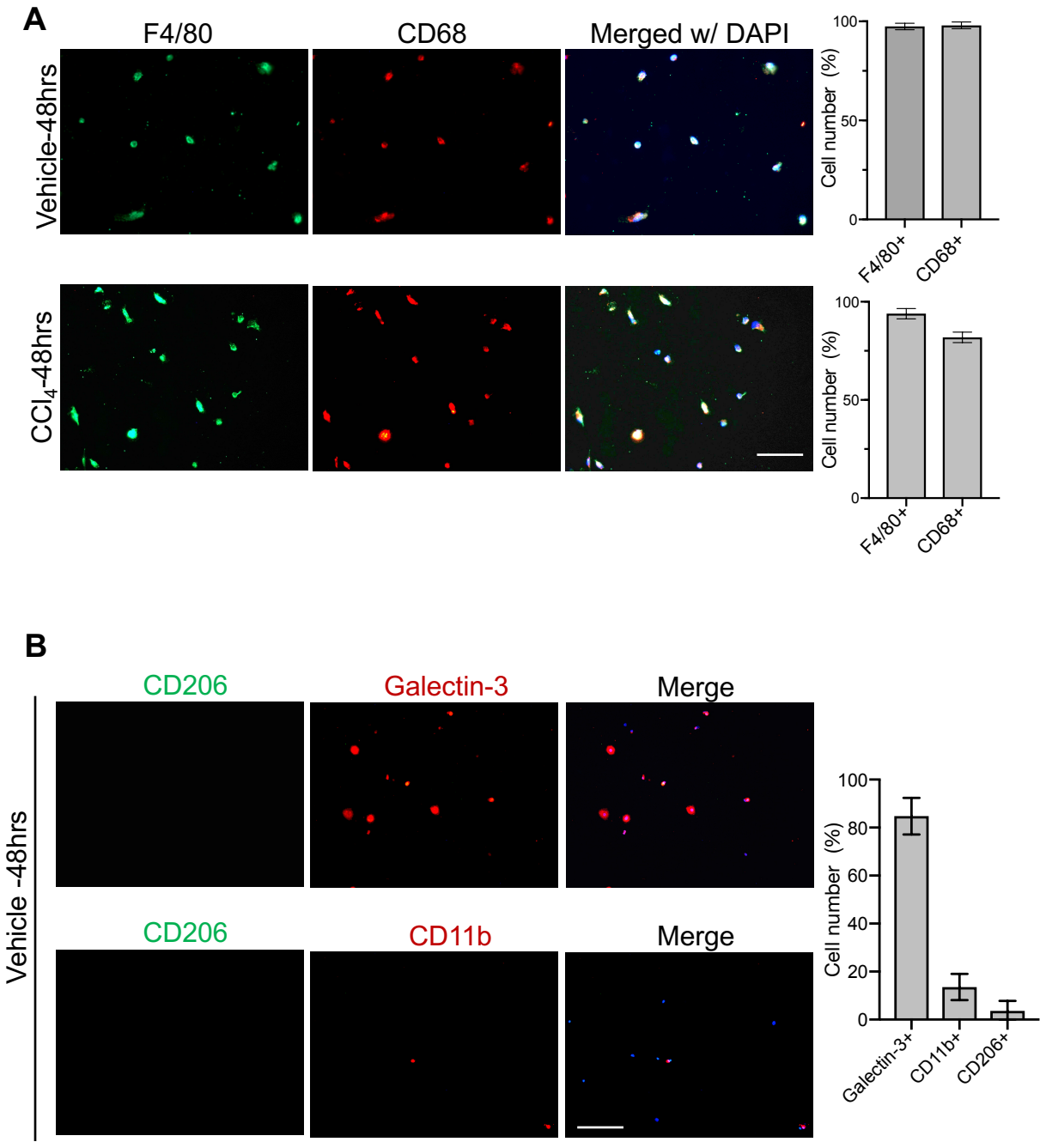


**Figure S1.** (A) *Ccn1*$^{WT/WT}$ liver macrophages isolated 48 hrs after injection of vehicle or $CCl_4$ were cultured overnight and stained with anti-CD68 and anti-F4/80 antibodies and counterstained with DAPI. (B) *Ccn1*$^{WT/WT}$ liver macrophages isolated 48 hrs after injection of vehicle were co-stained with anti-CD206 antibody and anti-Galectin-3 antibody or anti-CD206 antibody and anti-CD11b antibody. The percentages of positive cells were quantified (*n=4*). Data represents means ± SD. Scale bars: 100 μm.

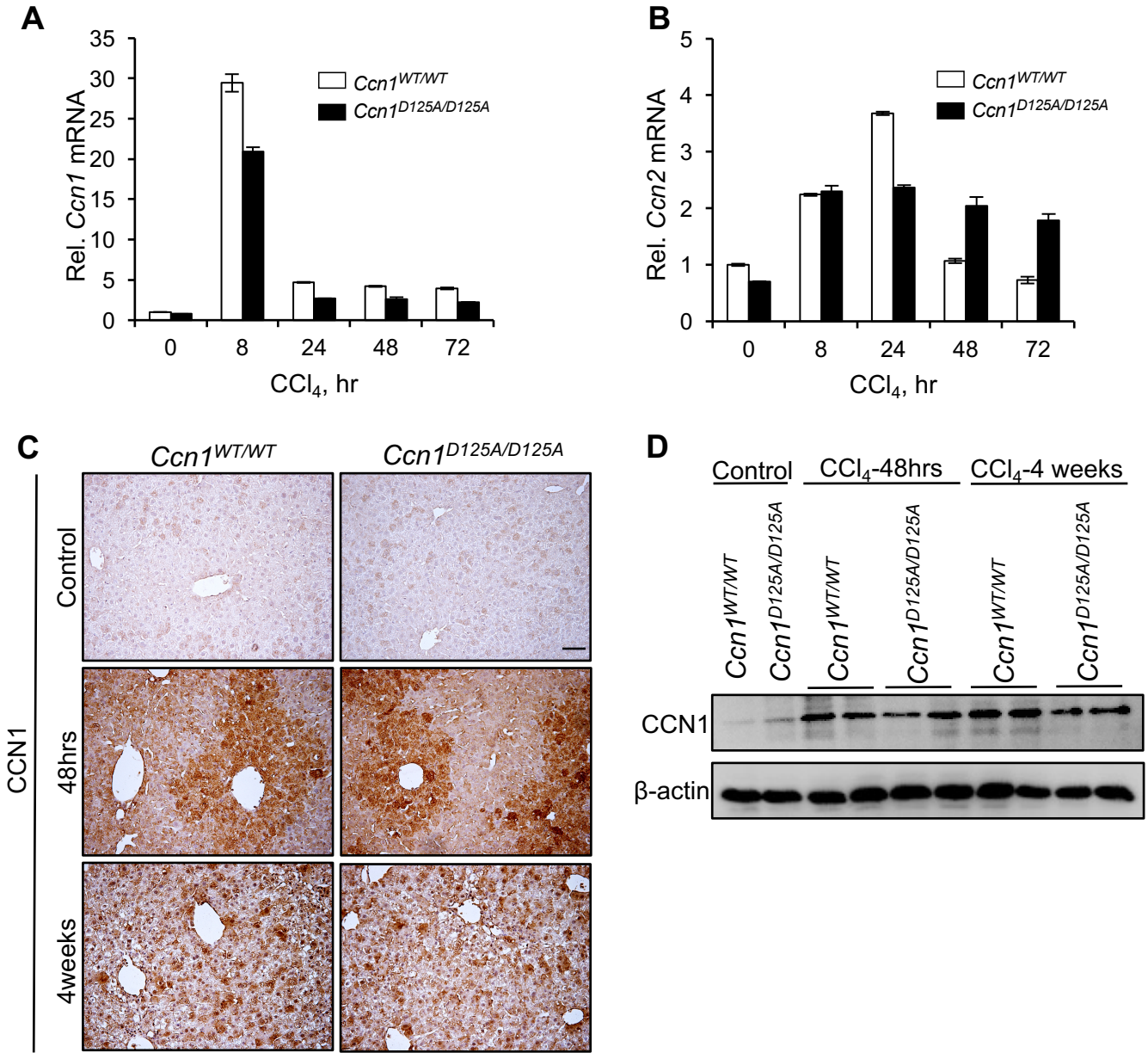


**Figure S2.** *Ccn1*$^{WT/WT}$ and *Ccn1*$^{D125A/D125A}$ mice were i.p. injected with $CCl_4$, and *Ccn1* (A) or *Ccn2* (B) expression was analyzed by qRT-PCR in liver RNA isolated at the indicated times ($n$=6). (C) Liver sections from *Ccn1*$^{WT/WT}$ and *Ccn1*$^{D125A/D125A}$ mice after injection with $CCl_4$ for indicated times were stained with anti-CCN1 antibody. (D) Immunoblots of protein extracts from the indicated livers were probed with antibodies against CCN1 and β-actin. Scale bars: 100 μm.

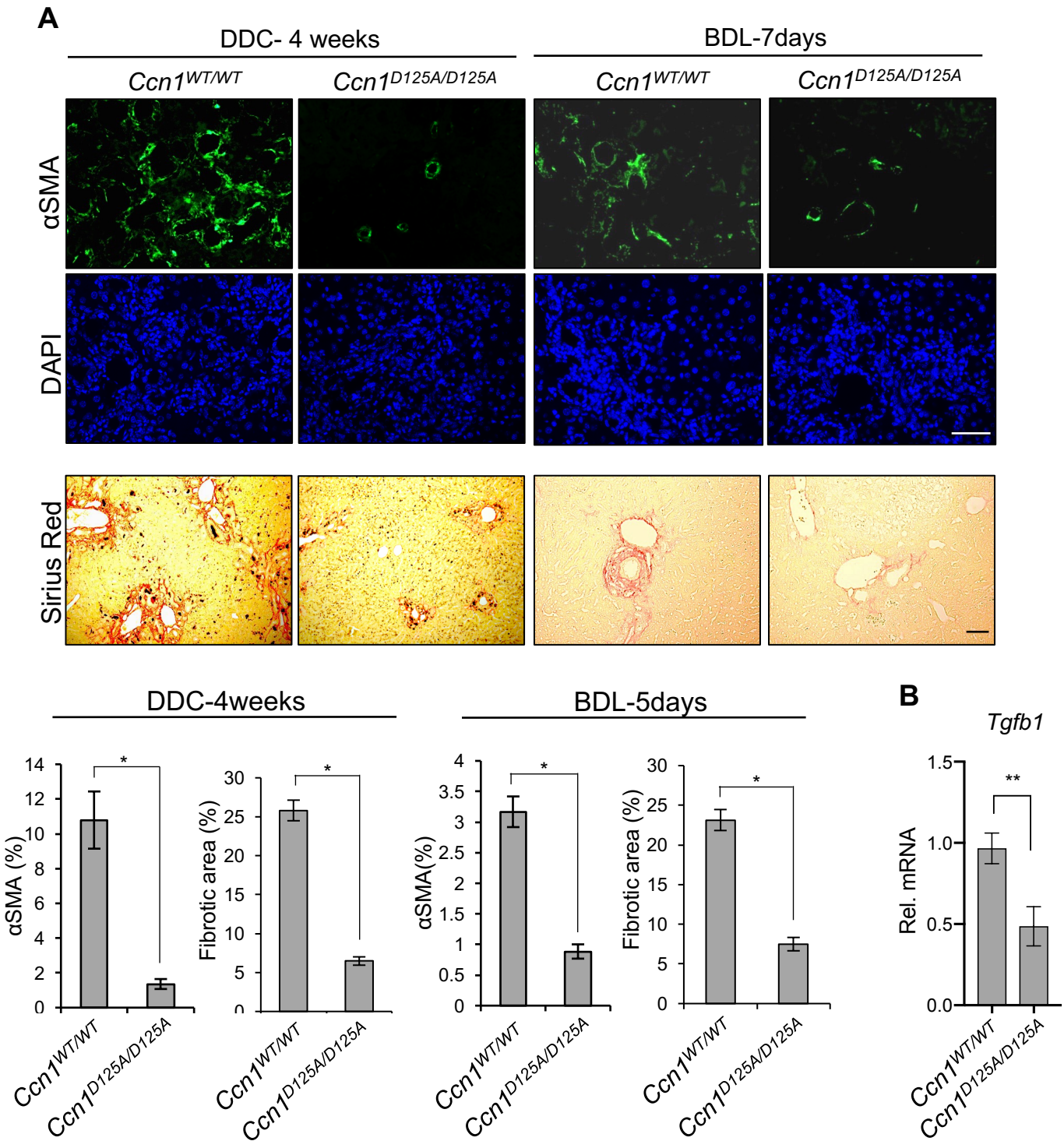


**Figure S3.** (A) Liver sections from *Ccn1*$^{WT/WT}$ and *Ccn1*$^{D125A/D125A}$ mice fed DDC diet for 4 weeks or subjected to BDL 7 days were immunostained for α-smooth muscle actin (αSMA, green) and counterstained with DAPI (*n*=6) or stained with Sirius Red to reveal collagen deposition. The fibrotic areas were measured by Image J. The percentages of fibrotic areas were assessed by Image J analysis of microphotographs of six randomly selected fields. (B) Expression of *Tgfb1* in *Ccn1*$^{WT/WT}$ and *Ccn1*$^{D125A/D125A}$ mice livers which were subjected to BDL for 7 days was assessed by qRT-PCR (*n=4*). . Data represent means ± SD. **P*<0.033, ***P*<0.002. Scale bars: 100 μm.

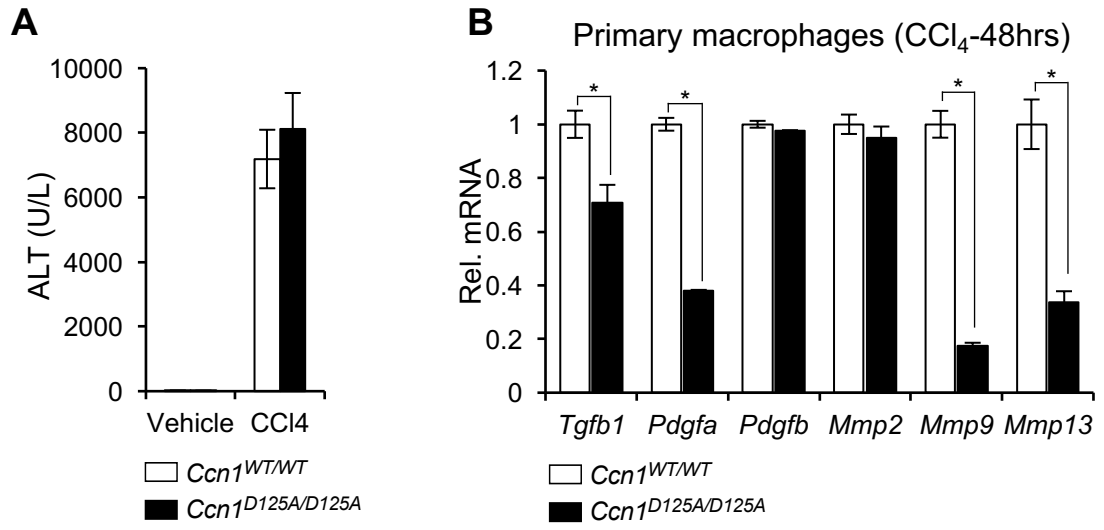


**Figure S4.** (A) Serum ALT levels were measured 48 hrs after $CCl_4$ injection (*n*=6). (B) Macrophages were isolated from injured livers and expression of indicated genes was assessed by qRT-PCR (*n=6*). . Data represents means ± SD.**P*<0.033.

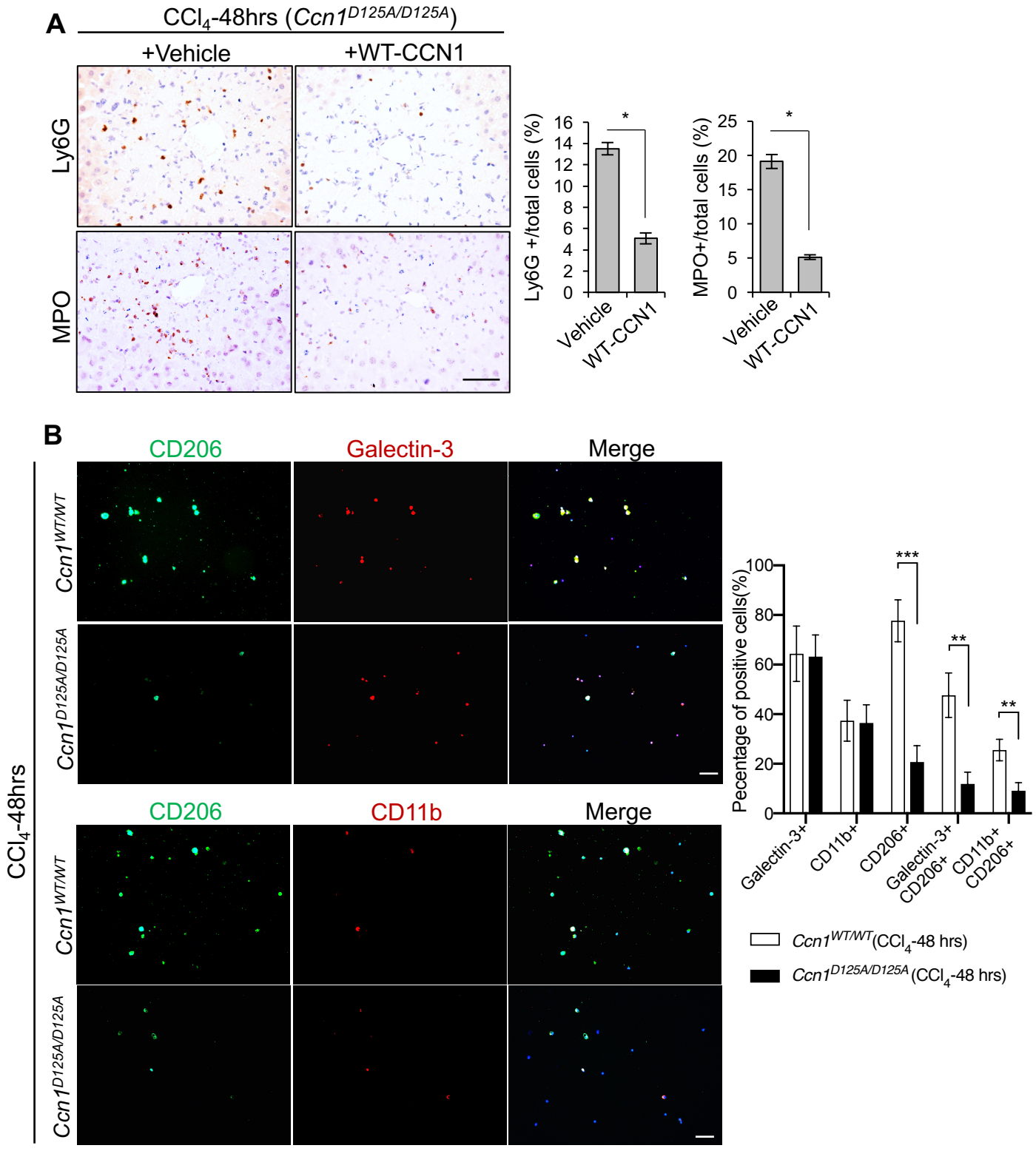


**Figure S5.** (A) *Ccn1*$^{D125A/D125A}$ mice were injected with $CCl_4$, followed by *i.p.* injections of either vehicle or CCN1 protein (1 mg/kg) at 4, 24, and 40 hrs thereafter. Livers were collected at 48 hrs after $CCl_4$ injection, and liver sections were stained with anti-Ly6G or anti-MPO antibody as indicated and counterstained with hematoxylin (blue). (B) *Ccn1*$^{WT/WT}$ and *Ccn1*$^{D125A/D125A}$ hepatic macrophages isolated 48 hrs after injection of $CCl_4$ were co-stained with CD206 and Galectin-3 or CD206 and CD11b. The percentages of positive cells were quantified (*n=4*). **P*<0.033, ***P*<0.002, ****P*<0.001. Data represents means ± SD. Scale bars: 100 μm.

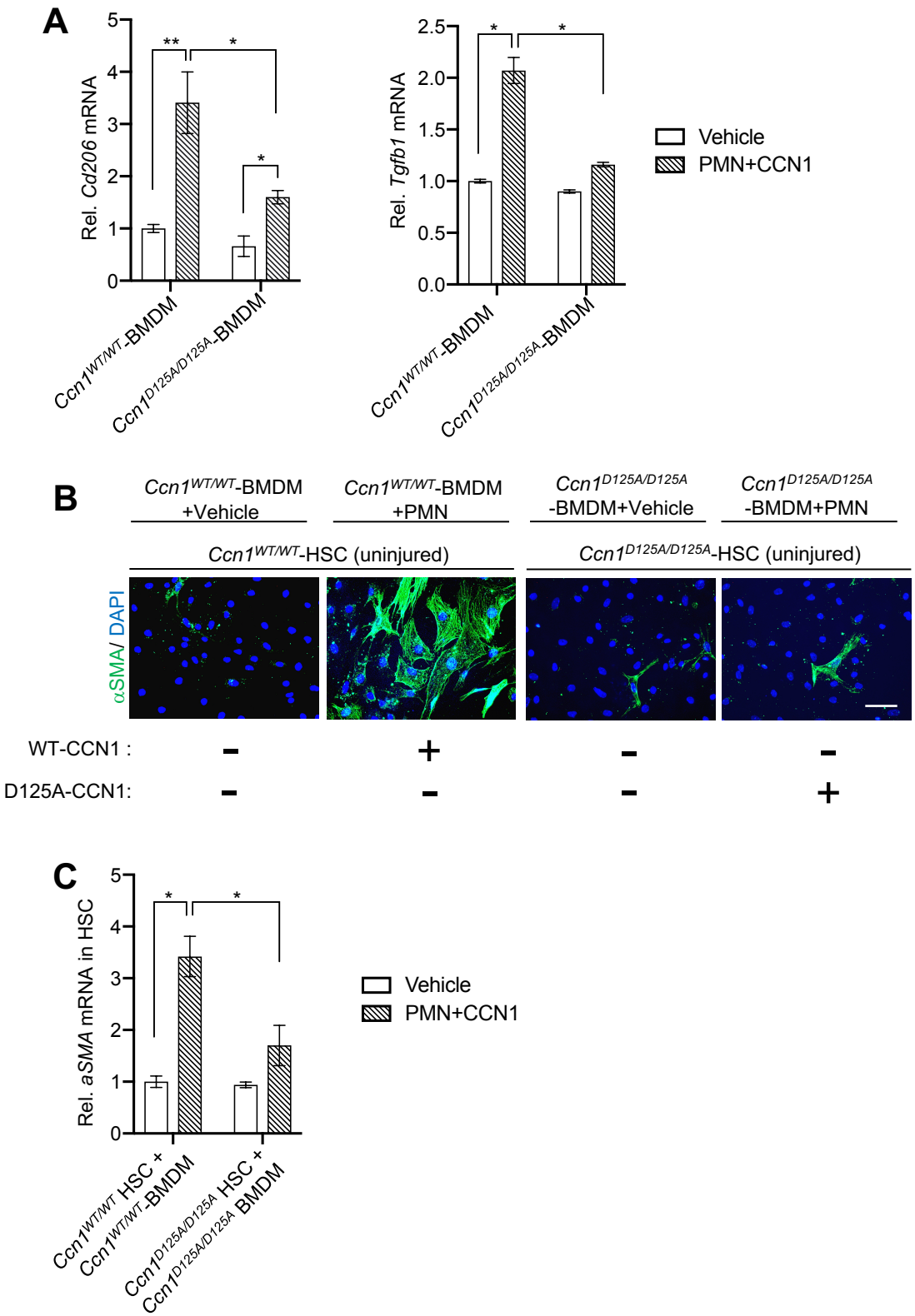


**Figure S6.** Bone marrow derived macrophages (BMMs) from *Ccn1*$^{WT/WT}$ and *Ccn1*$^{D125A/D125A}$ mice were incubated for 4 hrs with their own apoptotic neutrophils, which were pre-treated with their own type of CCN1. (A) The expression of *cd206* and *Tgfb1* were assessed by qRT-PCR (*n*=4). (B) HSCs isolated from uninjured *Ccn1*$^{WT/WT}$ and *Ccn1*$^{D125A/D125A}$ mice were co-cultured for 5 days with BMMs from *Ccn1*$^{WT/WT}$ and *Ccn1*$^{D125A/D125A}$ mice with or without apoptotic PMN and stained with anti-αSMA antibody. (C) The expression of *αSMA* was assessed by qRT-PCR (*n*=4). Data represents means ± SD. *$P$<0.033, **$P$<0.002. Scale bars: 100 μm.

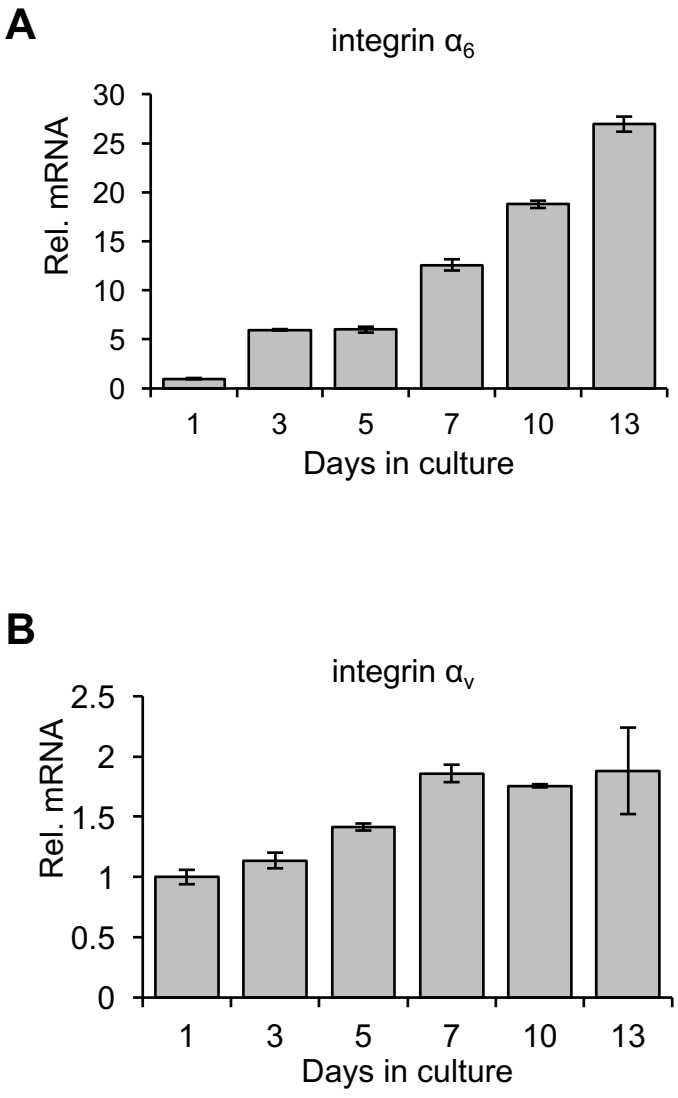


**Figure S7.** HSCs isolated from *Ccn1*$^{WT/WT}$ mice 48 hrs after injection with $CCl_4$ were grown in culture. (A) Integrin $\alpha_6$ mRNAs level and (B) Integrin $\alpha_v$ mRNAs level were measured by qRT-PCR (*n*=4). Data represents means ± SD.

| *Gene* | Orientation | Sequence (5' to 3') |
|---|---|---|
| *αSMA* | sense | ctgacagaggcaccactgaa |
| | antisense | gaaggaatagccacgctcag |
| *Tgfβ1* | sense | gttttgaccccgaggagc |
| | antisense | gagaagagagcgcagaatcca |
| *Ccn1* | sense | ggaactggcatctccaca |
| | antisense | tttgggccggtatttctt |
| *Ccn2* | sense | taggccctcagcctcact |
| | antisense | cttgacaggcttggggat |
| *Cyclophilin* | sense | ttcacaaaccacaatggcacaggg |
| | antisense | tgccgtccagccaatctgtcttat |
| *Col1a1* | sense | ccaagggtaacagcggtgaa |
| | antisense | cctcgttttccttcttctccg |
| *Mmp2* | sense | taacctggatgccgtcgt |
| | antisense | ttcaggtaataagcacccttgaa |
| *Mmp9* | sense | cgtcgtgatccccacttact |
| | antisense | aacacacagggtttgccttc |
| *Mmp13* | sense | agttgacaggctccgagaaa |
| | antisense | ggcactccacatcctggttt |
| *Pdgfα* | sense | gtgcgacctccaacctga |
| | antisense | ggctcatctcacctcacatct |
| *Pdgfβ* | sense | cggcctgtgactagaagtcc |
| | antisense | gagcttgaggcgtcttgg |
| *Egf* | sense | agaaacaccaagaccccaag |
| | antisense | tgtgcccattccatctatgtg |
| *Igf* | sense | accgaggggcttttacttca |
| | antisense | tggctcacctttccttctcc |

Table S1. Primer sequences used in this study.

| Elisa kit | Company and catalog number |
| --- | --- |
| TGF-β1 | BioLegend (436707) |
| Free active TGF-β1 | BioLegend (437707) |

Table S2. Elisa kits used in this study.

| Antibody | dilution | Company and catalog number |
|---|---|---|
| α-SMA | 1:200 | abcam (ab7817) |
| Ly6G | 1:300 | BD pharmigen (551460) |
| Cleaved-Caspase3 | 1:300 | Cell signaling (9661S) |
| CD206 | 1:500 | Cell signaling (24595T) |
| Galectin-3 | 1:300 | Cell signaling (89572S) |
| CD11b | 1:300 | Cell signaling (17800S) |
| F4/80 | 1:300 | Bio-Rad (MCA497RT) |
| MPO | 1:150 | invitrogen (PA5-16672) |
| CD68 | 1:200 | Abcam (ab53444) |

Table S3. Antibodies used in staining.

| Antibody | dilution | Company and catalog number |
|---|---|---|
| Anti-Phospho-Smad2 | 1:1000 | Cell signaling (18338) |
| anti-Smad2 | 1:1000 | Cell signaling (5339) |
| anti-CCN1 | 1:800 | R&D Systems (AF4055) |
| anti-β-actin | 1:20000 | Abcam (ab8226) |

Table S4. Antibodies used in Western blots