# Supplemental material

MMP-2 negatively regulates cardiac secreted phospholipase A$_2$ to modulate inflammation and fever

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Liver
Inflammation
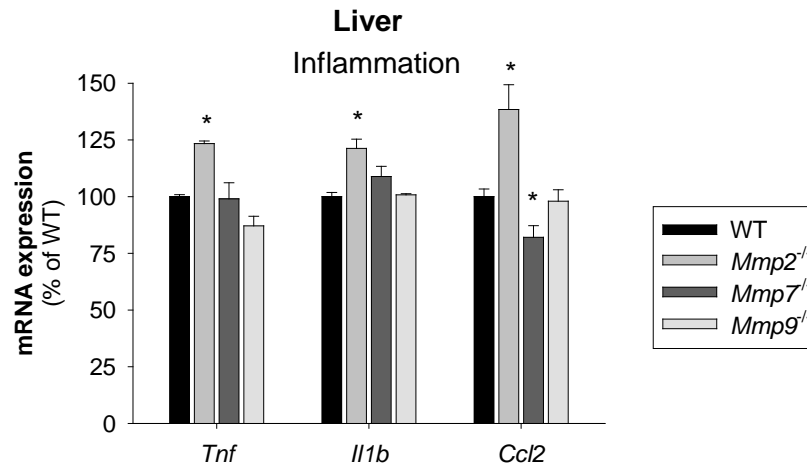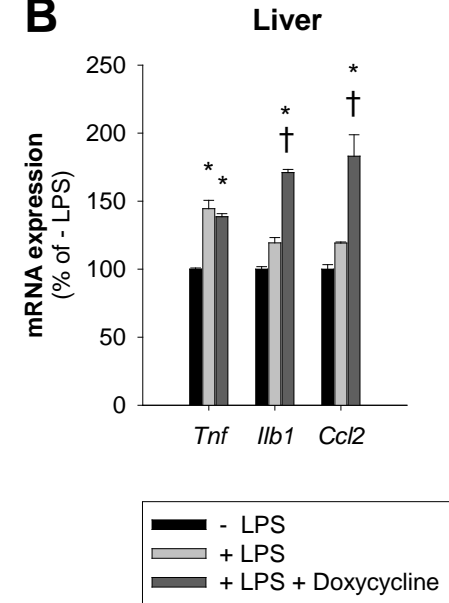
Supplemental Figure S1
qRT-PCR analysis of selected inflammatory marker genes in the livers of WT, *Mmp2*$^{-/-}$, *Mmp7*$^{-/-}$ and *Mmp9*$^{-/-}$ mice. *n*=3 for each genotype. Results are means ± sem. *:*P*≤0.05 *vs.* WT (control). All pairwise multiple comparisons *vs.* control group (Holm-Sidak method).
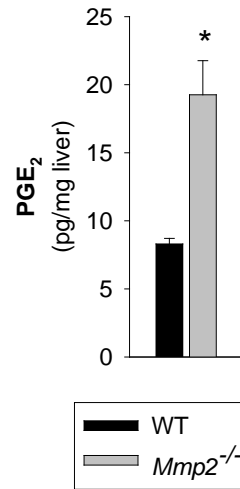
Supplemental Figure S2
Hepatic PGE$_2$ levels in mice 5 hours after intraperitoneal LPS (30 µg/kg) administration. Pools of n=3 were measured in duplicate. Results are means ± sem. *:P≤0.05 *vs.* WT. *t*-test.

A

LPS
(30 µg/kg)

Study group	Baseline Temperature (C)
- Doxycycline	37.23 ± 0.12
+ Doxycycline	37.23 ± 0.12

B Liver
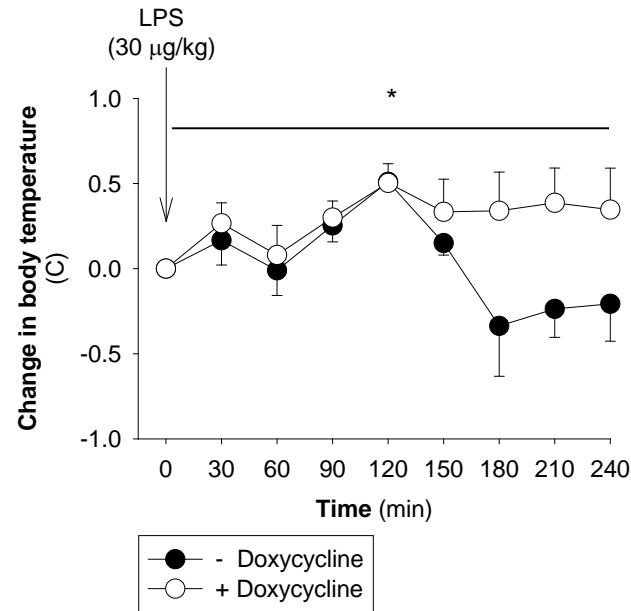
Supplemental Figure S3

LPS-induced fever response in mice administered the MMP inhibitor, doxycycline. This experiment was conducted in parallel with that indicated in Figure 8A. *n*=3. Doxycycline-treated mice received doxycycline (50 mg/kg/day) orally for two days, with the second dose immediately preceding injection of LPS.

(A) Body temperature was measured rectally before and after intraperitoneal injection of LPS. *:*P*≤0.05 *vs.* - Doxycycline. One way repeated measures ANOVA.
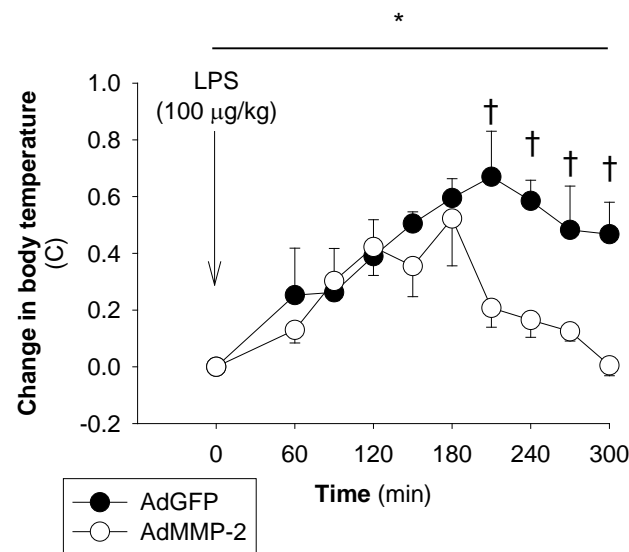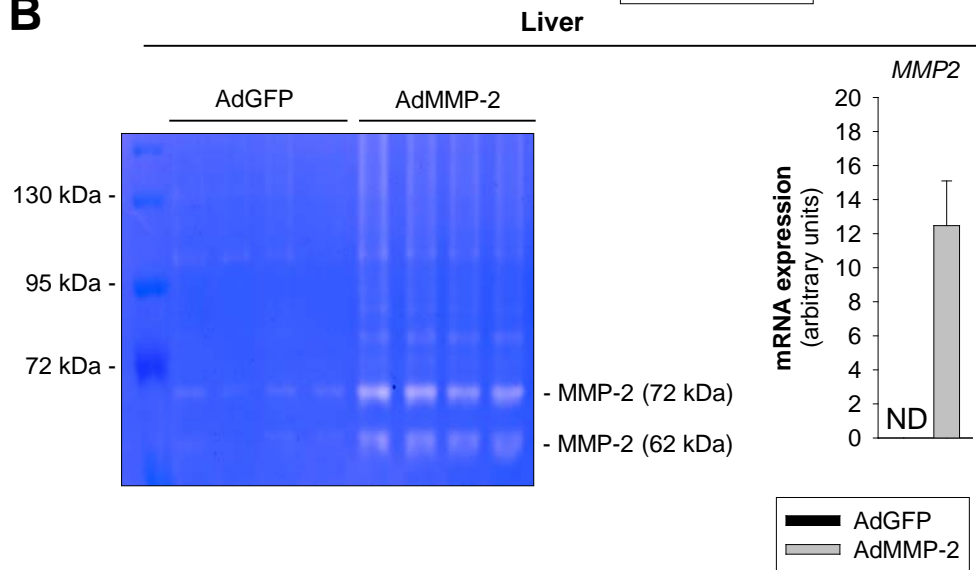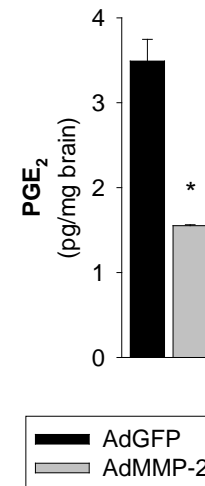
(B) Augmentation of selected hepatic inflammatory marker genes by doxycycline in mice administered LPS. qRT-PCR analysis of livers 5 hours after LPS (30 µg/kg) administration. *:*P*≤0.05 *vs.* – LPS. † *P*≤0.05 *vs.*+ LPS. All pairwise multiple comparisons *vs.* control group (Holm-Sidak method).

A

Study group	Baseline Temperature (C)
AdGFP	37.33 ± 0.05
AdMMP-2	37.53 ± 0.04

B

C

Supplemental Figure S4 (A) LPS-induced fever response of mice that overexpress MMP-2. WT mice received an intraperitoneal injection of AdMMP-2 or AdGFP (~10^8 pfu). Three days later the mice received an intraperitoneal injection of LPS (100 µg/kg). Body temperature was measured rectally before and after LPS. n=4. *:$P \leq 0.05$ vs. AdGFP. Friedman Repeated Measures Analysis of Variance on Ranks. †: $P \leq 0.05$ vs. AdGFP at indicated times. All pairwise multiple comparison procedures (Fisher LSD Method). (B) Confirmation of MMP-2 overexpression. MMP-2 expression in AdMMP-2 vs. AdGFP infected mice 5 hours after LPS (100 µg/kg) administration. Left: Gelatin zymography. Right: qRT-PCR. ND: not detected. n=4. (C) Hypothalamic PGE2 levels 5 hours after LPS (100 µg/kg). Pools of n=4 were measured in duplicate. *:$P \leq 0.05$ vs. AdGFP. *t*-test.