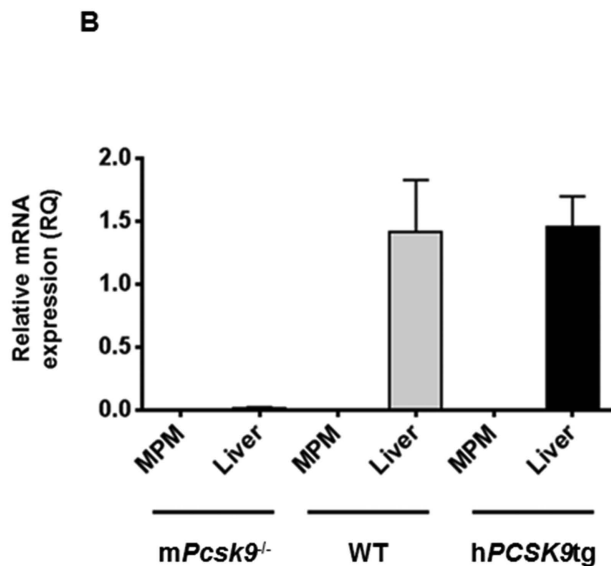
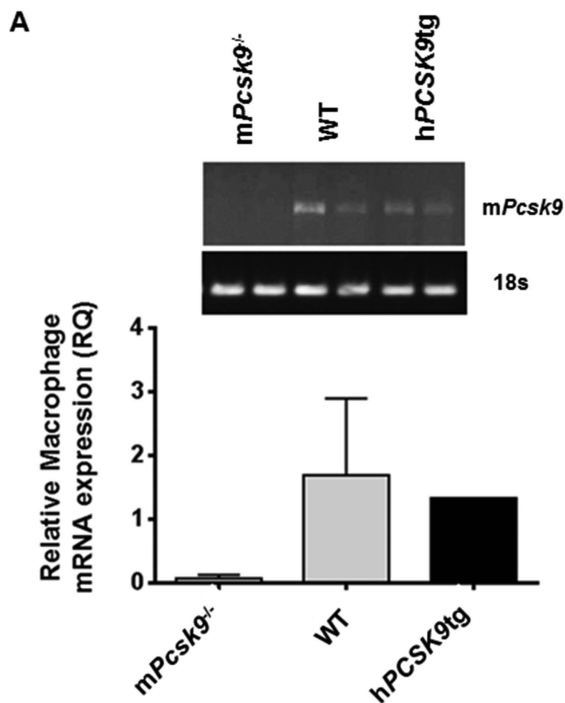
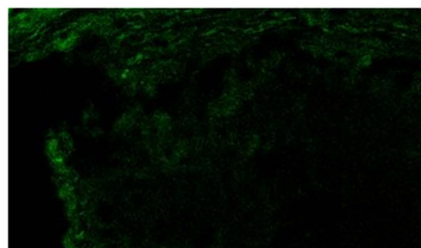
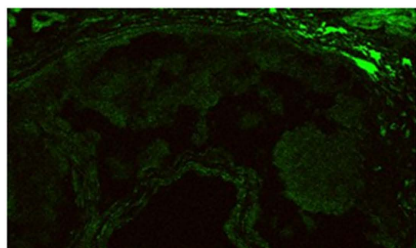


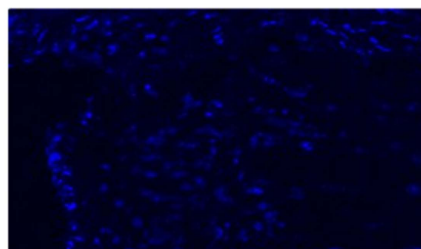
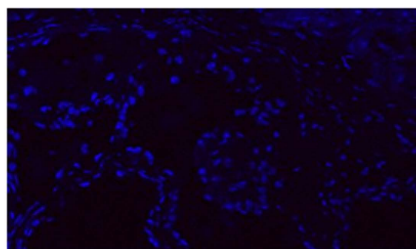
Supplementary Figure 1. (A) Immunoprecipitation of *hPCSK9* in liver, kidney, adrenals and MPM collected from *hPCSK9tg* mice and relative western blot analysis of LDLR and LRP1 (B) Flow cytometry analysis of surface LRP1 levels in MPM from *apoE^{-/-}* or *hPCSK9tg/apoE^{-/-}* mice.



Supplementary Figure 2. (A) Relative mRNA levels of *mPcsk9* in MPM from *mPcsk9*^{-/-}, WT and *hPcSK9*tg mice, as measured by PCR. (B) Relative mRNA levels of *mPcsk9* in MPM and livers from *mPcsk9*^{-/-}, WT and *hPcSK9*tg mice, as measured by QRT-PCR.



Anti-
human
488

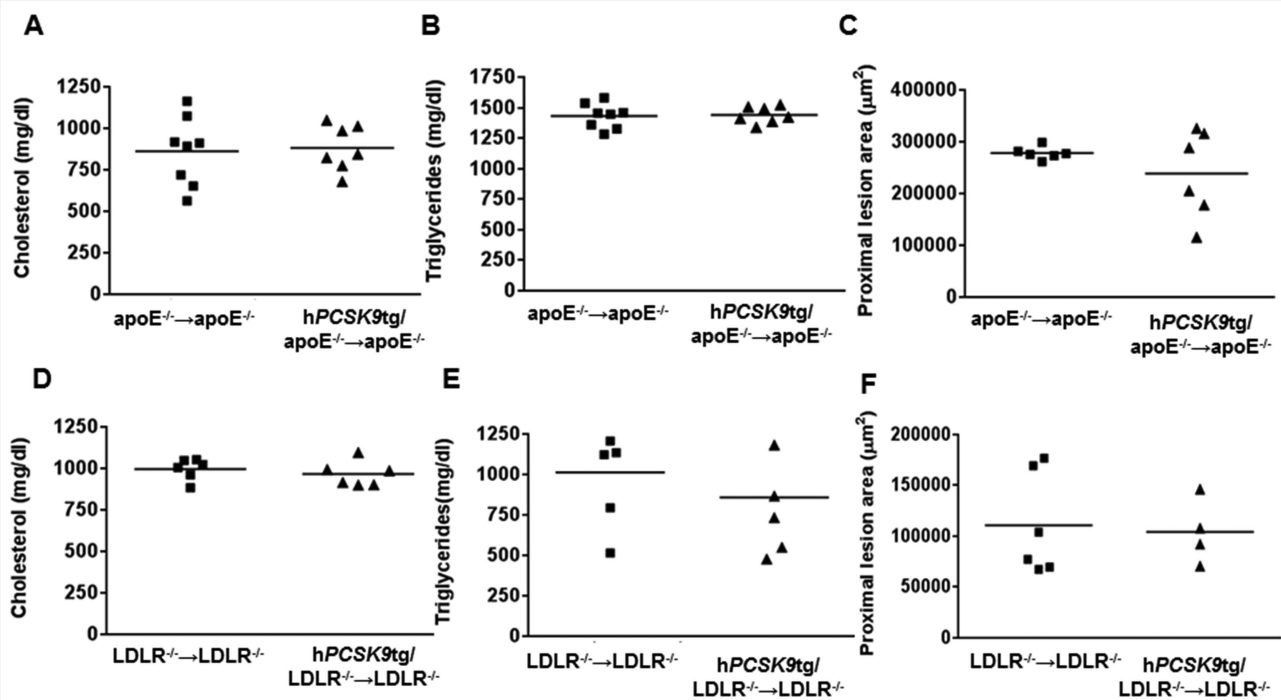


DAPI

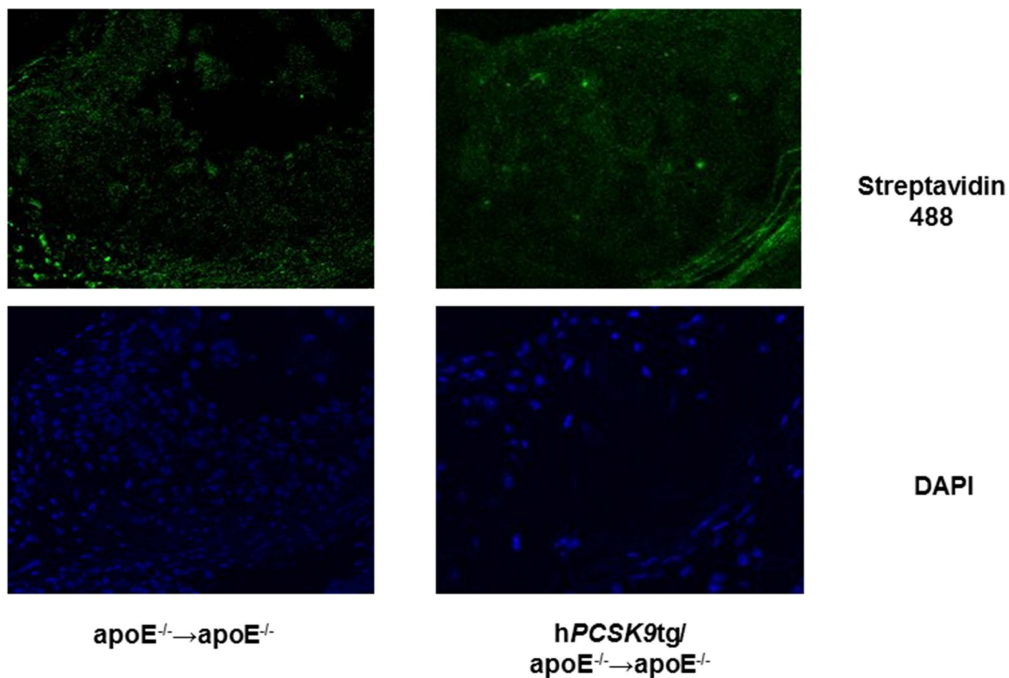
$apoE^{-/-} \rightarrow apoE^{-/-}$

$hPCSK9tg/$
 $apoE^{-/-} \rightarrow apoE^{-/-}$

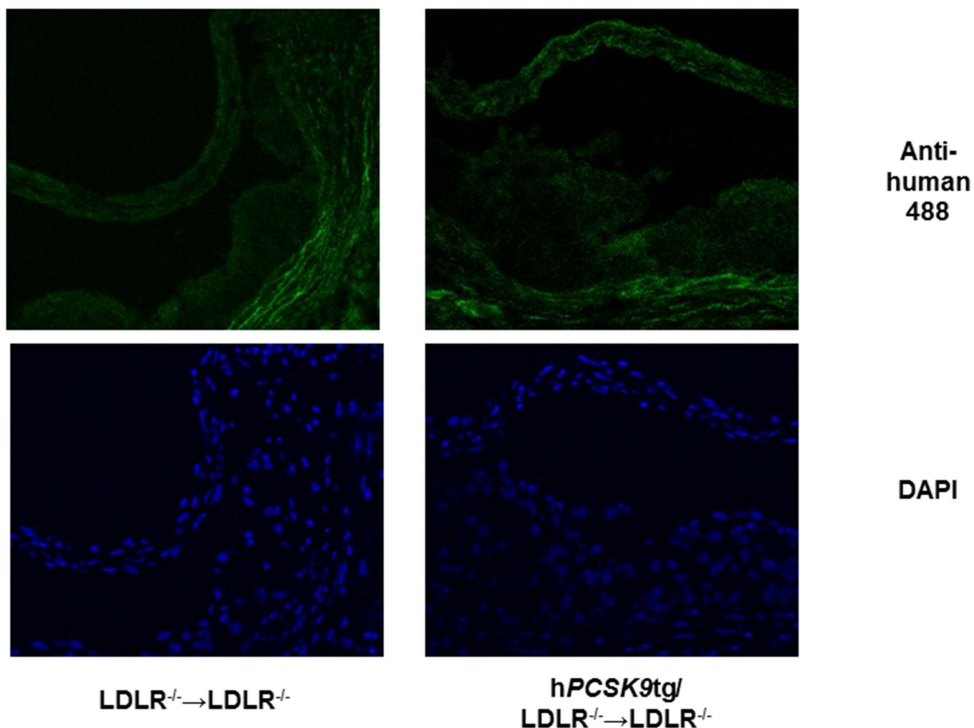
Supplementary Figure 3. Representative images showing negative control staining of lesions of proximal aortas in $apoE^{-/-} \rightarrow apoE^{-/-}$ or $hPCSK9tg/apoE^{-/-} \rightarrow apoE^{-/-}$ mice. In green: anti-human secondary antibody staining; in blue: DAPI.



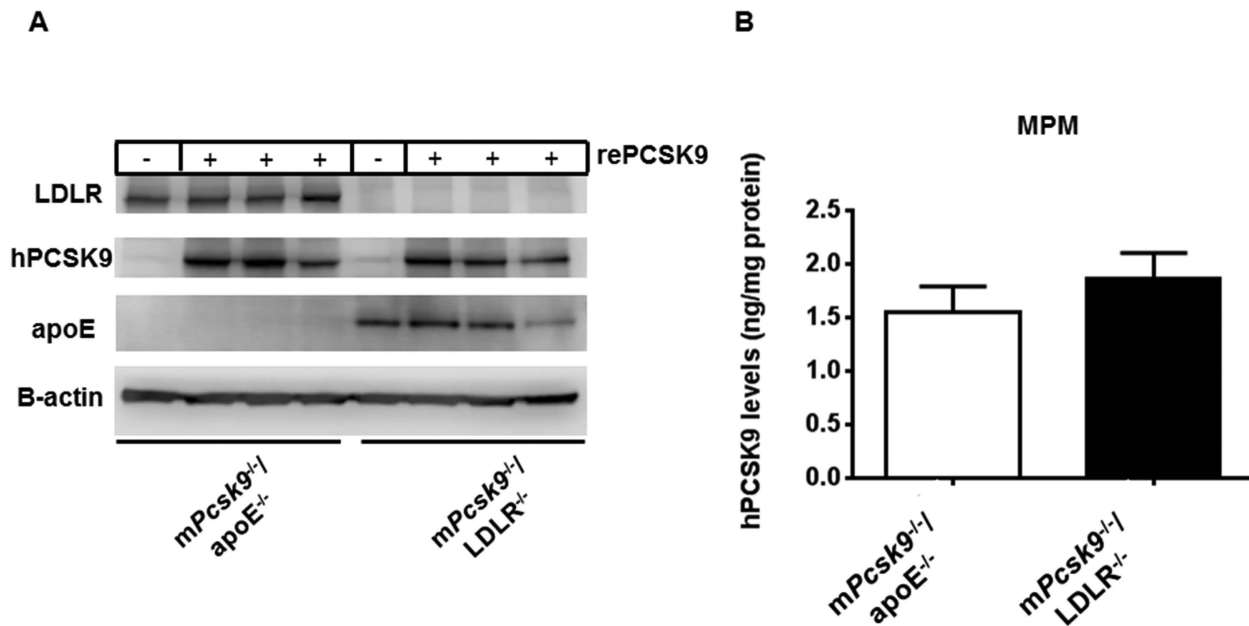
Supplementary figure 4. (A) Total serum cholesterol levels measured in apoE^{-/-}→apoE^{-/-} or hPCSK9tg/apoE^{-/-}→apoE^{-/-} (B) Serum triglyceride levels measured in apoE^{-/-}→apoE^{-/-} or hPCSK9tg/apoE^{-/-}→apoE^{-/-} (C) Quantitation of proximal lesion area in Oil red O stained proximal aortas of apoE^{-/-}→apoE^{-/-} or hPCSK9tg/apoE^{-/-}→apoE^{-/-} mice (D) Total serum cholesterol levels measured in LDLR^{-/-}→LDLR^{-/-} or hPCSK9tg/LDLR^{-/-}→LDLR^{-/-} mice (E) Serum triglyceride levels measured in LDLR^{-/-}→LDLR^{-/-} or hPCSK9tg/LDLR^{-/-}→LDLR^{-/-} mice (F) Quantitation of proximal lesion area in Oil red O stained proximal aortas of LDLR^{-/-}→LDLR^{-/-} or hPCSK9tg/LDLR^{-/-}→LDLR^{-/-} mice.



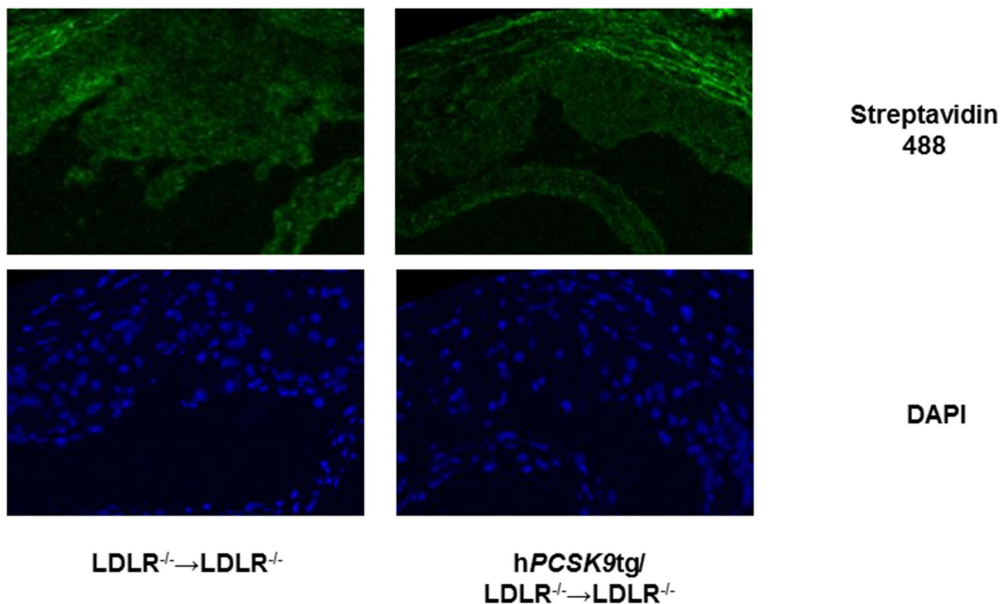
Supplementary Figure 5. Representative images showing negative control staining of lesions of proximal aortas in $apoE^{-/-} \rightarrow apoE^{-/-}$ or $hPCSK9tg/apoE^{-/-} \rightarrow apoE^{-/-}$ mice. In green: streptavidin 488 antibody staining; in blue: DAPI.



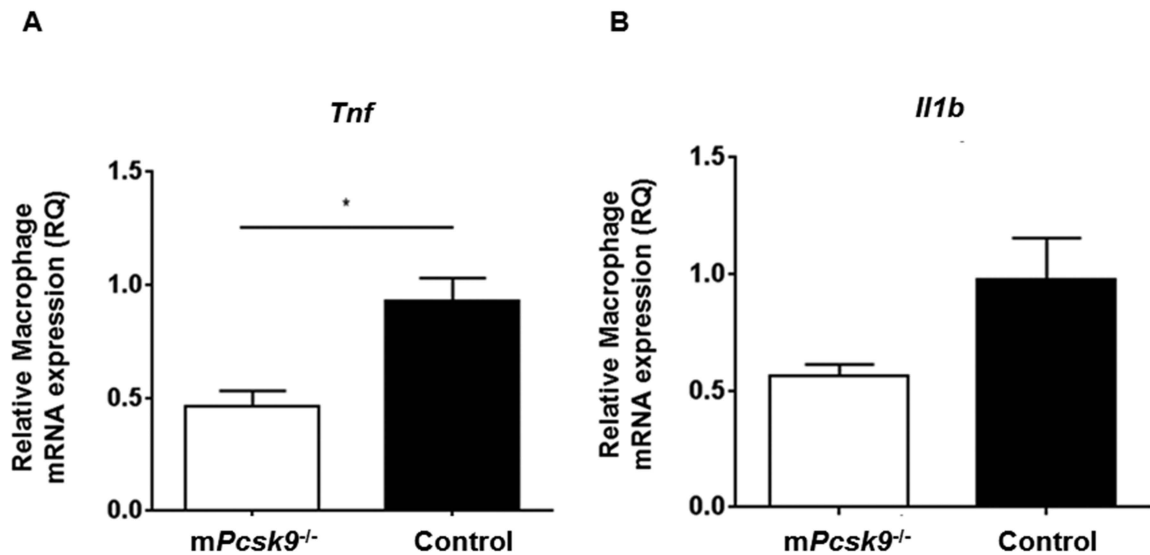
Supplementary Figure 6. Representative images showing negative control staining of lesions of proximal aortas in $LDLR^{-/-} \rightarrow LDLR^{-/-}$ or $hPCSK9tg/LDLR^{-/-} \rightarrow LDLR^{-/-}$ mice. In green: anti-human secondary antibody staining; in blue: DAPI.



Supplementary figure 7. (A) Western blot analysis of hPCSK9, LDLR and apoE in MPM from *mPcsk9^{-/-}/LDLR^{-/-}* or *mPcsk9^{+/-}/apoE^{-/-}* mice incubated overnight with recombinant hPCSK9 (rePCSK9) 1000ng/ml (B) Quantification of intracellular levels of hPCSK9 in MPM from *mPcsk9^{+/-}/LDLR^{-/-}* or *mPcsk9^{+/-}/apoE^{-/-}* mice incubated overnight with rePCSK9 1000ng/ml.



Supplementary Figure 8. Representative images showing negative control staining of lesions of proximal aortas in $LDLR^{-/-} \rightarrow LDLR^{-/-}$ or $hPCSK9tg / LDLR^{-/-} \rightarrow LDLR^{-/-}$ mice. In green: streptavidin 488 antibody staining; in blue: DAPI.



Supplementary figure 9. mRNA expression of *Tnf* (A) and *Il1b* (B) in LPS-stimulated MPM from *mPcsk9*^{-/-} and Control mice