SUPPLEMENTAL MATERIAL

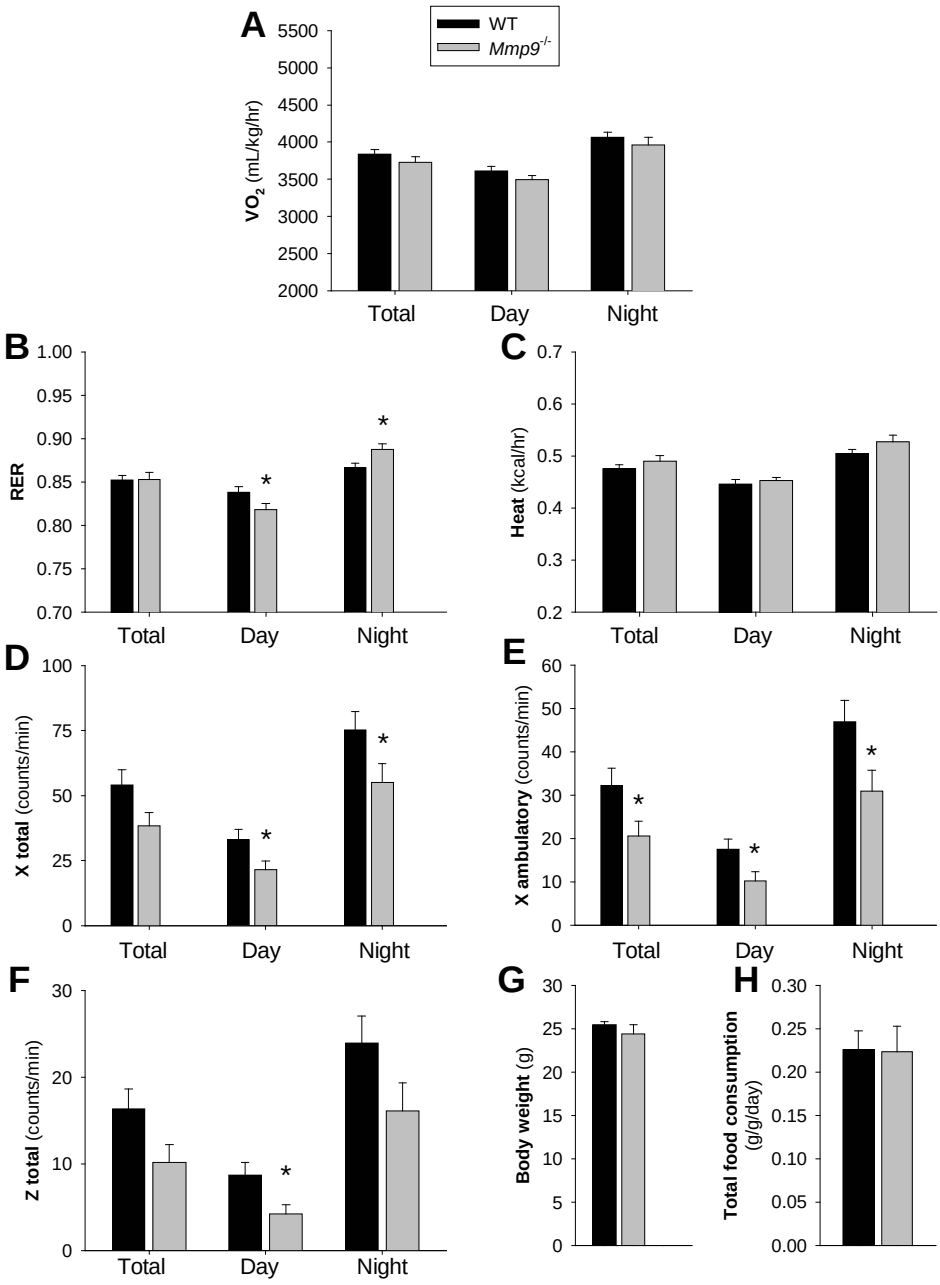

Figure S1. Systemic metabolic profile of MMP-9 deficient mice.
(A) Oxygen consumption. (B) Carbon dioxide production. (C) Heat / Energy expenditure (normalized to body weight). (D-F) Locomotor activity. (G) Body weight. (H) Total food consumption. The studies were conducted in metabolic cages. n=7 WT mice, n=5 *Mmp9*$^{-/-}$ mice. *: $P \leq 0.05$ *vs*. WT.

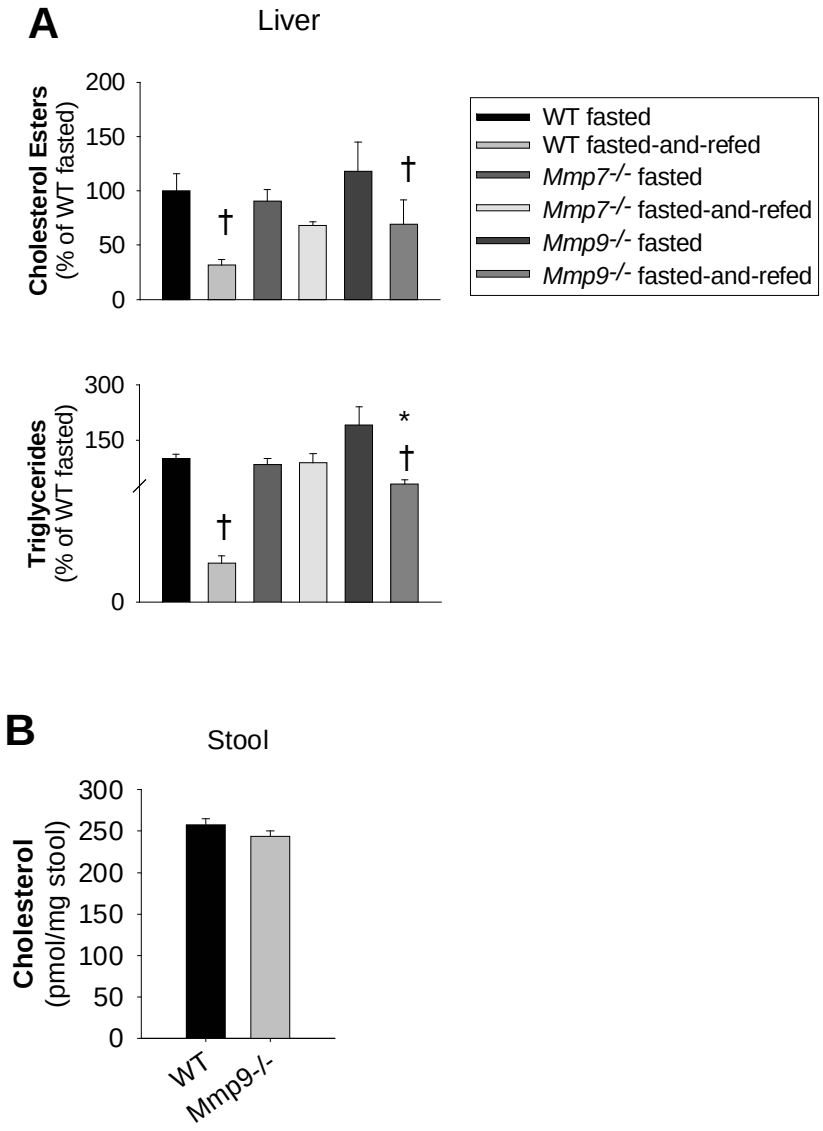

Figure S2. Supplemental quantitative analysis of lipids.
(A) Esterified lipids were elevated in livers from *Mmp9*$^{-/-}$ mice compared to livers from WT mice, particularly when the mice were fasted-and-refed a high carbohydrate diet. In contrast to Mmp9-/- mice, mice lacking MMP-7 (*Mmp7*$^{-/-}$) had a different hepatic lipid profile. *n*=4 mice *per* group, except *n*=3 for *Mmp7*$^{-/-}$ fasted-and-refed. †$P \leq 0.05$ *vs*. fasted for each genotype. *:$P \leq 0.05$ *vs*. WT fasted-and-refed.
(B) Cholesterol excretion was unchanged in *Mmp9*$^{-/-}$ mice. *n*=4 mice *per* genotype.

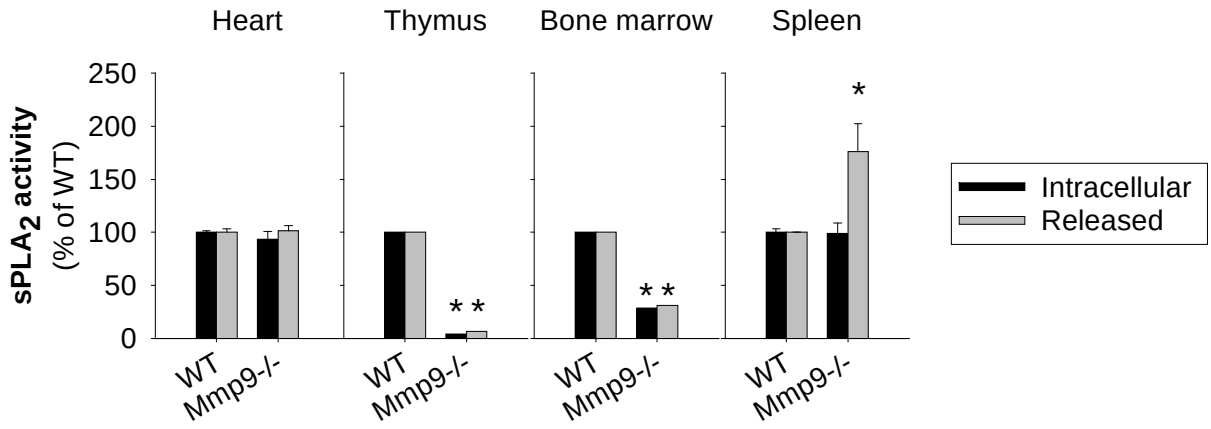

Figure S3. Spleen is a likely source of plasma sPLA$_2$ in MMP-9-deficient mice. sPLA$_2$ activity was analyzed in duplicate using pools of the indicated tissues. *n*=3 WT and *n*=4 *Mmp9*$^{-/-}$ mice. *: *P*<0.05 *vs*. WT.

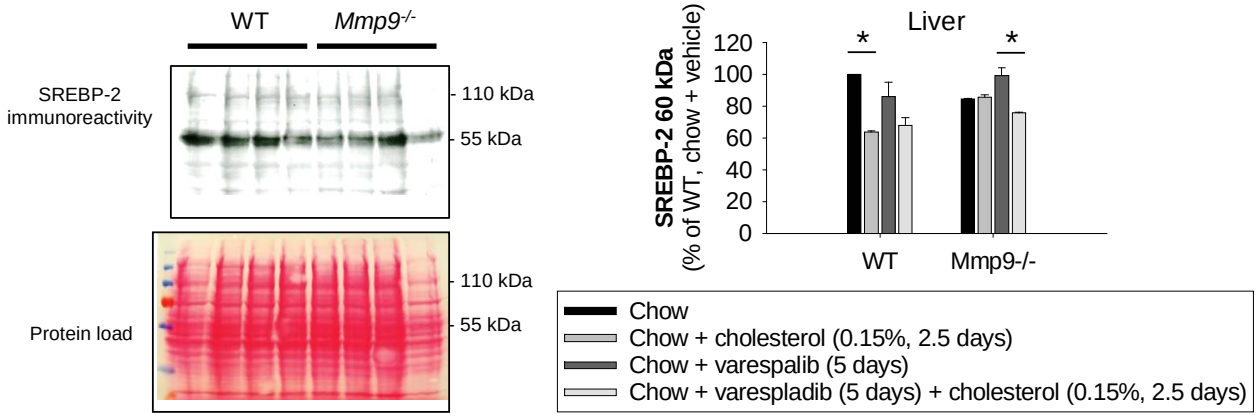

Figure S4. SREBP-2 expression in response to dietary cholesterol and varespladib. ***Left***: Western blot showing amount of hepatic SREBP-2 protein in *Mmp9*$^{-/-}$ mice in response to varespladib and dietary cholesterol supplementation. The experiment involved n=4 to 5 mice *per* group (or treatment). For analysis, livers were pooled, homogenized and the fraction containing nuclei was subjected to western blot analysis with SREBP-2 antibodies. ***Right***: Quantitative analysis for two independent preparations and western blots. *: $P \leq 0.05$ *vs*. untreated.

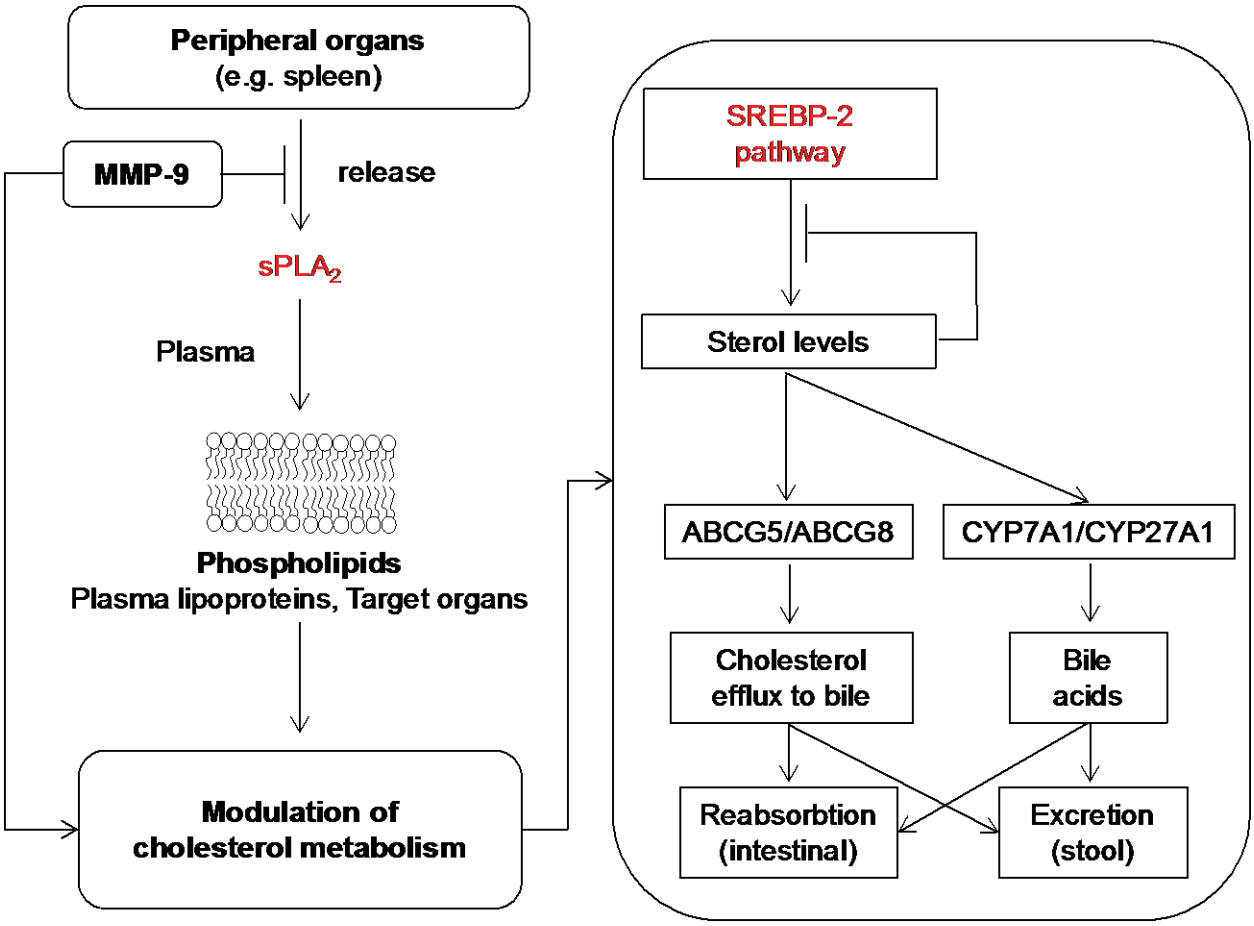

Figure S5. Proposed model. MMP-9 regulates cholesterol metabolism through PLA_2-dependent and PLA_2-independent mechanisms. Important elements are: peripheral organs (e.g., the spleen) acting as source of plasma $sPLA_2$ activity and MMP-9 (inhibitor of $sPLA_2$ release from peripheral organs). Once in the circulation, $sPLA_2$ acts on plasma lipoproteins or target organs (e.g., the liver) to release lipid mediators from phospholipids that ultimately influence cholesterol metabolism. Furthermore, the direct action of MMP-9 in the liver may influence hepatic cholesterol through as yet unclear PLA_2-independent pathways.

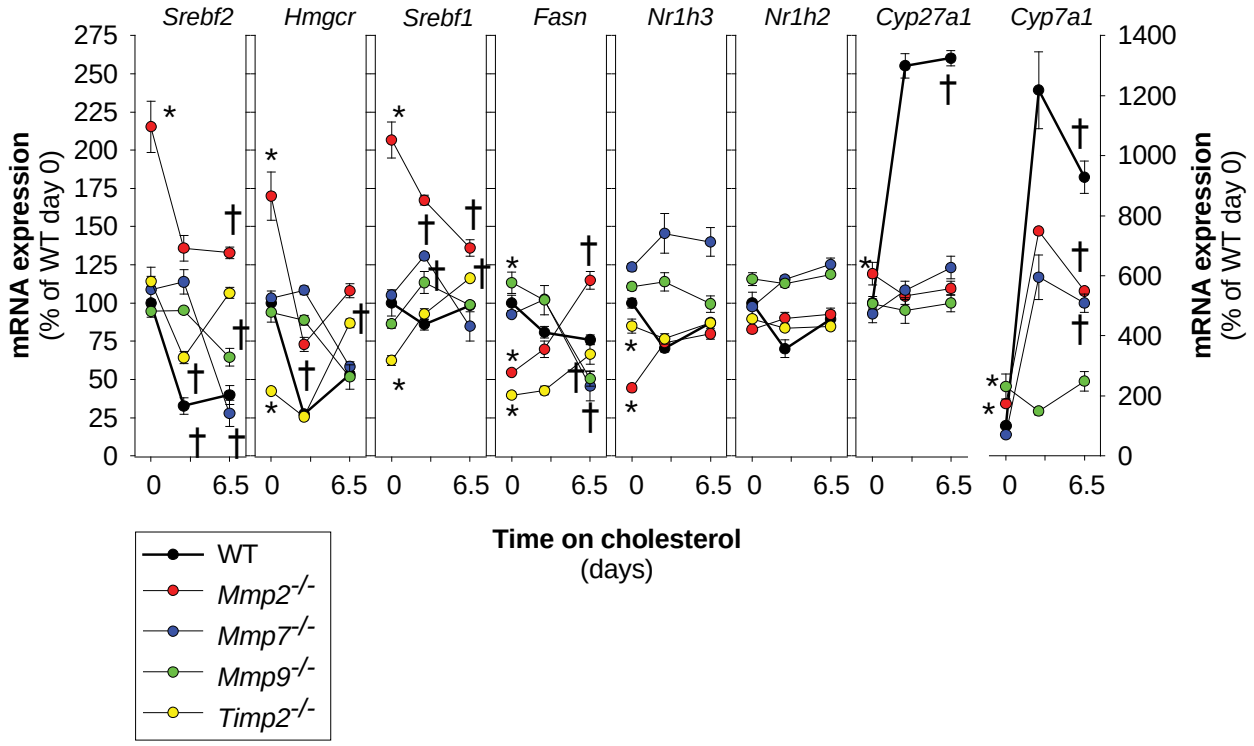

Figure S6. Supplement to Figure 7A containing the quantitative analysis of hepatic transcriptional responses to dietary cholesterol for the indicated genes and genotypes. n=6 WT mice, n=8 *Mmp2*$^{-/-}$ mice, n=5 *Mmp7*$^{-/-}$ mice, n=5 *Mmp9*$^{-/-}$ mice and n=5 *Timp2*$^{-/-}$ mice. *: $P \leq 0.05$ *vs*. WT. †: $P \leq 0.05$ *vs*. 0 days on cholesterol.

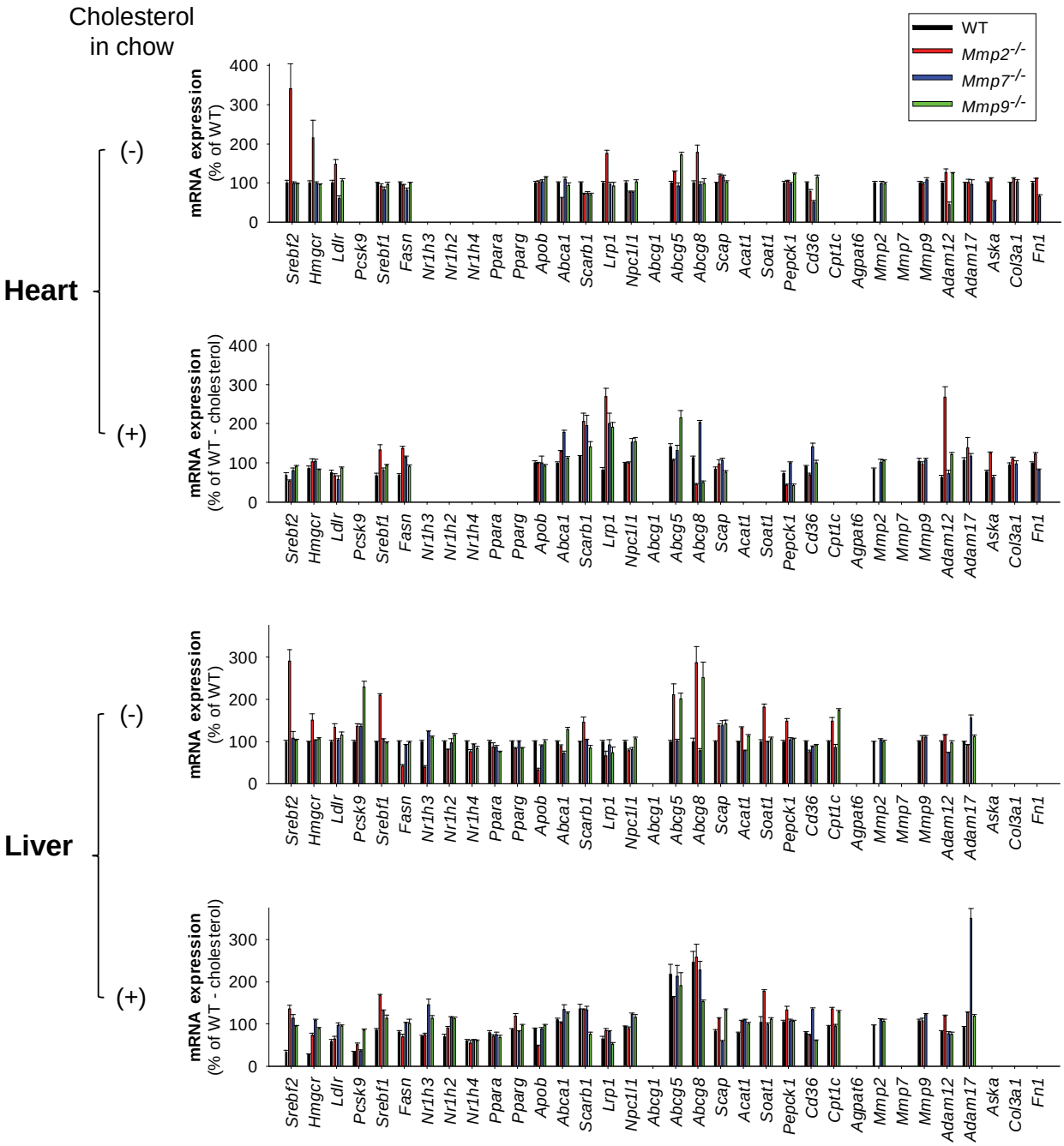

Figure S7. Extended quantitative analysis of the relative mRNA expression of cardiac and hepatic lipid metabolic and metalloproteinase genes and their response to dietary supplementation with 0.15% cholesterol for 2.5 days in mice deficient in one of several MMPs. *n*=6 WT mice, *n*=8 *Mmp2*$^{-/-}$ mice, *n*=5 *Mmp7*$^{-/-}$ mice, *n*=5 *Mmp9*$^{-/-}$ mice. Slots without bars: Gene expression was not determined.