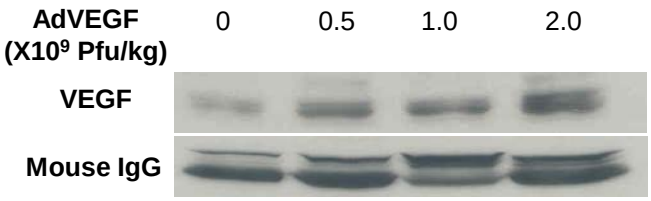
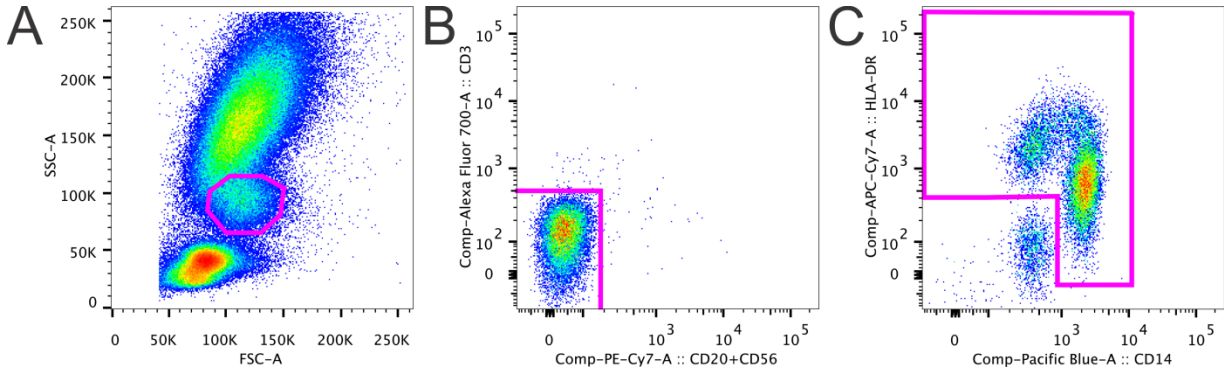
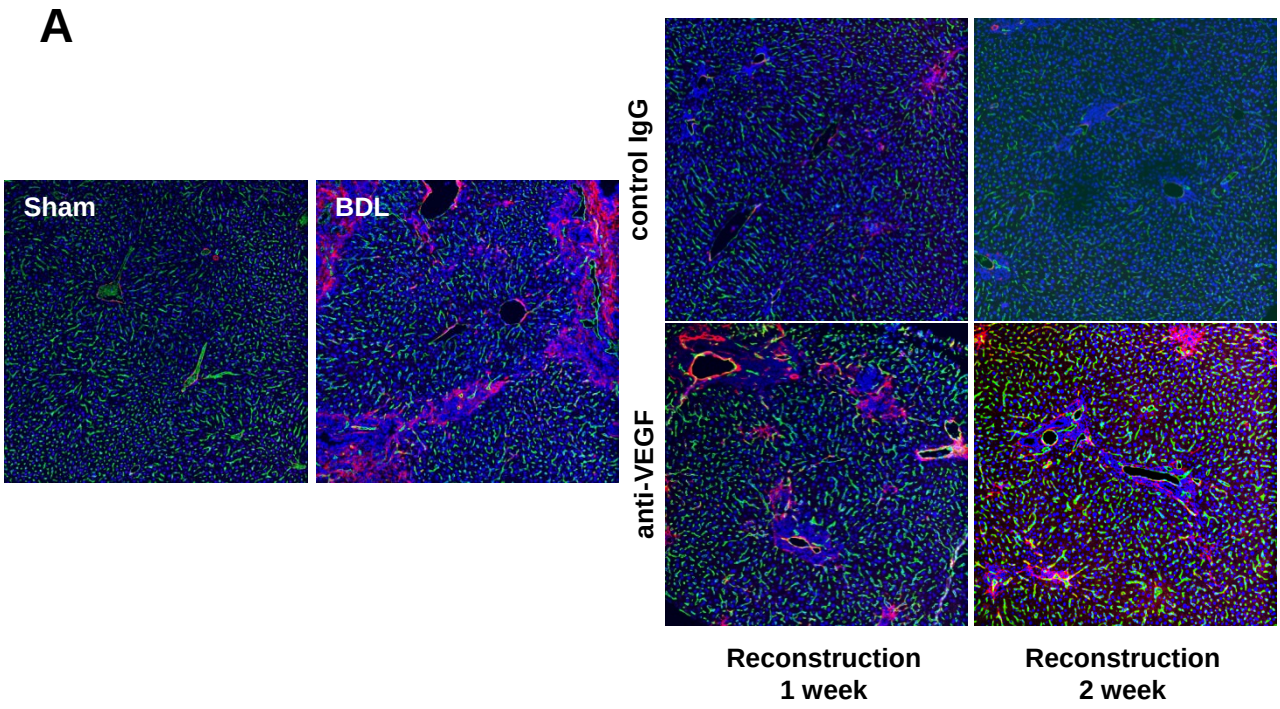
Supplementary Figure 1

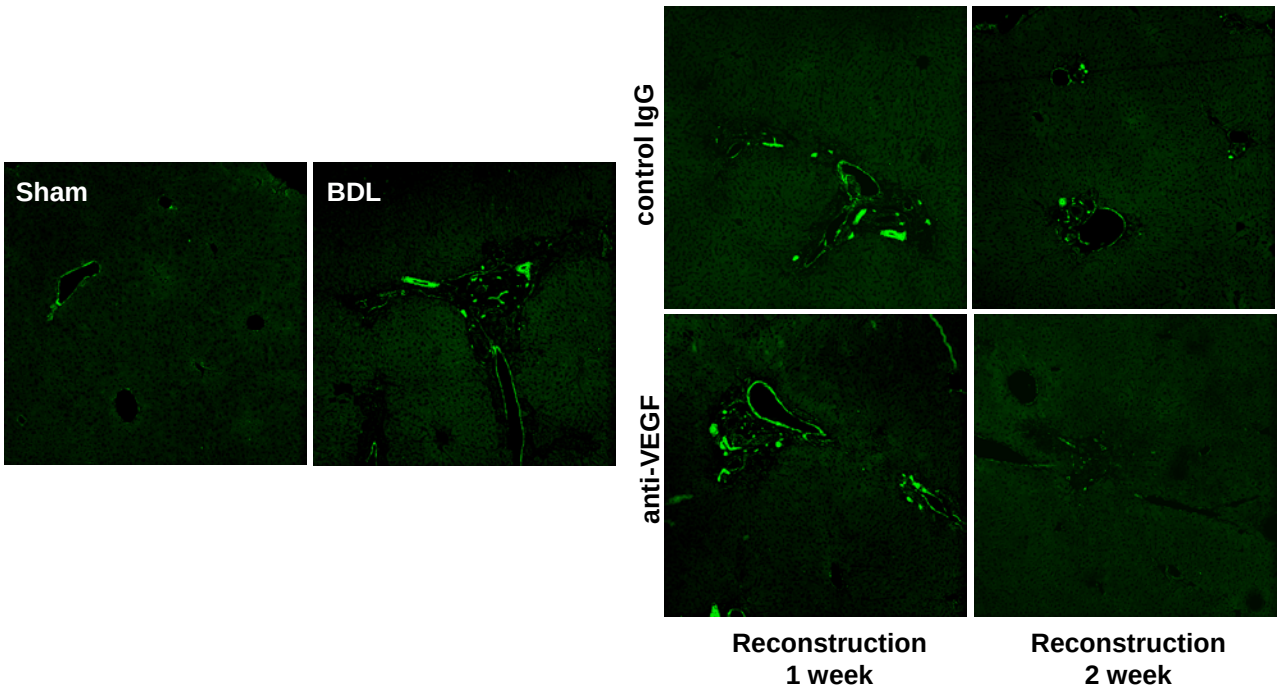


Supplementary Figure 2



Supplementary Figure 3





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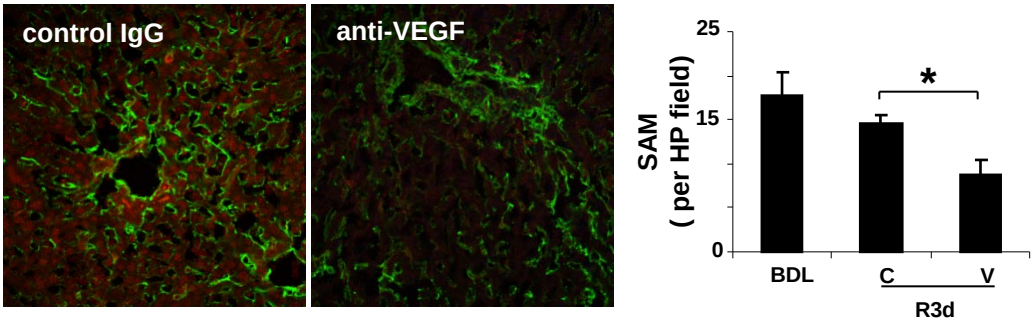

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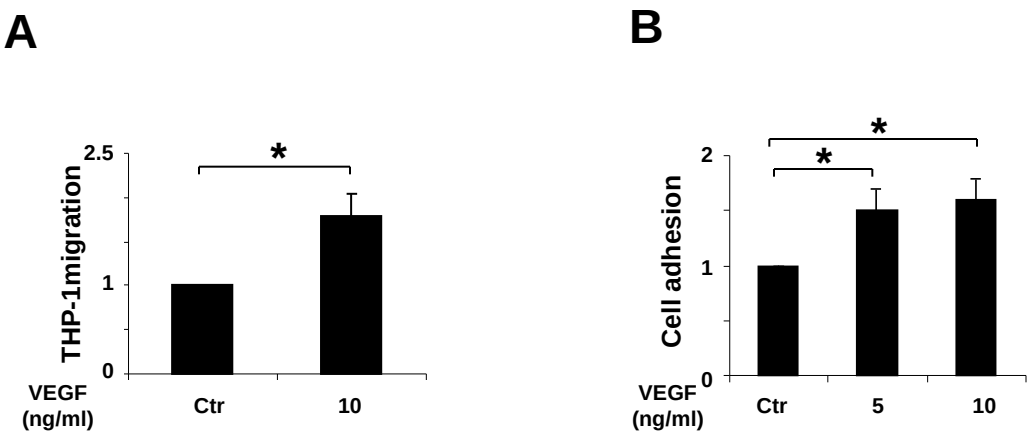

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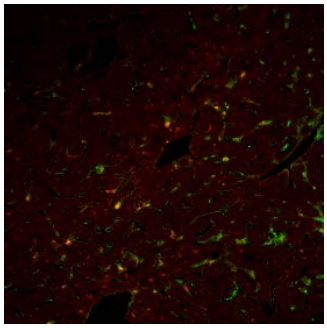

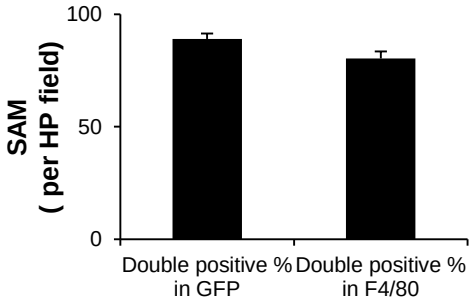

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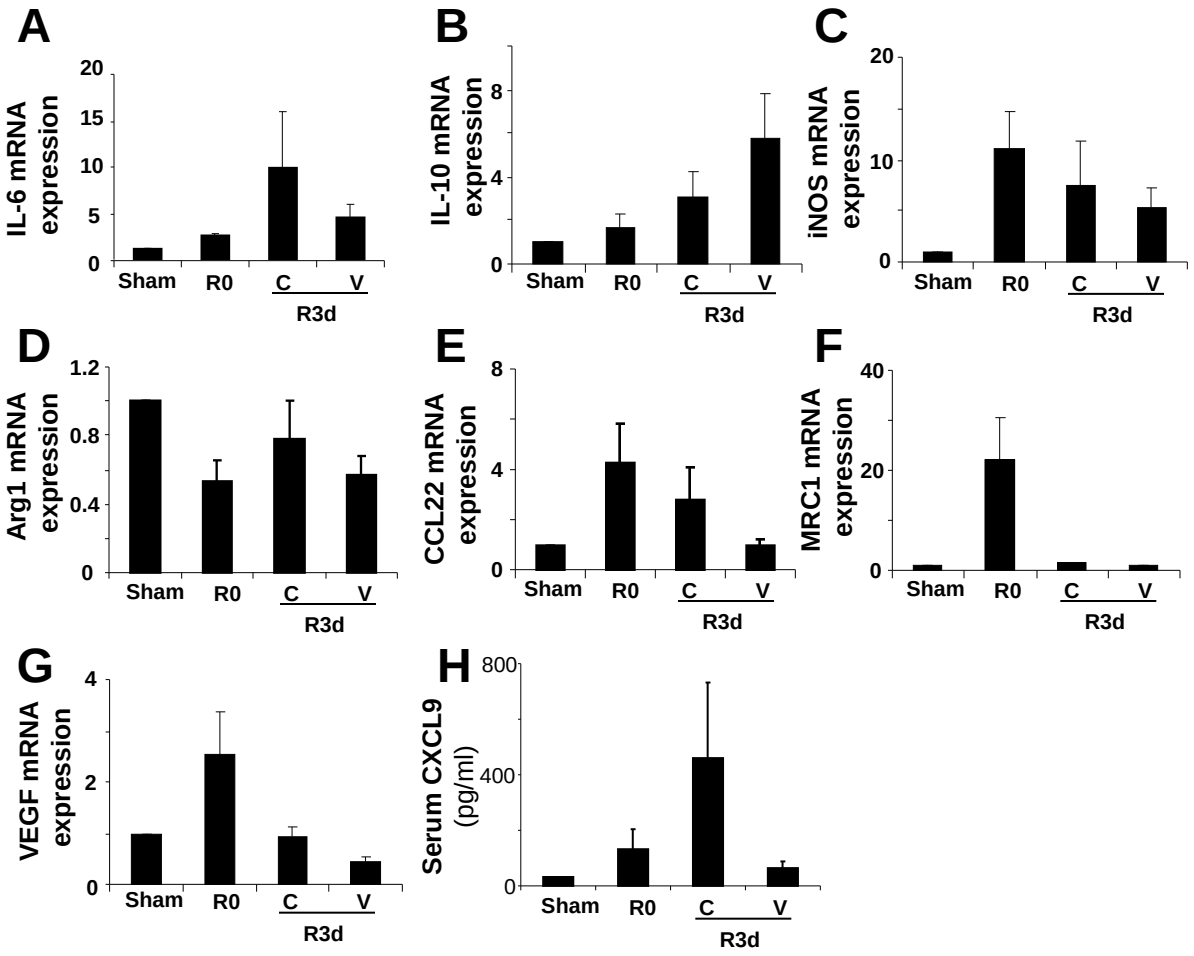

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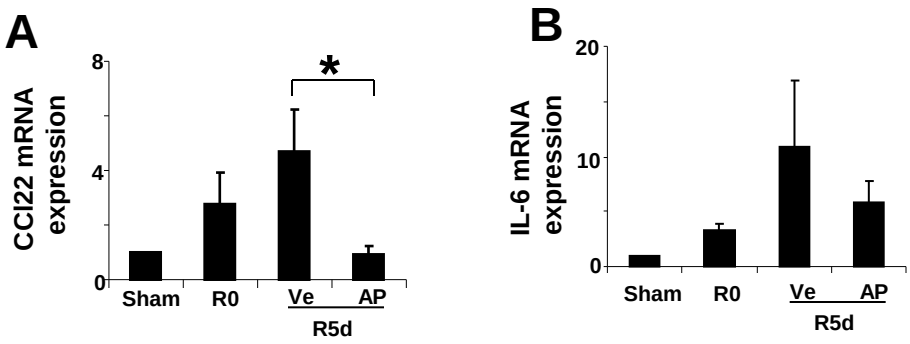
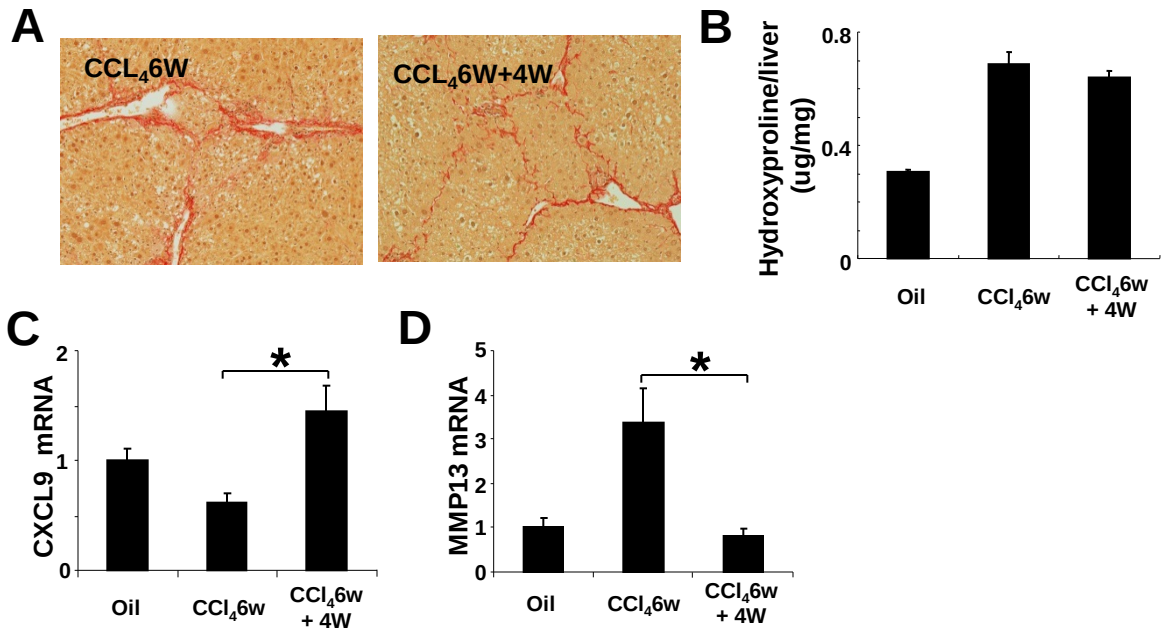
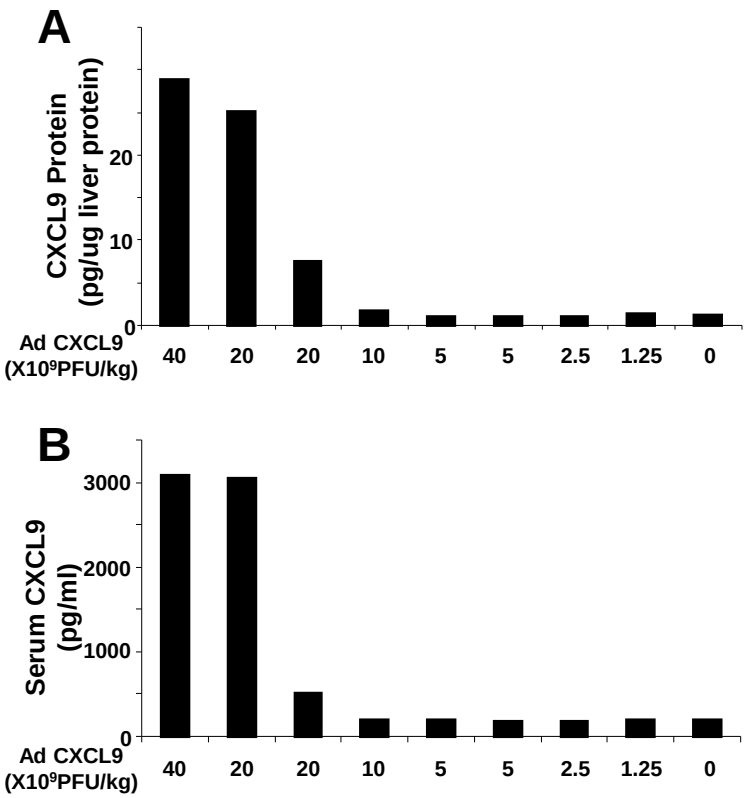


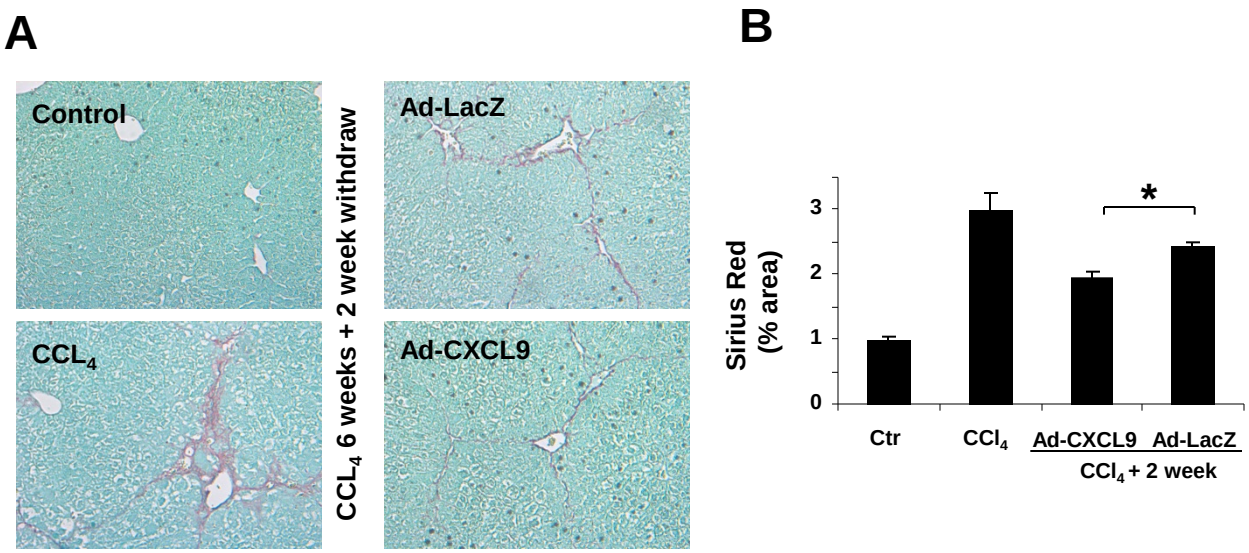
Supplementary Figure 9



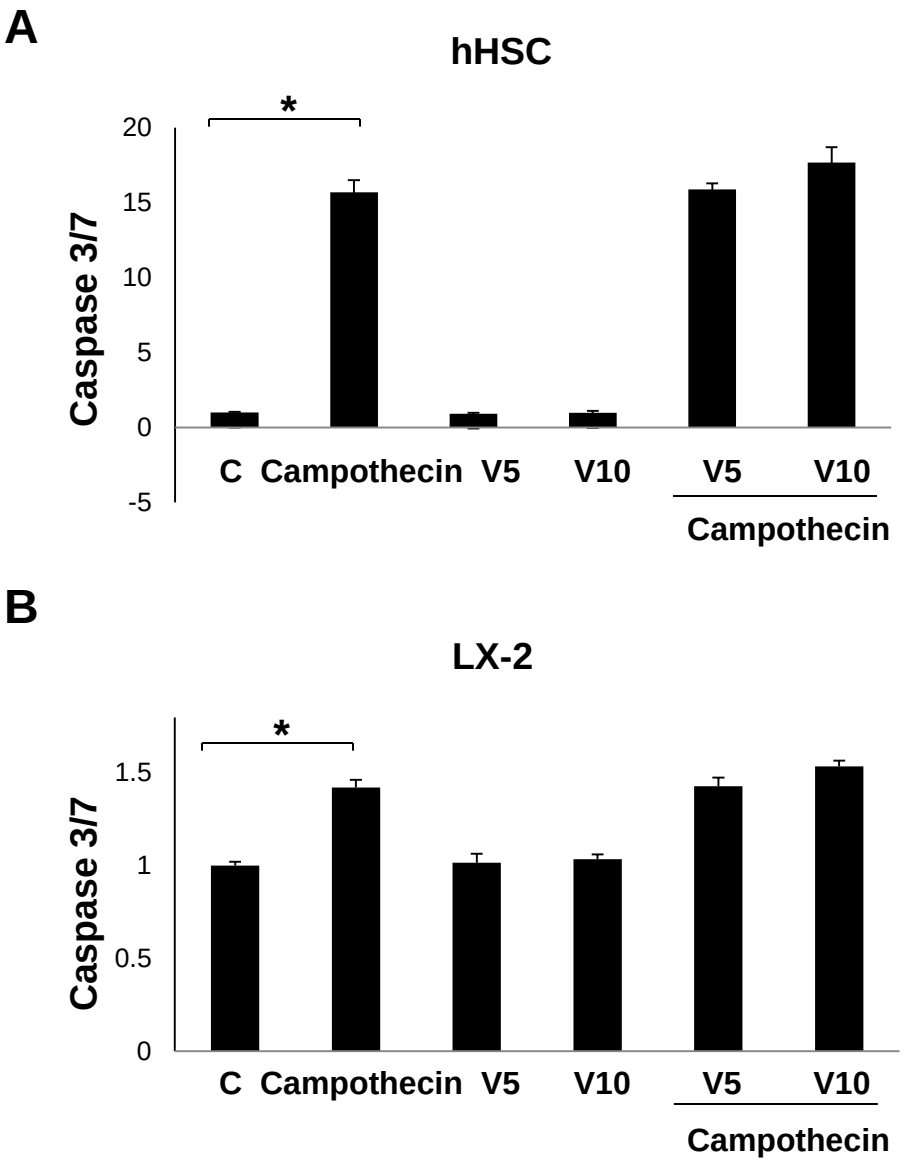
Supplementary Figure 10



Supplementary Figure 11



Supplementary Figure 12



Supplementary Figure 1. VEGF expression in AdVEGF-treated mice. C57BL/6 mice were subjected to different doses of AdVEGF to determine the ideal dosage for in vivo study. Most mice died after receiving doses higher than 4×10^9 PFU/kg. Three days after virus injection, mice were sacrificed. Total liver lysates were subject to Western blot analysis for VEGF.

Supplementary Figure 2. Gating sequence employed for the isolation of human peripheral blood monocytes by fluorescence-activated cell sorting. (*A*) Initial gating based on light scatter properties characteristic of monocytes (SSC, side scatter: orthogonally scattered light; FSC, forward scatter: light scattered at low forward angles). (*B*) Exclusion of contaminating $CD3^+$ T cells, $CD20^+$ B cells and $CD56^+$ natural killer cells. (*C*) Exclusion of contaminating $HLA\text{-}DR^-CD14^{dim}$ granulocytes. A representative from 5 experiments is shown.

Supplementary Figure 3. Aquaporin and von Willibrand factor (vWF) expression during fibrosis resolution in murine cholestatic fibrosis resolution model. C57BL/6 mice received VEGF-neutralizing antibody (anti-VEGF) or control antibody (IP ×2/week for 1 or 2 weeks), after 2 weeks of BDL followed by CJ. One week and 2 weeks after CJ, livers were harvested and subjected to analysis. Immunofluorescence for aquaporin (*green*) and SMA (*red*) are shown in (*A*) and immunofluorescence for vWF (*green*) is showed in (*B*).

Supplementary Figure 4. Anti-VEGF antibody decreases SAM during fibrosis resolution. C57BL/6 mice received 1 dose VEGF-neutralizing antibody (anti-VEGF) or control antibody, after 2 weeks of BDL followed by CJ. Three days after CJ, livers were harvested and subjected to analysis. Immunofluorescence for collagen I (*green*) and macrophage marker CD68 (*red*) were used to identify SAM in frozen section. Anti-VEGF–treated group showed decrease in SAM compared with control IgG-treated group. Quantification data showed. (R3d: BDL 2 weeks plus CJ for 3 days; C: control IgG; V: anti-VEGF antibody; $^{*}P < .05$).

Supplementary Figure 5. VEGF increases migration of THP-1 cells and adhesion between THP-1 and HUVEC. Transwell-insert with florescent dye-labeled monocyte cell line (THP-1) was placed in 12-well dishes with Dulbecco's modified Eagle medium containing VEGF (10 ng/mL). Cell migration was measured 1 hour later by florescence detection. VEGF-stimulated THP-1 cell migration showed in (*A*). To evaluate the effect of VEGF on monocyte adhesion, HUVEC were treated with VEGF for 12 hours before co-culture with florescent dye–labeled THP-1 cells for an additional 3 hours. Cells were washed and fluorescence was measured to determine cell adhesion (*B*).

Supplementary Figure 6. Macrophage in MAFIA mice. MAFIA mice were subjected to sham. In situ GFP (*green*) and F4/80 (*red*) double staining was performed. Double-positive percent in GFP or in F4/80 showed CSFR1-positive cell infiltration in MAFIA mice (200×, n = 7).

Supplementary Figure 7. Cytokine expression during fibrosis resolution after VEGF-neutralizing antibody treatment. After BDL + CJ, C57BL/6 mice receive 1 dose of VEGF-neutralizing antibody (anti-VEGF) or control antibody. Three days later, mice were sacrificed and total liver mRNA was isolated. Total liver mRNA was subjected to real-time PCR for interleukin (IL)-6 (*A*), IL-10 (*B*), inducible nitric oxide synthase (iNOS) (*C*), Arginase 1 (Arg1) (*D*), CC chemokine ligand 22 (CCL22) (*E*), mannose receptor (MRC1) (*F*), and VEGF (*G*). Serum CXCL9 concentration (*H*) was measured using commercial enzyme-linked immunosorbent assay kit (pg/mL) (R0: BDL 2 weeks without CJ; R3d: BDL 2 weeks plus CJ for 3 days; C: control IgG; V anti-VEGF antibody; $^{*}P < .05$).

Supplementary Figure 8. CC chemokine ligand 22 (CCL22) and interleukin (IL)-6 mRNA levels after macrophage depletion during fibrosis resolution. After CJ+BDL, MAFIA mice were treated with vehicle or AP20187 daily for 5 days. Total liver mRNA was subjected to real-time PCR for CCL22 and IL-6. CCL22 (*A*) elevation during fibrosis resolution was attenuated after Kupffer cell depletion with AP20187 in MAFIA mice. IL-6 was also reduced but not statistically significant (*B*). (R0: BDL 2 weeks without CJ; R5d: BDL 2 weeks plus CJ for 5 days; Ve, vehicle; AP, AP 20187; $^{*}P < .05$).

Supplementary Figure 9. CXCL9 and MMP13 expression in CCl4-induced liver fibrosis resolution model. C57BL/6 mice were sacrificed after treated with CCl4 or olive oil for 6 weeks. Another group of animals were allowed to have 4 weeks recovery after treatment with CCl4 or olive oil for 6 weeks ($CCl_4$6w+4W). Sirius Red staining and hydroxyproline content were shown in (*A*) and (*B*), respectively. Total liver mRNA was subjected to real-time PCR analysis to evaluate CXCL9 (*C*) and MMP13 (*D*) (n = 8; $^{*}P < .05$).

Supplementary Figure 10. CXCL9 expression in Ad-CXCL9–treated mice. C57BL/6 mice were subjected to different doses of AdCXCL9 to determine the ideal dosage for in vivo study. Three days after virus injection, mice were sacrificed. Liver (*A*) and serum (*B*) CXCL9 level were measured by enzyme-linked immunosorbent assay (each bar indicates one individual animal; no obvious toxicity was seen at any dose).

Supplementary Figure 11. CXCL9 overexpression promotes fibrosis resolution in CCl4 fibrosis regression model. After 6 weeks of CCl4 treatment, mice were injected with adenovirus-expressing mouse CXCL9 (AdCXCL9) or LacZ (single dose 1×10^{10} PFU/kg through tail vein). Mice were sacrificed 2 weeks after discontinuation of CCl4. Sirius Red stain is shown in (*A*) and quantified in (*B*) ($^{*}P < .05$).

Supplementary Figure 12. Caspase 3/7 assay in VEGF-treated HSC and LX-2. Human HSC (*A*) and LX-2 (*B*) were used to evaluate whether VEGF regulates HSC resistance to apoptosis. Camptothecin (10 uM) was used as an apoptosis inducer (V5: VEGF 5 ng/mL; V10: VEGF 10 ng/mL).

Supplementary Table 1

Primer sequence

Mouse		Sequence	Size
CSF1r	Sense	GACCTGCTCCACTTCTCCAG	305
	Antisense	GGGTTCAGACCAAGCGAGAAG	
Ncf1	Sense	AGCCCCTTGACAGTCCCGAC	151
	Antisense	TCCAGGAGCTTATGAATGACC	
CXCL-9	Sense	TCTTGGGCATCATCTTCCTGG	122
	Antisense	GAGGTCTTTGAGGGATTTGTAGTGG	
MMP-13	Sense	CCAGAACTTCCCAACCATGT	200
	Antisense	GTCTTCCCCGTGTTCTCAAA	
MMP-2	Sense	CAACGGTCGGGAATACAGCAG	353
	Antisense	CCAGGAAAGTGAACGGGAAGA	
MMP-9	Sense	GCTGACTACGATAAGGACGGC	284
	Antisense	AGGAAGACGAAGGGGAAGACG	
IL-6	sense	GAGCCCACCAAGAACGATAG	229
	anti-sense	TCCACGATTTCCCAGAGAAC	
IL10	Sense	TGTGAAAATAAGAGCAAGGCAGTG	85
	Antisense	CATTCATGGCCTTGTAGACACC	
iNOS	Sense	CAGCTGGGCTGTACAAACCTT	95
	Antisense	CATTGGAAGTGAAGCGTTTCG	
MRC1	Sense	GCAAATGGAGCCGTCTGTGC	300
	Antisense	CTCGTGGATCTCCGTGACAC	
Arg1	Sense	CAGAAGAATGGAAGAGTCAG	250
	Antisense	CAGATATGCAGGGAGTCACC	
CCL-22	Sense	AAGACAGTATCTGCTGCCAGG	141
	Antisense	GATCGGCACAGATATCTCGG	
VEGF	Sense	TTACTGCTGTACCTCCACC	189
	Antisense	ACAGGACGGCTTGAAGATG	
β-actin	Sense	AGAGGGAAATCGTGCGTGAC	138
	Antisense	CAATAGTGATGACCTGGCCGT	
Human			
MMP-13	Sense	TTCACTTTGAGGATACAGGCAA	129
	Antisense	CACCAATTCCTGGGAAGTCT	
GAPDH	Sense	CTCTGCTCCTCCTGTTCGAC	144
	Antisense	TTAAAAGCAGCCCTGGTGAC	

Supplementary Table 2

Antibodies used for peripheral blood monocyte isolation

Target	Supplier	Host/Source	Clone/ID	Isotype	Label	µg/100µl blood
HLA-DR[a]	BD[b] Bioscience	Mouse mc[c]	L243	IgG_{2a},κ	APC[d]-Cy7[e]	0.0625 µg
CD14[f]	BD Pharmingen	Mouse mc	M5E2	IgG_{2a},κ	Pacific Blue	0.5 µg
CD3[g]	BD Pharmingen	Mouse mc	SP34-2	$IgG_{1,}\lambda$	Alexa Fluor 700	0.25 µg
CD20[h]	BD Bioscience	Mouse mc	L27	IgG_{1},κ	PE[i]-Cy7	0.25 µg
CD56[j]	BD Pharmingen	Mouse mc	B159	IgG_{1},κ	PE-Cy7	0.03 µg

[a], HLA-DR major histocompatibility complex class II cell surface receptor; [b], BD, Becton Dickinson and Company; [c], mc, monoclonal; [d], APC, allophycocyanin; [e], Cy7, cyanine 7; [f], monocyte differentiation antigen CD14; [g], CD3 T cell co-receptor; [h], CD20 antigen, [i], PE, phycoerythrin; [j], CD56 antigen (neural cell adhesion molecule 1; NCAM1)