

Figure S1

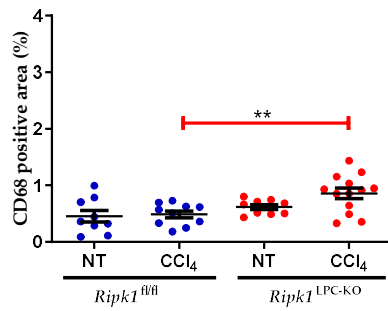


Figure S1: Macrophage infiltration analysis in non-treated and CCl₄-treated *Ripk1^{fl/fl}* and *Ripk1^{LPC-KO}* mice. *Ripk1^{fl/fl}* and *Ripk1^{LPC-KO}* mice were force-fed either with olive oil alone (control; NT for non-treated) or containing CCl₄ (dose of 2.4 g/kg body weight), 24 h before sample collection. Signal quantification of anti-CD68 positive area. For the graph, each dot represents an individual and errors bars are expressed as means ± SEM (** p < 0.01).

Figure S2

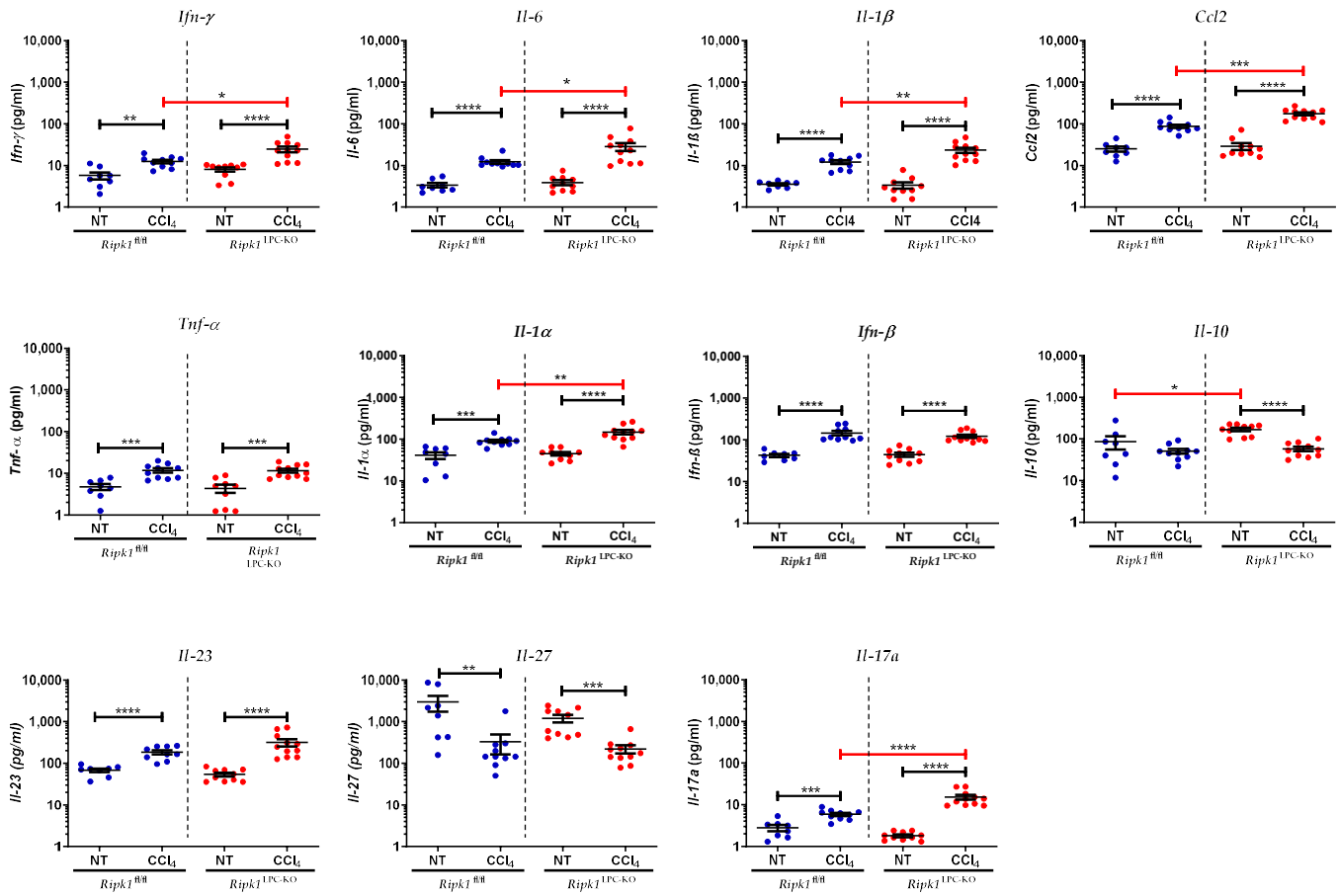
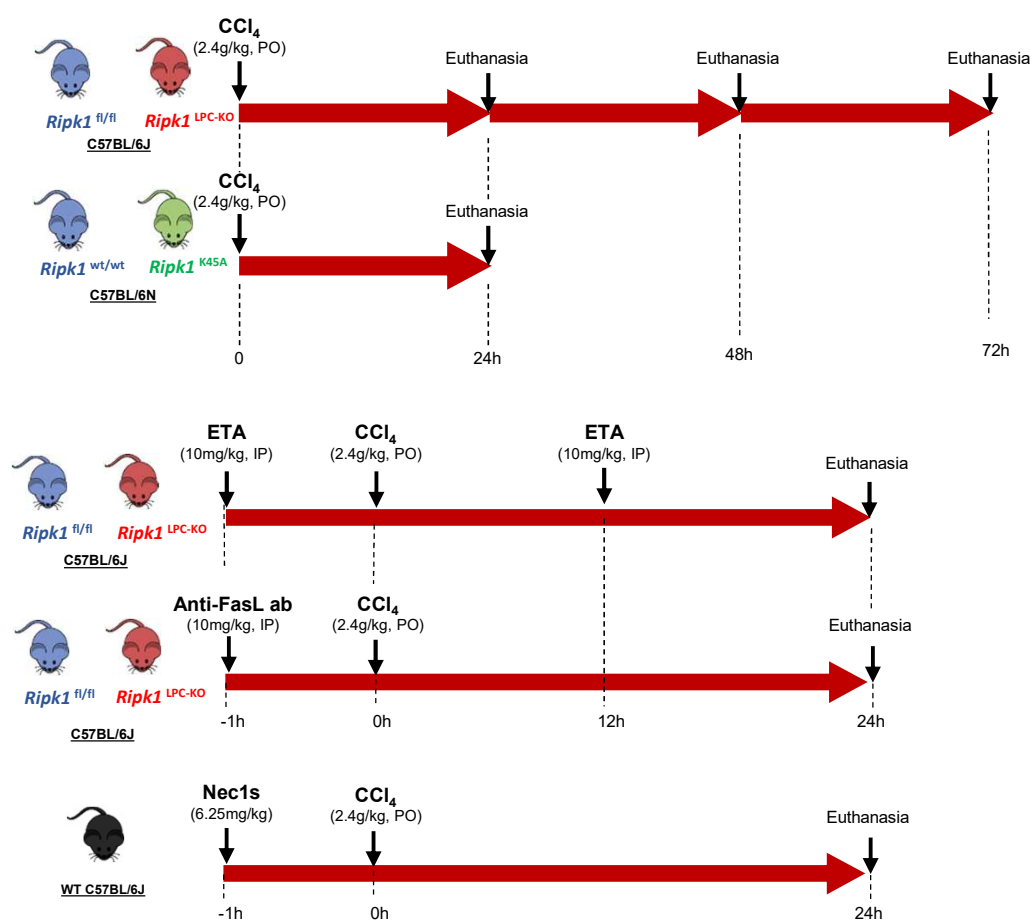


Figure S2: Serum levels of cytokines in non-treated and CCl₄-treated *Ripk1^{fl/fl}* and *Ripk1^{LPC-KO}* mice. *Ripk1^{fl/fl}* and *Ripk1^{LPC-KO}* mice were force-fed either with olive oil alone (control; NT for non-treated) or containing CCl₄ (dose of 2.4 g/kg body weight), 24 h before serum collection. Murine cytokines were captured by a bead-based immunoassay (BioLegend's LEGENDplex™ Mouse Inflammation Panel, multi-analyte flow assay kit) and quantified on a LSR X-20 Fortessa™ flow cytometer (BD Biosciences). For all graphs, each dot represents an individual and errors bars are expressed as means ± SEM (* p < 0.05; ** p < 0.01; *** p < 0.001 and **** p < 0.0001).

Figure S3



LPC : Liver parenchymal cells

K45A : Kinase Dead (KD)

Figure S3: Experimental design. *Ripk1*^{LPC-KO} (red; LPC-KO, Liver Parenchymal Cell – Knock Out) and *Ripk1*^{K45A} (green; Kinase Dead, KD) C57BL/6 mice along with their respective WT littermates (blue; *Ripk1*^{fl/fl} [fl, floxed] and *Ripk1*^{wt/wt} [wt, wild-type]) were force-fed with olive oil alone (non-treated, NT) or containing CCl₄ with a final administered dose of 2.4g/kg (PO, Per Os). When used, etanercept (ETA) or anti-FasL antibody (ab) or vehicle (PBS) were intraperitoneally (IP) injected at 10 mg/kg, 1 hour before CCl₄ treatment, and 12 hour later for a second dose of ETA. In another experiment, Nec-1s or vehicle (PBS-DMSO 6%) was intravenously injected at 6.25 mg/kg 1 hour before CCl₄ treatment. Analysis were conducted 12, 24, 48 or 72 hours post CCl₄ administration as shown in the diagram.

Figure S4

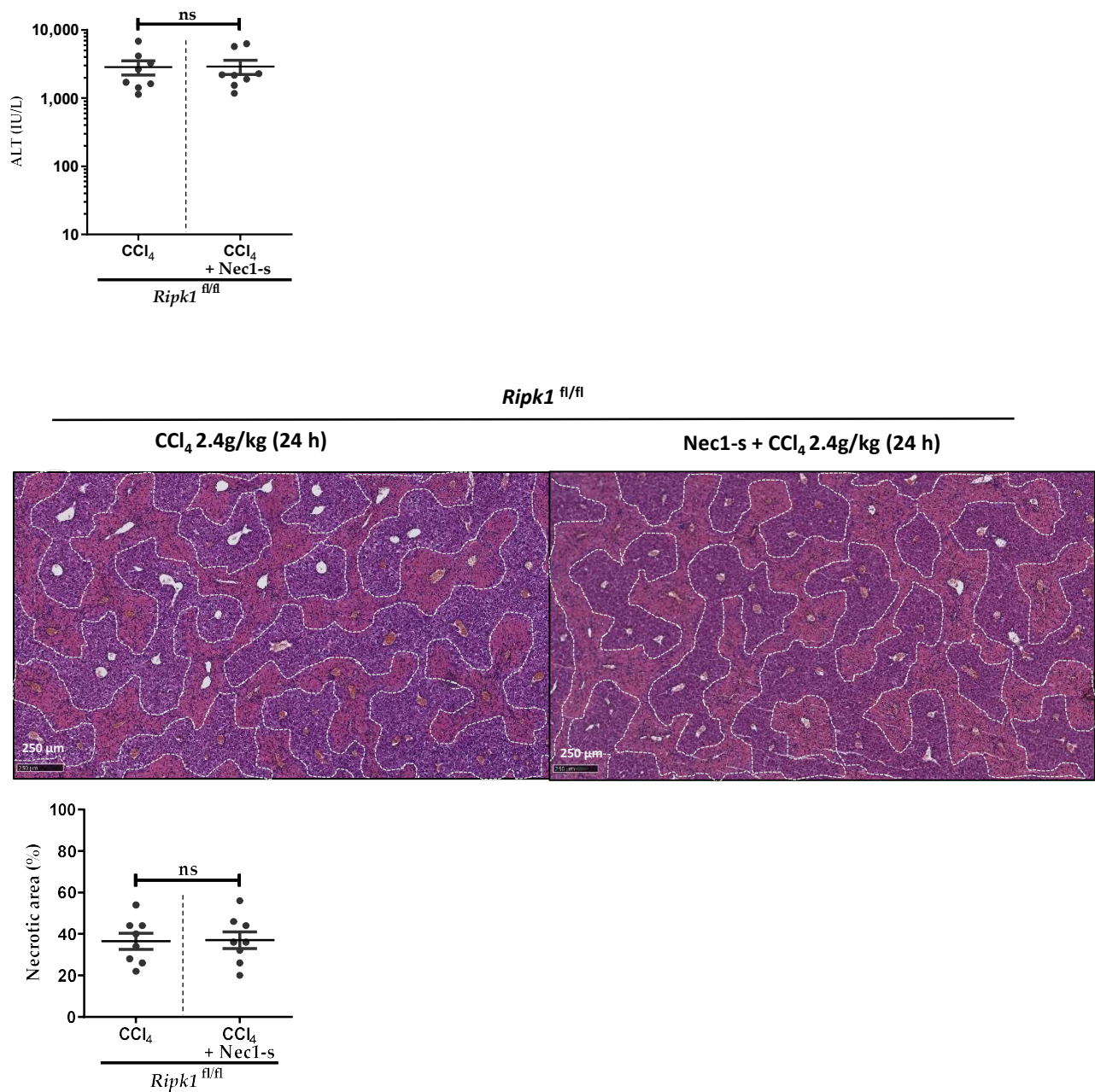


Figure S4: No contribution of RIPK1 kinase activity during CCl₄-induced hepatotoxicity. C57BL/6J *Ripk1*^{fl/fl} mice were forced with olive oil containing CCl₄ (dose of 2.4 g/kg body weight), 24 hours before sample collection. Levels of serum alanine aminotransferase (ALT). Representative pictures of liver tissue sections stained by H&E with necrotic area quantifications. For all graphs, each dot represents an individual and errors bars are expressed as means ± SEM (ns, non-significant).

Table S1

Mouse Gene	Forward	Reverse
18S	5'-CGCCGCTAGAGGTGAAATTC-3'	5'-TTGGCAAATGCTTTCGCTC-3'
<i>Hmox-1</i>	5'-AGGTACACATCCAAGCCGAGA-3'	5'-CATCACCAGCTTAAAGCCTTCT-3'
<i>Nfe2l2</i> (Nrf-2)	5'-TAGATGACCATGAGTCGCTTGC-3'	5'-GCCAAACTTGCTCCATGTCC-3'
<i>Cybb</i> (Nox-2)	5'-AGTGCGTGTGCTCGACAA-3'	5'-GCGGTGTGCAGTGCTATCAT-3'
<i>Nqo1</i>	5'-AGGATGGGAGGTACTCGAATC-3'	5'-AGGCGTCCTTCCTTATATGCTA-3'
<i>Il-6</i>	5'-CGATGATGCACTTGCAGA-3'	5'-CTCTGAAGGACTCTGGCTTTG-3'
<i>Ifn-γ</i>	5'-AAGACAATCAGGCCATCAGC-3'	5'-CAGCAGCGACTCCTTTTCC-3'
<i>Il-1b</i>	5'-GCCACCTTTTGACAGTGATGAG-3'	5'-GACAGCCCAGGTCAAAGGTT-3'
<i>Ccl2</i>	5'-TCCCAATGAGTAGGCTGGAG-3'	5'-TCTGGACCCATTCTTCTTG-3'
<i>Rela</i> (NFKBp65)	5'-GACCCCTGTCCTCTCACATCCG-3'	5'-CAGCTCCCAGAGTCCGGTT-3'
<i>Nfkbia</i> (IκBα)	5'-TGAAGGACGAGGAGTACGAGC-3'	5'-TTCGTGGATGATTGCCAAGTG-3'
<i>Tnfaip3</i> (A20)	5'-TGCCCAGTCTGTAGTCTTCG-3'	5'-AGTTGTTCAAGCATGGTCCT-3'
<i>Cflar</i> (cFLIP)	5'-GAGGCCAGCTCTCTTTTGCT-3'	5'-TCCACGGTTGCTTTGTCTGT-3'
<i>Ikkb-γ</i> (Nemo)	5'-GGTGGAGAGACTGAGCTTGG-3'	5'-CCTCTAAAGCTTGCCGATCC-3'
<i>Saa1</i>	5'-TGTTACGAGGCTTTCCAAG-3'	5'-GTCCTCTGCCGAAGAATTCC-3'
<i>Cxcl1</i>	5'-CGCCTATCGCCAATGAGC-3'	5'-GAACCAAGGGAGCTTCAGG-3'
<i>Ccl20</i>	5'-TCTGCTCTTCCTTGCTTTGG-3'	5'-TCACCCAGTTCTGCTTTG-3'
<i>Tnf-α</i>	5'-TAGCTCCCAGAAAAGCAAGC-3'	5'-TTTTCTGGAGGGAGATGTGG-3'
<i>Tnfrsf1a</i> (TNFR1)	5'-ATCGAGAGGCTGGAGATGC-3'	5'-GGCGGGATTCTCAGAGC-3'
<i>Tnfrsf1b</i> (TNFR2)	5'-CGCTGGTCTTCGAACTGC-3'	5'-CAGGAGGACACTTAGCACAGC-3'
<i>Fas</i>	5'-CTCCGAGTTTAAAGCTGAGG-3'	5'-TGTAATCCTTCCCTTCTGTGC-3'
<i>FasL</i>	5'-GCAGCAGCCCATGAATTACC-3'	5'-GGTAATTCATGGGCTGCTGC-3'
<i>Tnfsf10</i> (TRAIL)	5'-TGAGAACCTTTCAGGACACC-3'	5'-GGCCTAAGGTCTTCCATCC-3'
<i>Tnfrsf10b</i> (TRAIL-R2)	5'-CCGGGCAGATCACTACACC-3'	5'-AGACAGGGTCCTCTTGATGG-3'

Table S1: Primer sequences