figure S3**



Serum cytokine concentrations. ApoE<sup>-/-</sup> and C57BL/6 mice were fed high-fat diet or normal chow for four weeks before receiving a bm12 heart transplant. Mice were sacrificed at the time of rejection, and pooled serum for each group was assayed for expression of IL-1α, IFN-γ, TNF-α, IL-12p70, IL-2, IL-4, IL-6 and IL-17 by multiplex ELISA. A) Serum cytokine level of IL-2, IL-6 and IL-17 expressed in pg/ml in C57BL/6 mice fed normal chow (white bars), C57BL/6 mice fed a high-fat diet (light grey bars), ApoE<sup>-/-</sup> mice fed normal chow (dark grey bars), and ApoE<sup>-/-</sup> mice fed a high-fat diet (black bars). *n*=6 mice per group. B) Serum cytokine level of IL-1α, IFN-γ, TNF-α, or IL-12p70, and IL-4 expressed in pg/ml in C57BL/6 mice fed normal chow (white bars), C57BL/6 mice fed a high-fat diet (light grey bars), ApoE<sup>-/-</sup> mice fed normal chow (dark

grey bars), and ApoE<sup>-/-</sup> mice fed a high-fat diet (black bars). *n*=6 mice per group. Asterisk represents *P*<0.05.

**Figure S4**



Lymphocytes populations not affected by hyperlipidemia.. ApoE<sup>-/-</sup> and C57BL/6 mice were fed high-fat diet or normal chow for four weeks before receiving a bm12 heart transplant. Mice were sacrificed at the time of rejection, and A. the frequencies of CD4<sup>+</sup>, CD8<sup>+</sup>, B220<sup>+</sup> and CD11b/c<sup>+</sup> cells were assayed by cell surface staining and flow cytometry. Naïve C57BL/6 mice fed normal chow (white bars) were used as a control. *n*

>5 in each group. B. The frequency of CD44<sup>hi</sup> cells was determined by flow cytometry.

Data is shown gated on CD4<sup>+</sup>FoxP3<sup>-</sup> n>4 in each group.