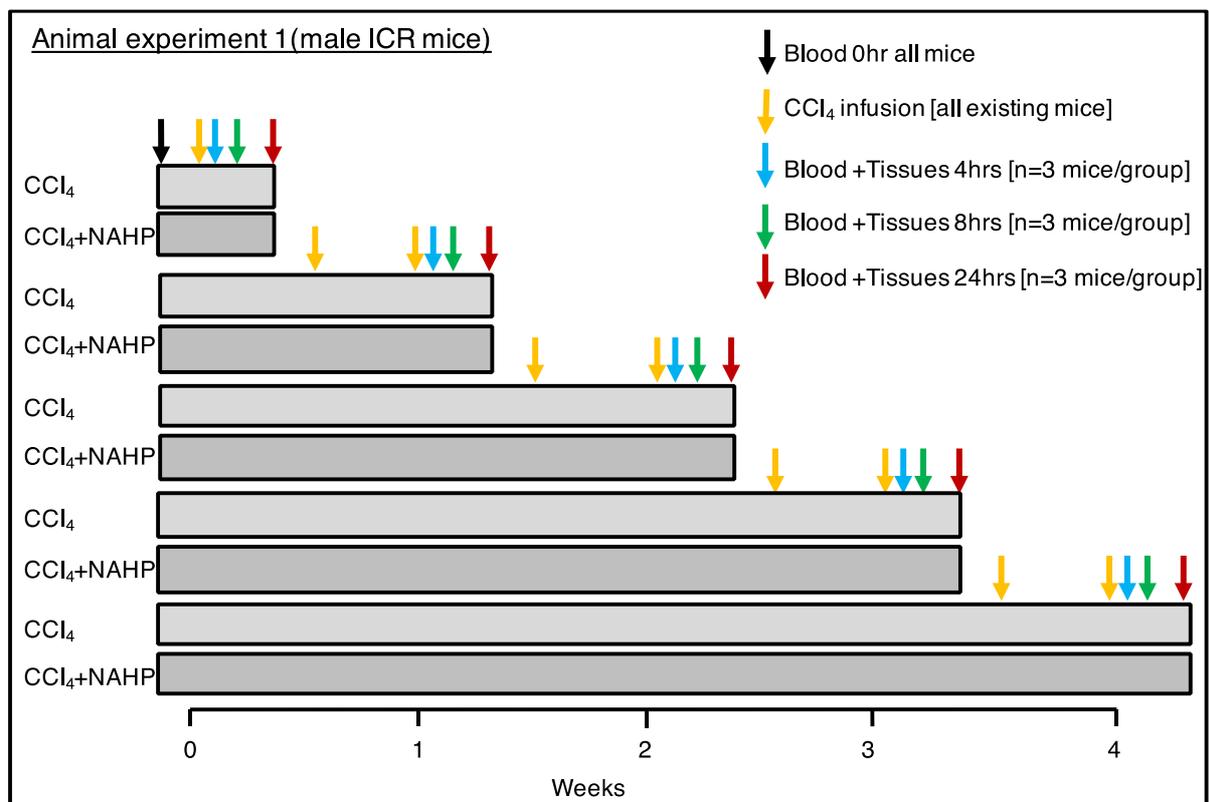


Supplementary data

**Extracellular histones stimulate collagen expression in vitro and promote liver fibrogenesis in mouse model via TLR4-MyD88 signalling pathway**

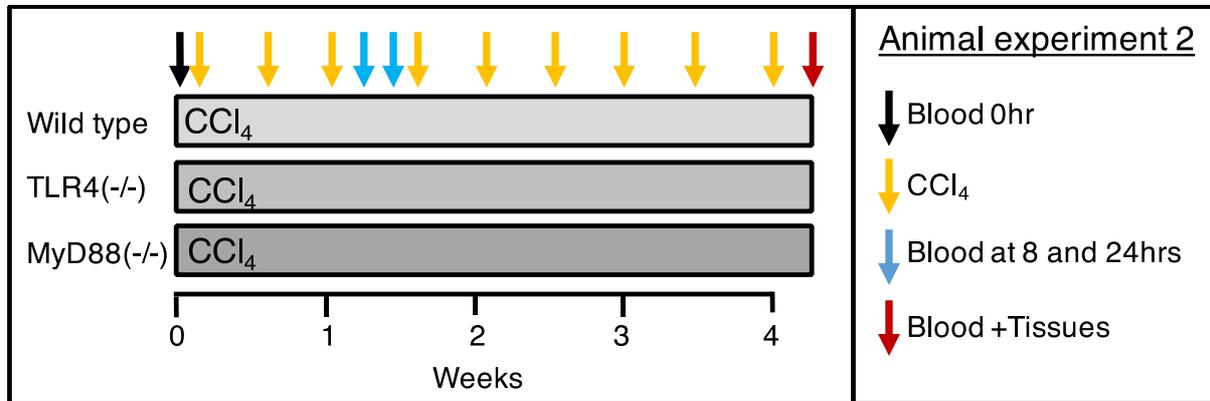
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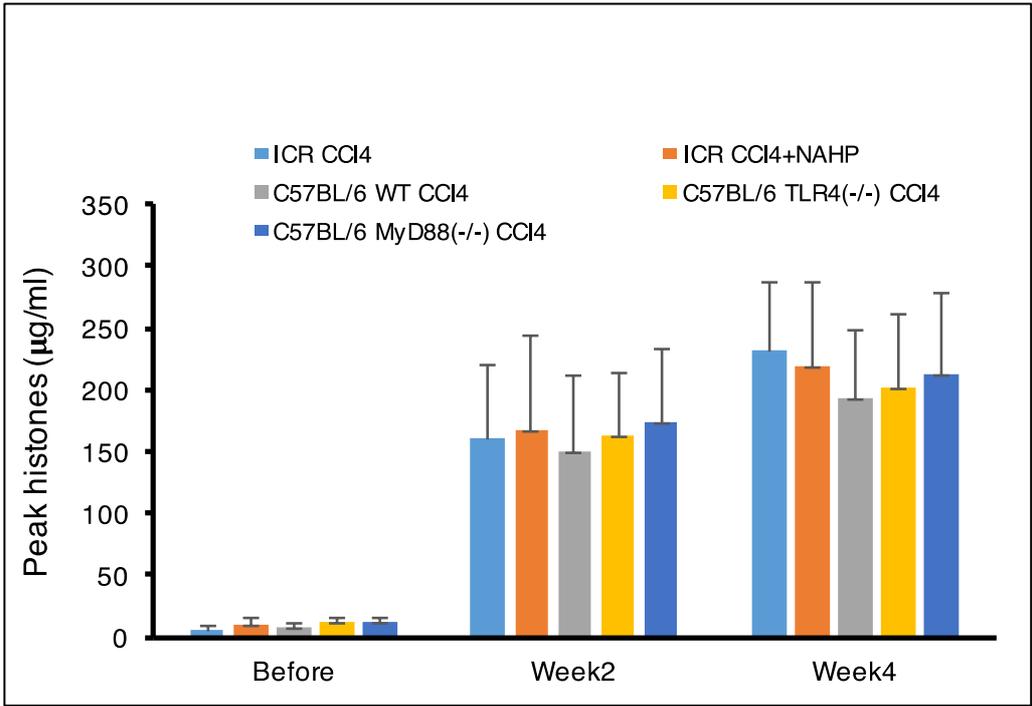


**Supplemental Figure S1. Diagrams of animal experiment 1.** ICR mice were used, 3 mice per group per time point. Blood samples were taken from each mouse before the experiments (black arrow). CCl<sub>4</sub>, 5  $\mu$ l/g of 25% (w/v) in olive, was injected intraperitoneally (i.p) 2 doses per week with interval of 84 hours (yellow arrow). NAHP: on the day of CCl<sub>4</sub> injection, 8  $\mu$ l/g (4 $\mu$ g/ml in saline, filtered for sterility) were injected subcutaneously (s.c) every 8h. On the remaining days, 8  $\mu$ l/g NAHP were injected s.c every 12hrs. Each group had 3 mice euthanized

at each time point: 4h (blue arrow), 8h (green arrow), and 24h (red arrow) after first CCl<sub>4</sub> dose of each week and both blood and tissues were collected.



**Supplemental Figure S2. Diagram of experiment 2.** C57BL/6 mice, wild type, TLR4 knockout and MyD88 knockout mice, 8 per group, were used. CCl<sub>4</sub> was injected intraperitoneally (i.p) 2 doses per week with interval of 84 hours (yellow arrow). Blood were taken before experiments as indicated by a black arrow and from 4 mice each group at 8h and 4 mice at 24h after first dose of CCl<sub>4</sub> of second week as indicated by blue arrows. By the end of 4 weeks, all mice were euthanized with blood and organs collected as indicated by a red arrow.



**Supplemental Figure S3. Comparable peak levels of circulating histones after CCl4**

**treatment.** Means±SD of histone levels in blood samples taken before experiment(Before),

8h and 24h after first dose of CCl4 in week 2 (Week2) and 24hrs after the last dose in week 4

(Week4) are presented.