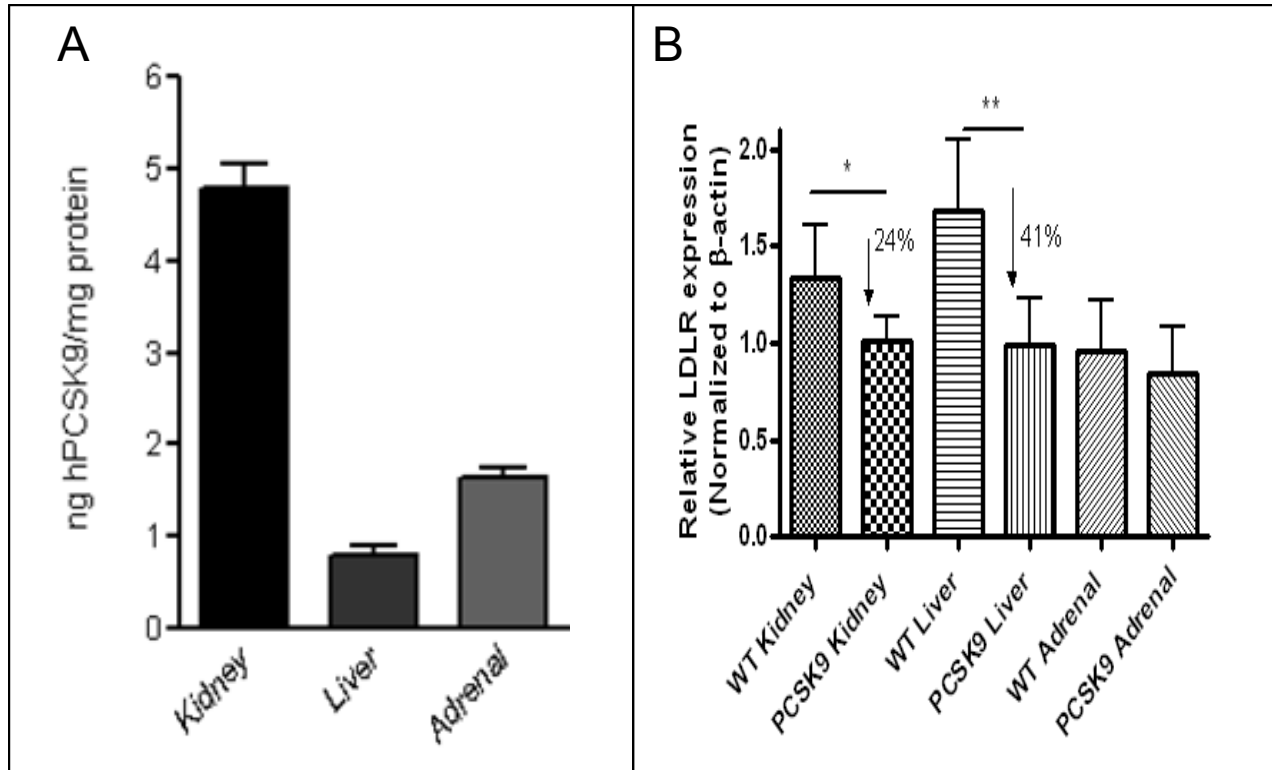
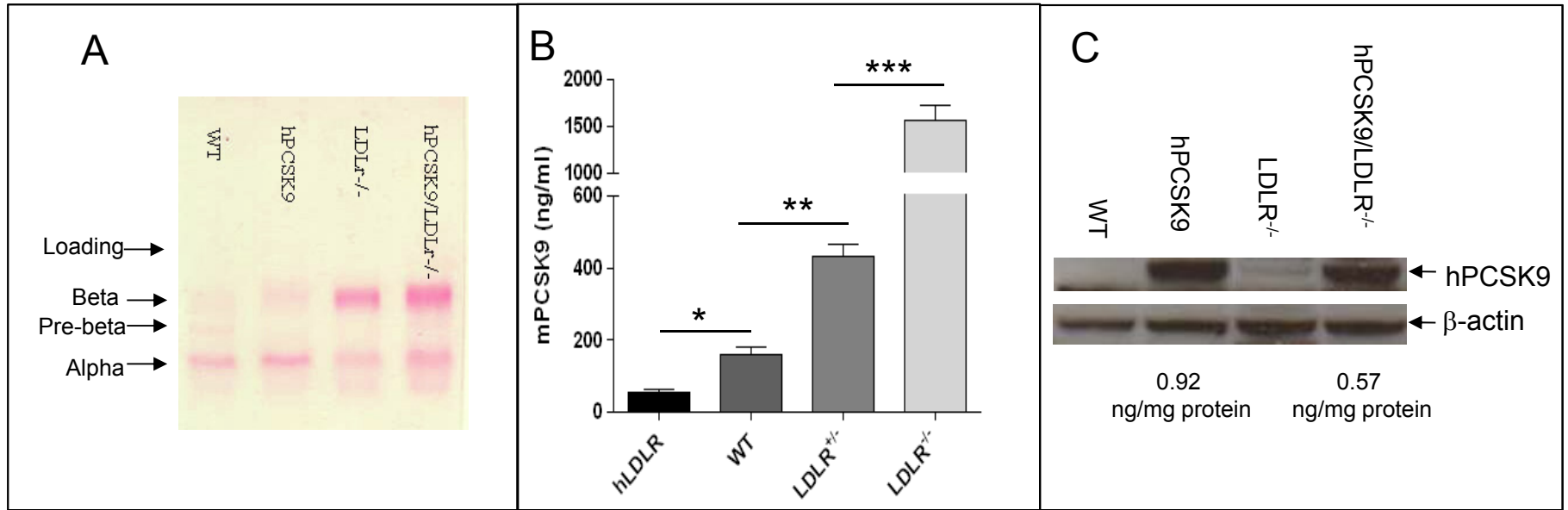


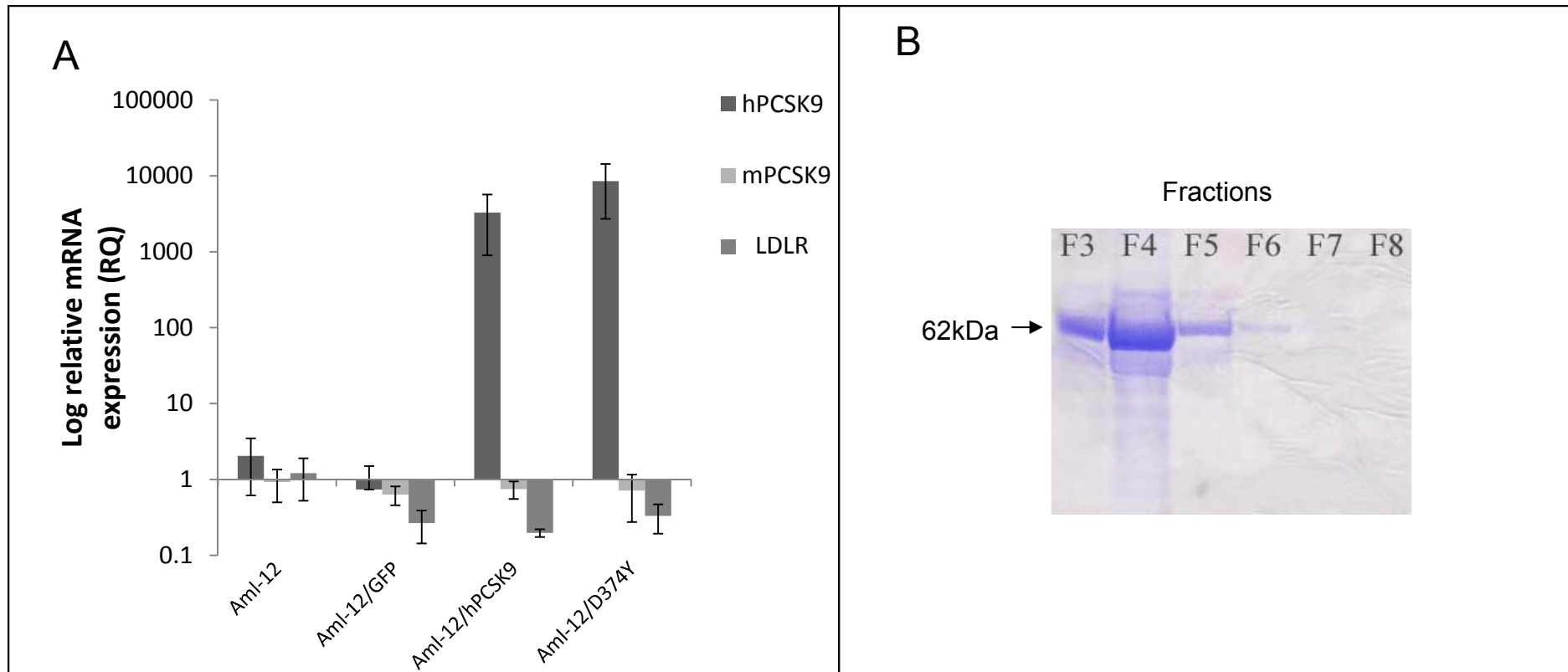
SUPPLEMENTAL MATERIAL



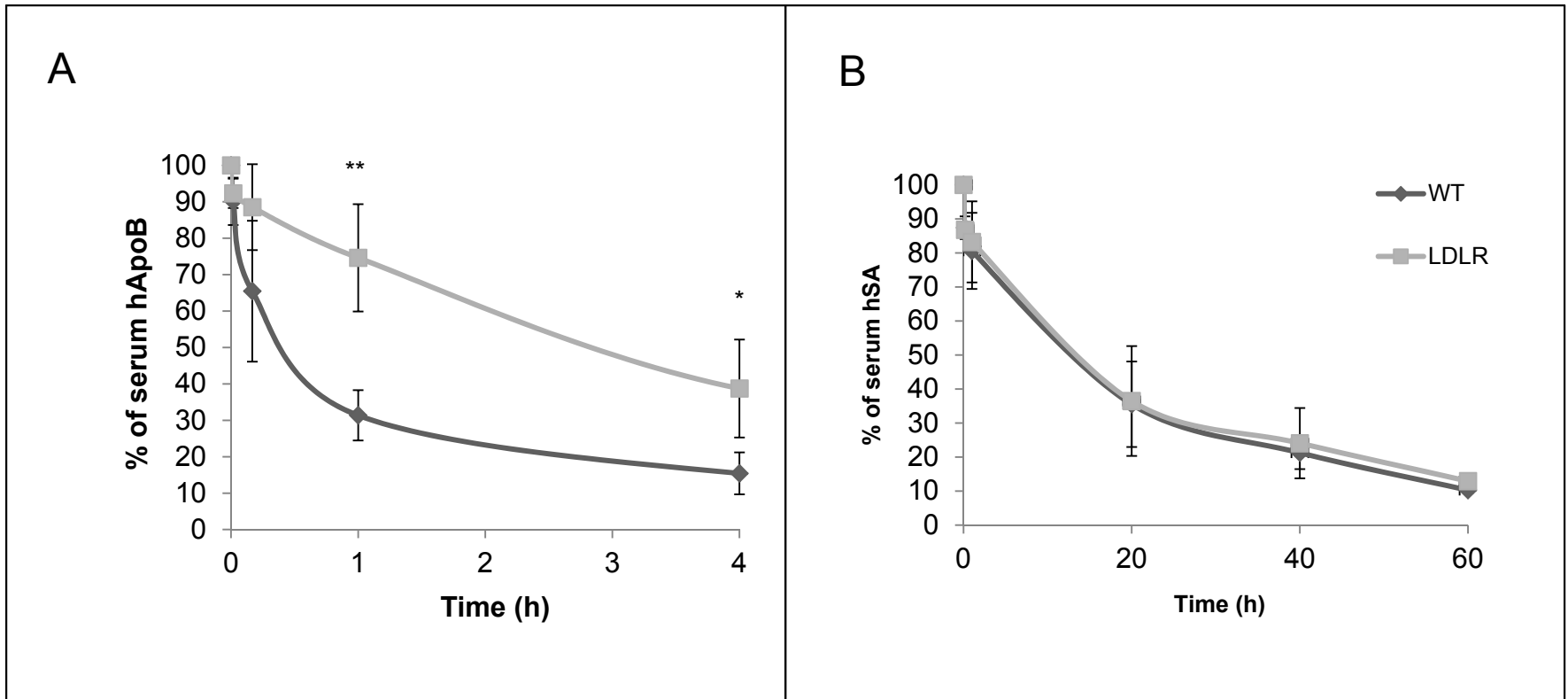
Supplementary figure 1: (A) ELISA quantification of hPCSK9 in tissues of transgenic mice. (B) Effect of hPCSK9 expression *in-vivo*: quantification of immunoblots for hepatic LDLR levels normalized to β -actin (n=4-6). (*p<0.05, ** p<0.01).



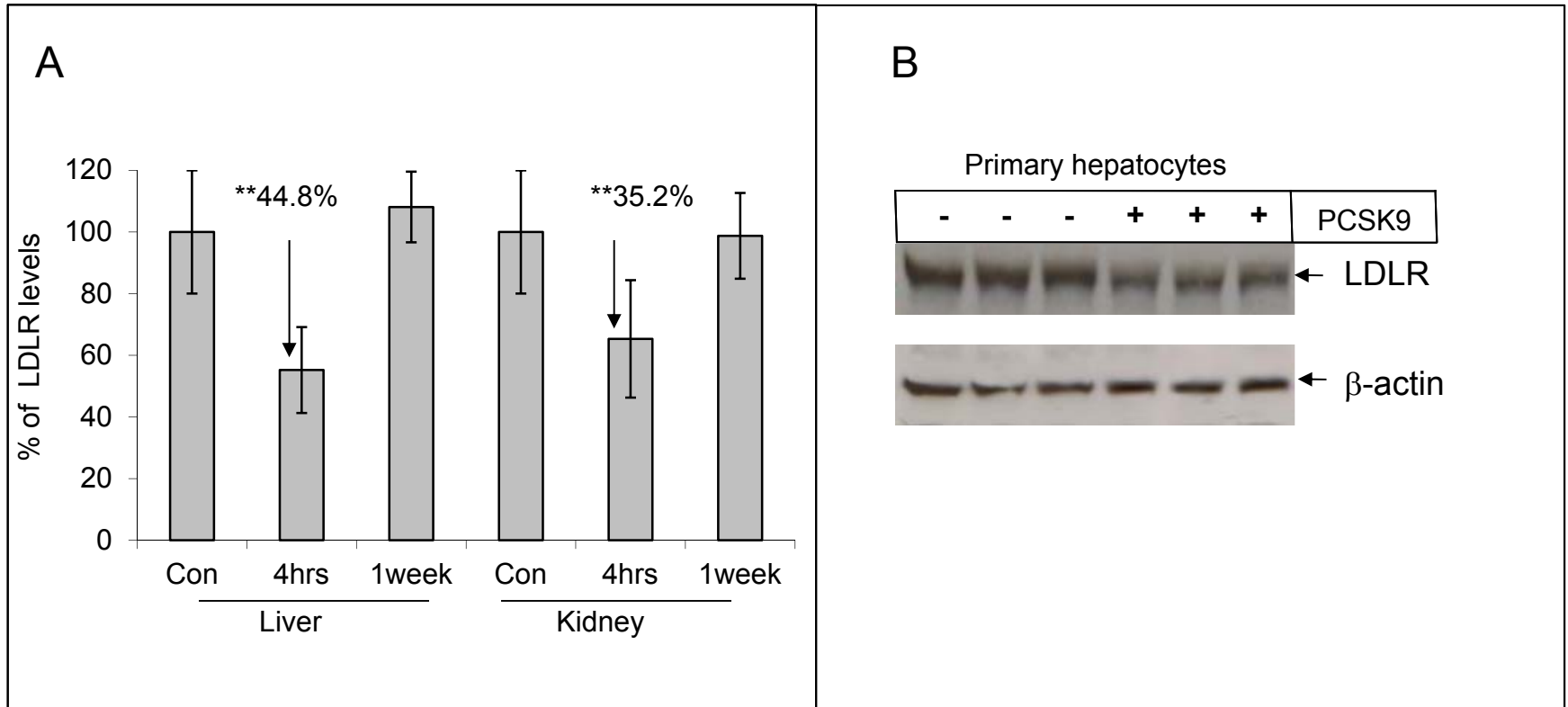
Supplementary figure 2: (A) Agarose gel separation of serum lipoproteins. (B) mPCSK9 levels. (C) Immunoblot and ELISA quantification of hPCSK9 in liver of controls and transgenic mice.



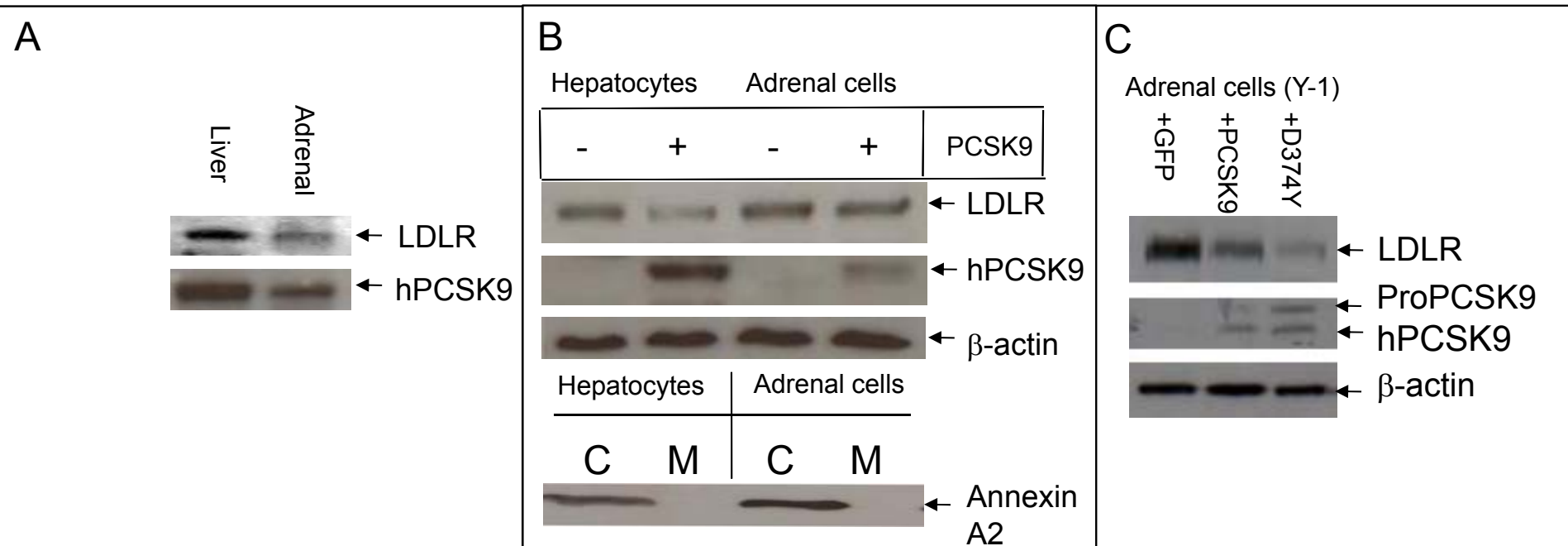
Supplementary figure 3: (A) qRT-PCR for hPCSK9, mPCSK9 and LDLR in Aml-12 cells transduced with pWPI-GFP, pWPI-hPCSK9, or pWPI-D374Y gain of function mutation. (B) Coomassie blue stain of His-tagged eluted fraction from “ProBond” Nickel column of media from HEK293T cell transduced with pWPI-hPCSK9 lentivirus.



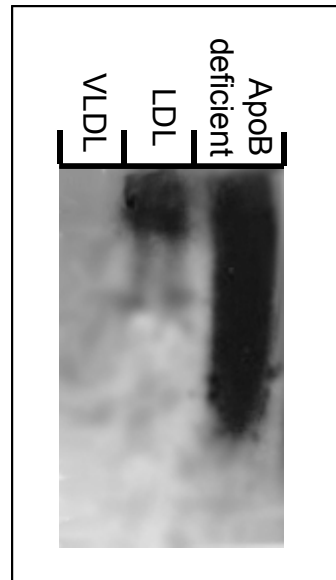
Supplementary figure 4: Turnover of human serum albumin and human LDL in mice. (A) Clearance of human LDL injected to WT or LDLR^{-/-} mice (n=3), (B) Clearance of human serum albumin injected to WT or LDLR^{-/-} mice (n=3), (*p<0.05, ** p<0.01).



Supplementary figure 5: (A) Quantification of immunoblots for hepatic and renal LDLR normalized to β -actin (n=3). (B) Immunoblot for LDLR, and beta actin in primary hepatocyte upon addition of hPCSK9 (500 ng/ml) for 4hrs, (p<0.01).



Supplementary figure 6: Effect of hPCSK9 in the adrenals. (A) Immunoblot of LDLR after co-immunoprecipitation with hPCSK9 of adrenal and liver from hPCSK9tg mice. (B) Immunoblot for LDLR, PCSK9, beta actin and annexinA2 in hepatocytes (AML-12) and adrenal (Y-1) cells (C=cell, M=media). (C) immunoblot of mouse adrenal cells (Y-1) transduced with GFP (control), PCSK9, or PCSK9 GOF mutation (D374Y).



Supplementary figure 7: hPCSK9 immunoblot for FPLC fractions treated with cross linker DSP (0.5mM, 30 min) on a native gel (4-16%).

%mPCSK9				%hPCSK9			
fraction				fraction			
mice	IDL/LDL	HDL	LPDS	mice	IDL/LDL	HDL	LPDS
WT	0.8	2.6	96.7	WT	N/D	N/D	N/D
hPCSK9	3.3	0.6	96.1	hPCSK9	0.8	3.0	95.5

Supplementary table 1: Serum mPCSK9 and hPCSK9 distribution after high-salt (KBr) ultracentrifugal separation of lipoproteins from hPCSK9 transgenic mouse serum, measured by PCSK9 ELISA and presented as % of total PCSK9.