Table S1A. Patient background characterstics for PBMC FACS analysis (Figure 1A and B)

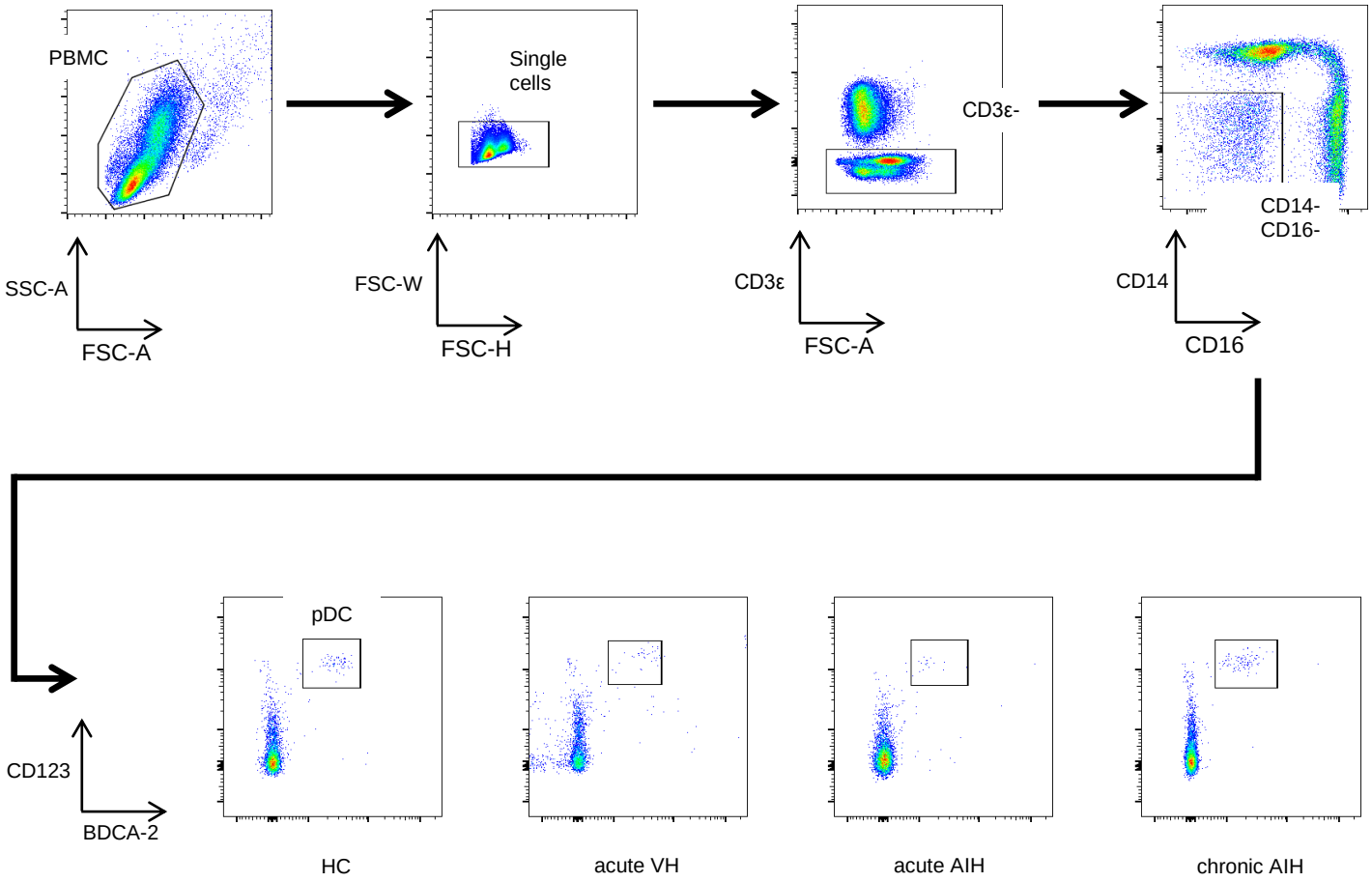
Patient groups	Viral infection	Sex (M/F)	Median values [Min-Max] Age (y)	ALT (IU/L)	AST (IU/L)	T-Bil (mg/dL)	ALP (IU/L)	GGTP (IU/L)	PT-INR	PLT (10^4/μL)	IgG (mg/dL)	IgM (mg/dL)	ANA titer>1:80,n (%)	IAIHG scoring[#1]	Simplified scoring[#2]
Healthy controls (n=21)	-	11/10	34.0 [30-55]	15.5 [6-39]	-	-	-	-	-	-	-	-	-	-	-
Acute viral hepatitis (n=7)	HAV(1)/HBV(4)/ HEV(1)/EBV(1)	6/1	47.0 [17-59]	1312 [495-6426]	1118 [629- 6145]	5.2 [2.7- 22.5]	565 [305- 1269]	189 [65- 682]	1.62 [0.95- 2.21]	12.1 [5.4- 31.7]	1275 [630- 2246]	151 [86- 877]	-	-	-
Acute autoimmune hepatitis (n=8)	-	1/7	49.5 [28-79]	669 [396-1234]	786 [363- 1140]	15.7 [7.8- 25.1]	526 [336- 837]	147 [29- 244]	1.78 [1.13- 2.68]	20.3 [13.0- 32.2]	1368 [1021-4862]	150 [51- 229]	3 (37.5%)	16 [11- 17]	5.5 [4- 7]
Chronic autoimmune hepatitis (n=7)	-	0/7	53.0 [24-79]	78 [24- 173]	57 [30- 225]	1.1 [0.5- 14.6]	251 [152- 515]	68 [23- 136]	1.10 [1.00- 1.78]	18.5 [6.6- 32.3]	1998 [946- 2873]	146 [41- 267]	5 (71.4%)	15 [10- 18]	7 [5- 7]

Table S1B. Patient background characterstics for liver IHC analysis (Figure 1C and D)

Patient groups	Viral infection	Sex (M/F)	Median values [Min-Max] Age (y)	ALT (IU/L)	AST (IU/L)	T-Bil (mg/dL)	ALP (IU/L)	GGTP (IU/L)	PT-INR	PLT (10^4/μL)	IgG (mg/dL)	IgM (mg/dL)	ANA titer>1:80,n (%)	IAIHG scoring[#1]	Simplified scoring[#2]
Liver metastasis (Non-tumor part as control) (n=6)	-	3/3	34 [30-55]	12.5 [8- 20]	20 [12- 25]	0.6 [0.5- 1.9]	238 [161- 365]	10 [18- 142]	0.96 [0.9- 1.13]	20.9 [18.1- 27.7]	-	-	-	-	-
Acute autoimmune hepatitis (n=5)	-	1/4	41 [28-56]	143 [58-657]	241 [53-1066]	8.7 [3.7- 25.1]	340 [256- 462]	49 [29- 126]	2.4 [1.86- 2.90]	16.1 [8.2- 26.6]	1874 [1121-3475]	147 [93- 205]	3 (60%)	12 [6- 22]	7 [3- 8]

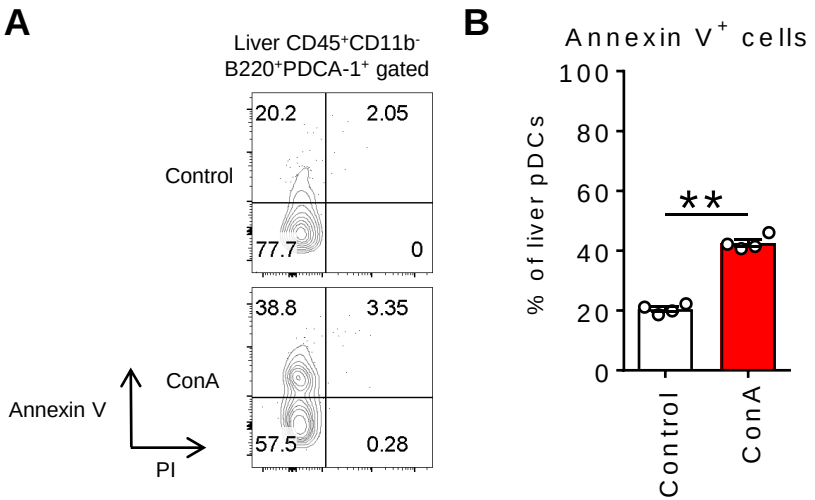
Supplemental Table 1. Patient background characteristics

Data are shown as median with ranges in brackets. Notes: #1. Alvarez F et al. J Hepatol 1999. #2. Hennes EM et al. Hepatology 2008. Abbreviations: AIH, autoimmune hepatitis; HAV, hepatitis A virus; HBV, hepatitis B virus; HEV, hepatitis E virus; EBV, Epstein–Barr virus; M, male; F, female; AST, aspartate aminotransferase; ALT, alanine aminotransferase; T-Bil, total bilirubin; ALP, alkaline phosphatase; GGTP, γ- glutamyl transpeptidase; PT-INR, prothrombin time–international ratio; PLT, platelet count; Ig, immunoglobulin; ANA, antinuclear antibody; IAIHG, International Autoimmune Hepatitis Group.



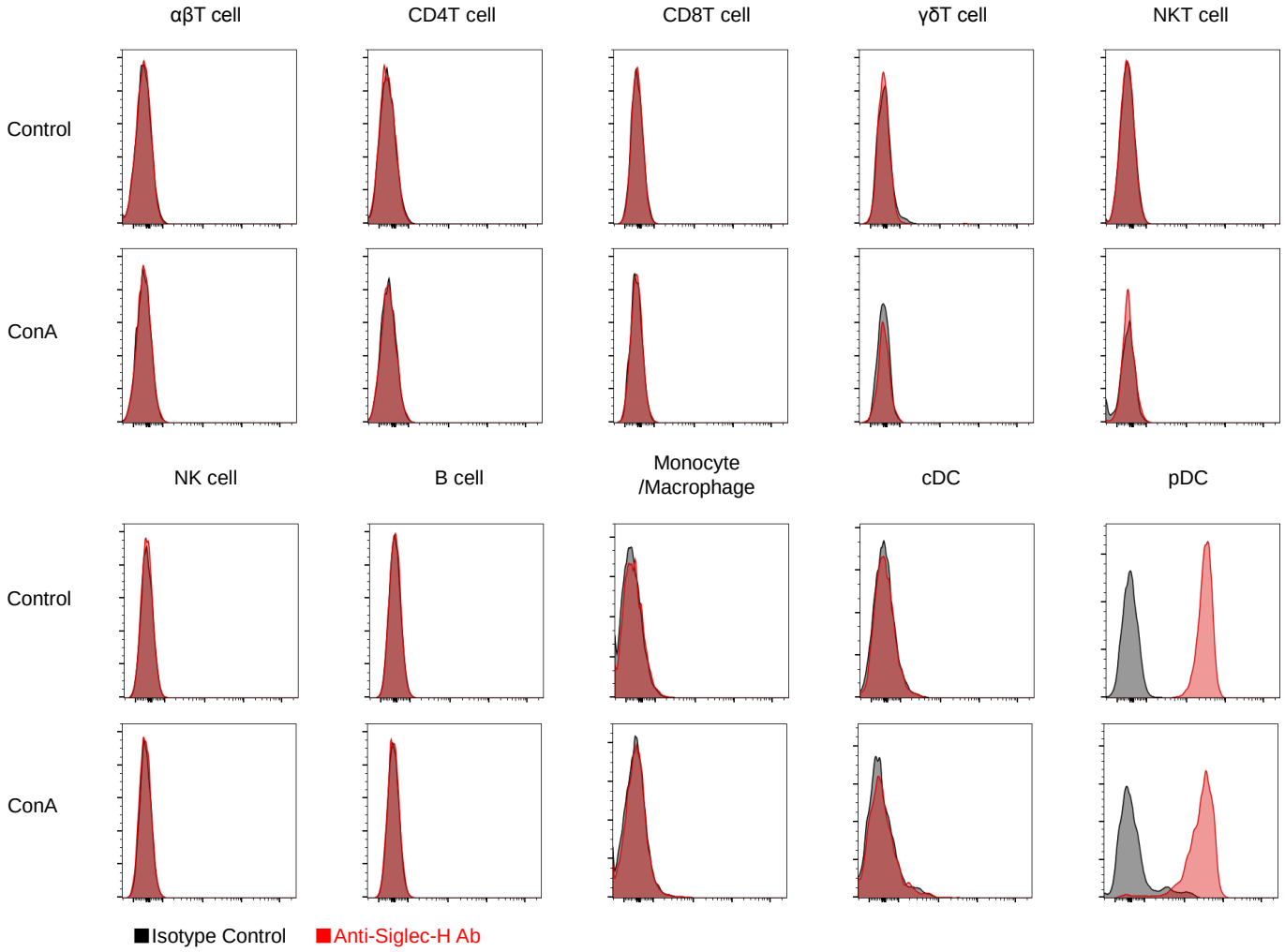
Supplemental Figure 1. The gating strategy of FACS analysis in human PBMC study.

Figure S1 Koda et. al.



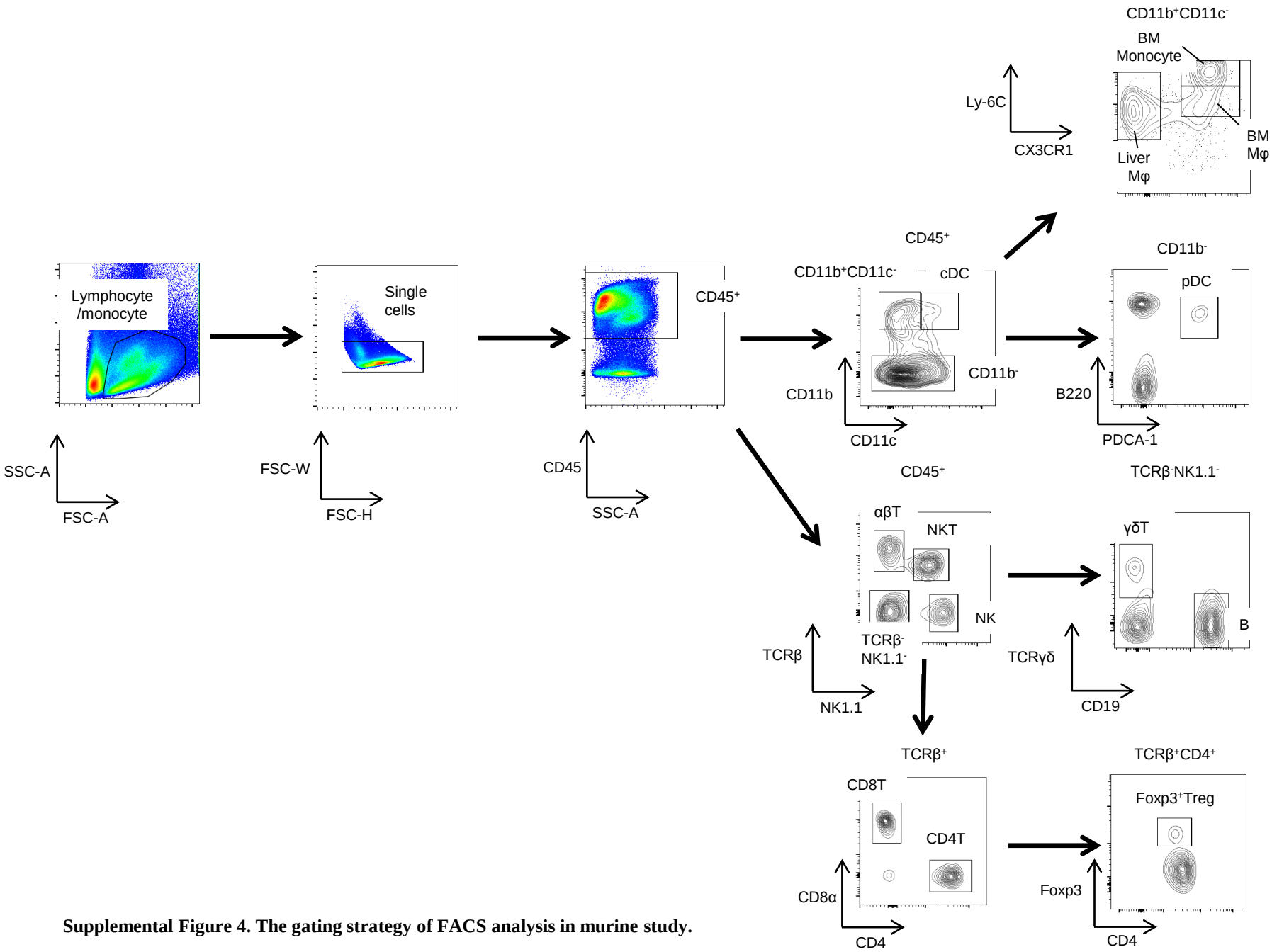
Supplemental Figure 2 Liver pDCs are prone to apoptosis during ConA-induced inflammation.
(A) Representative Annexin V and PI staining and (B) Mean percentages of Annexin V^+ cells in liver pDCs. Data represent the mean ± SEM (n=4 per group). **p <0.01 by Student's t test. Data are representative from two independent experiments.

Figure S2 Koda et. al.



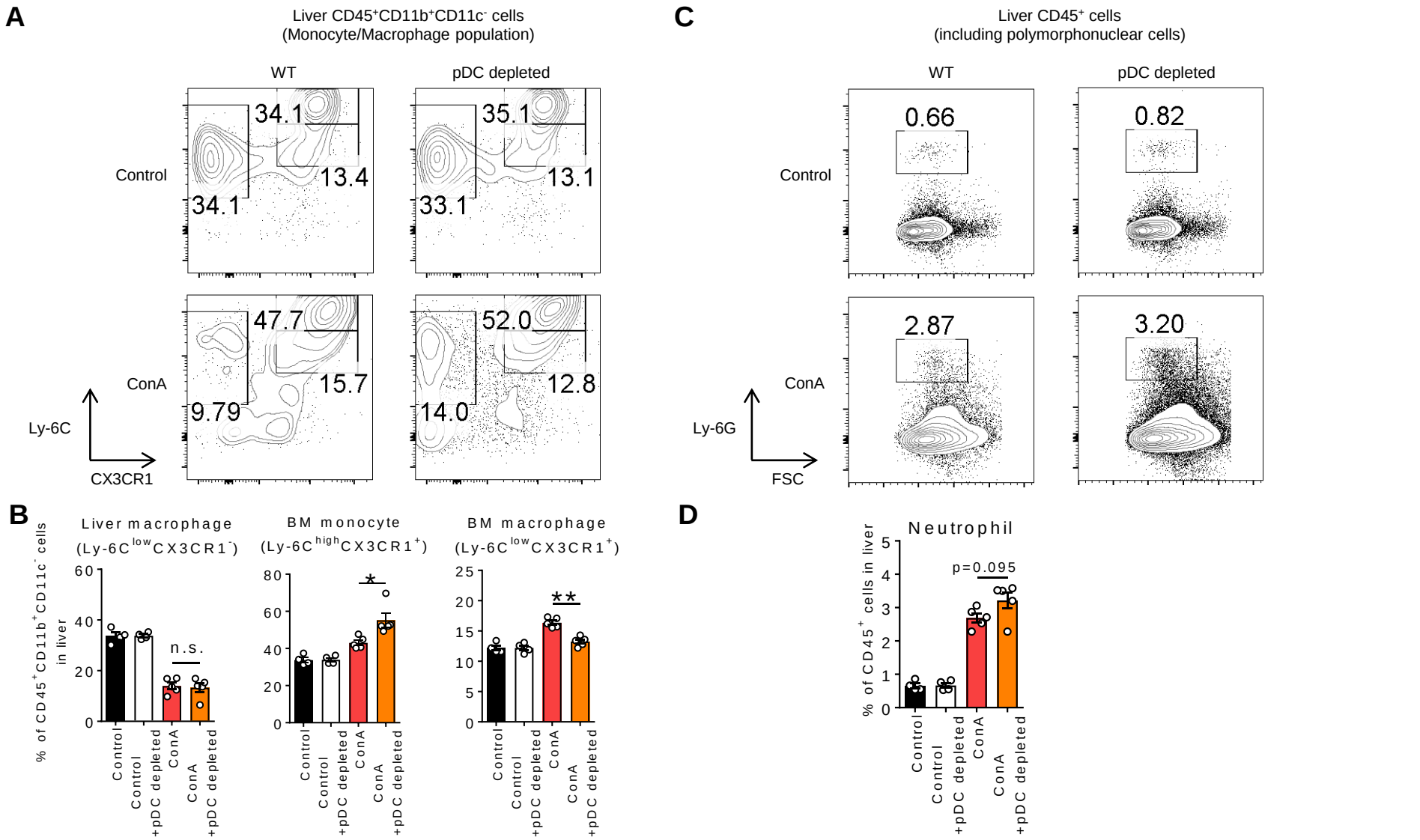
Supplemental Figure 3. Siglec-H is specifically expressed on pDCs in steady state and inflammatory condition.
Representative Siglec-H histograms of various immune cells in the liver of control or ConA (15 mg/kg, 18h) treated mice. Data are representative from over three independent experiments.

Figure S3 Koda et. al.



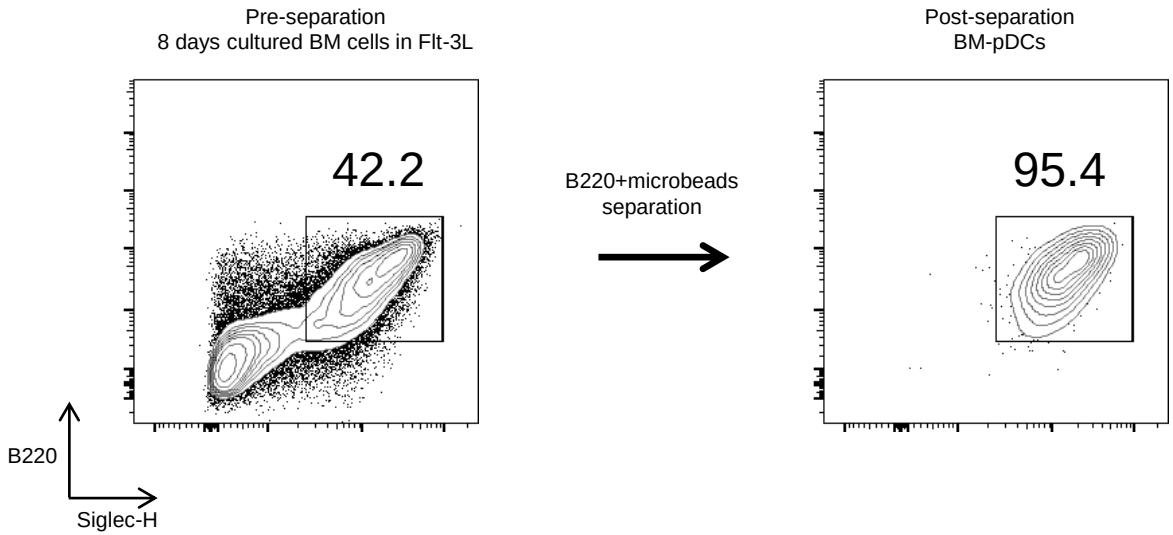
Supplemental Figure 4. The gating strategy of FACS analysis in murine study.

Figure S4 Koda et. al.



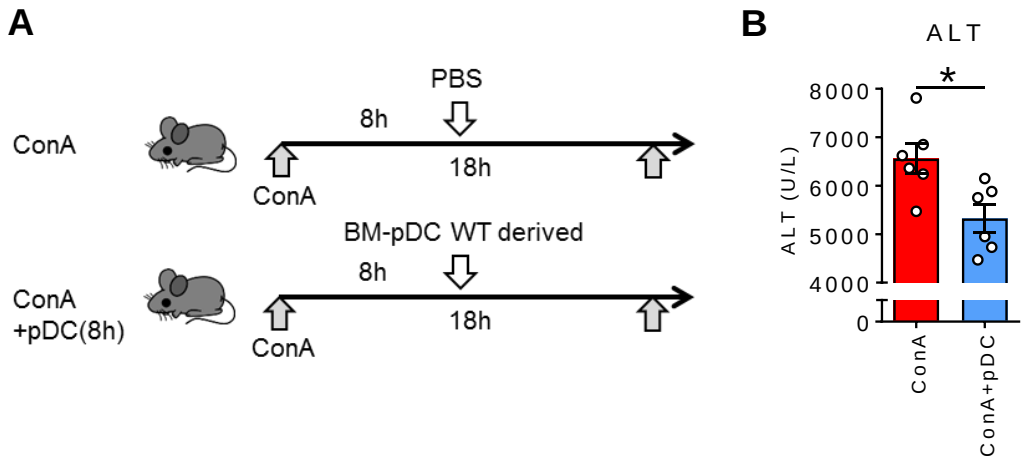
Supplemental Figure 5. Characterization of monocytes/macrophages and neutrophils in pDCs depleted mice in steady state and inflammatory condition.
(A) Representative Ly-6C and CX3CR1 staining of $CD45^+CD11b^+CD11c^-$-gated liver MNCs. $CD45^+CD11b^+CD11c^-$-gated liver MNCs was distinguished as liver macrophages ($Ly\text{-}6C^{low}CX3CR1^-$), bone marrow (BM) derived monocytes ($Ly\text{-}6C^{hig}hCX3CR1^+$), and BM derived macrophages ($Ly\text{-}6C^{low}CX3CR1^+$).(B) Mean percentages of each cells in $CD45^+CD11b^+CD11c^-$-gated liver MNCs. (C) Representative Ly-6G staining of $CD45^+$ gated liver immune cells. To analyze neutrophils, percoll gradient separation was performed by only 40% percoll. Following centrifugation, immune cells including polymorphonuclear cells were collected at the lower layer, washed, and hemolyzed. (D) Mean percentages of neutrophils in liver $CD45^+$ cells. Data represent the mean ± SEM (n = 4 for the control or control+pDCs-depleted group; n = 5 for the ConA or ConA+pDCs-depleted group). *$p < 0.05$, **$p < 0.01$ by Student's t test. Data are representative from two independent experiments.

Figure S5 Koda et. al.



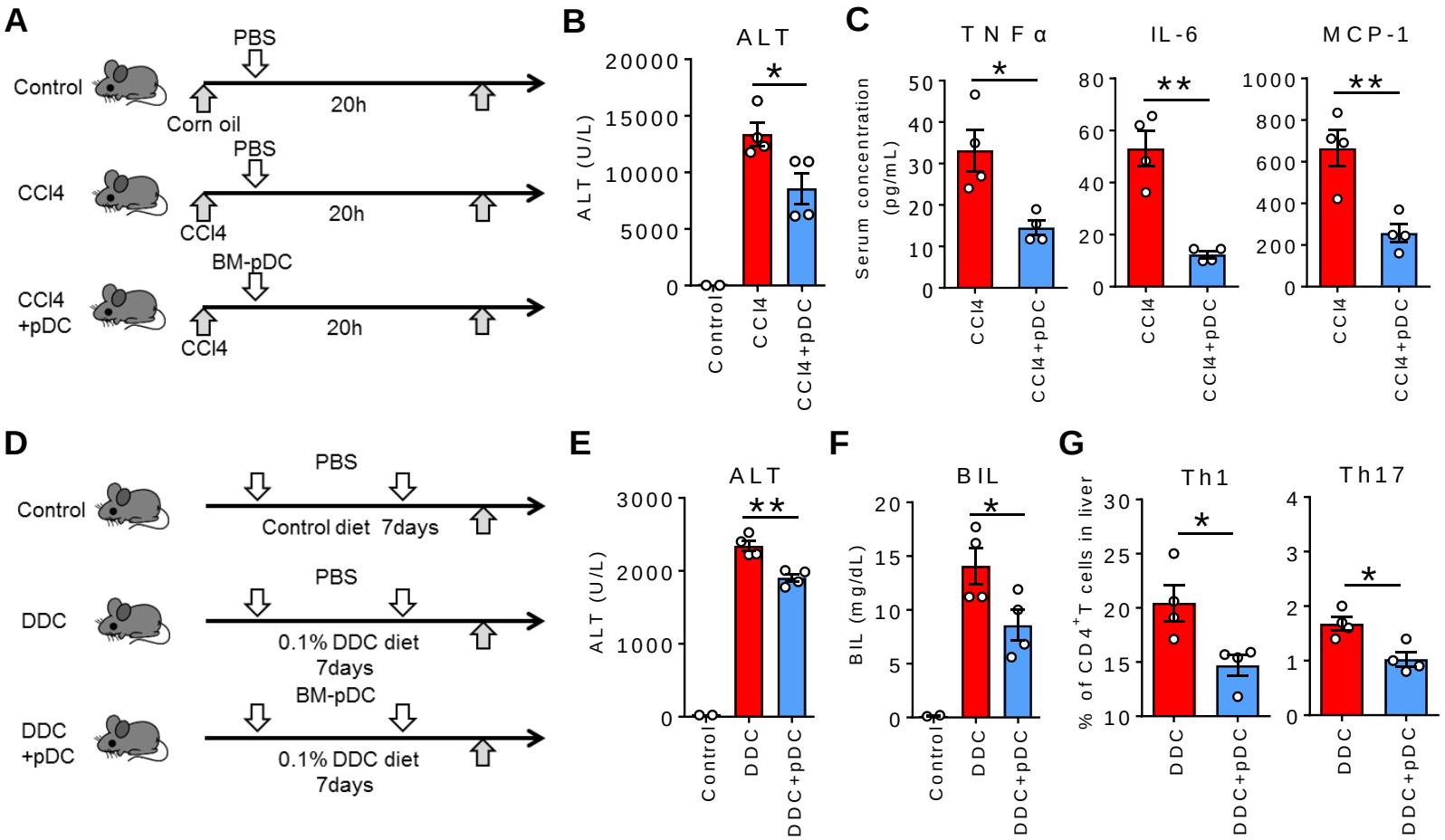
Supplemental Figure 6. BM-pDC separation in this study.

Figure S6 Koda et. al.



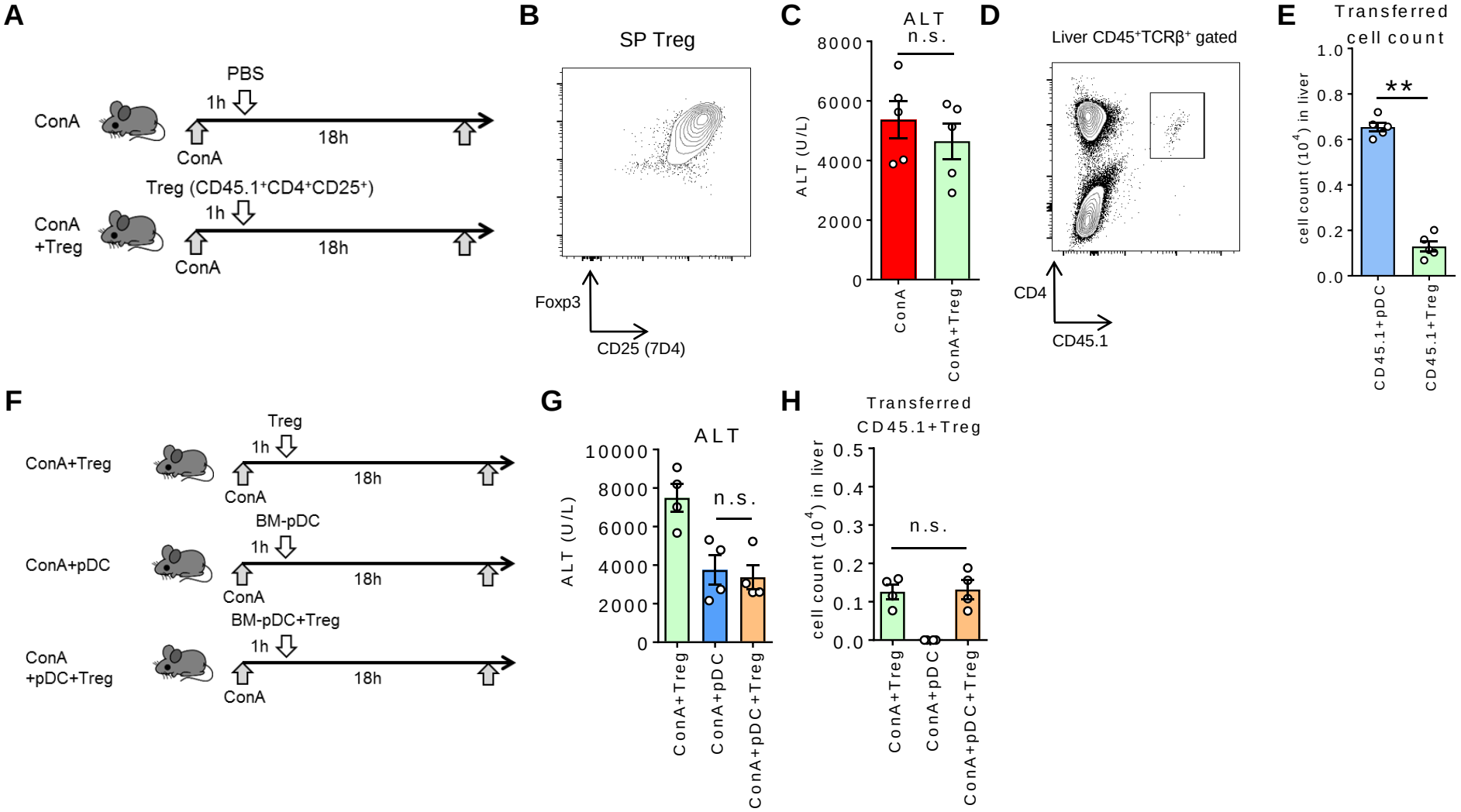
Supplemental Figure 7. Adoptive transfer of BM-pDCs at a late stage of disease also ameliorates ConA-induced liver inflammation.
(A) Study design. ConA (15 mg/kg) was intravenously injected into the tail vein of mice. 8 hours later, the mice were intravenously inoculated with Flt-3L-proliferated BM-pDCs (2×10^6 cells/200 µL PBS) or 200 µL PBS alone. All mice were sacrificed and analyzed 18 h after the ConA injection. (B) Serum ALT levels. Data represent the mean ± SEM (n = 6 per group). *p <0.05 by Student's t test. Data are combined from two independent experiments.

Figure S7 Koda et. al.



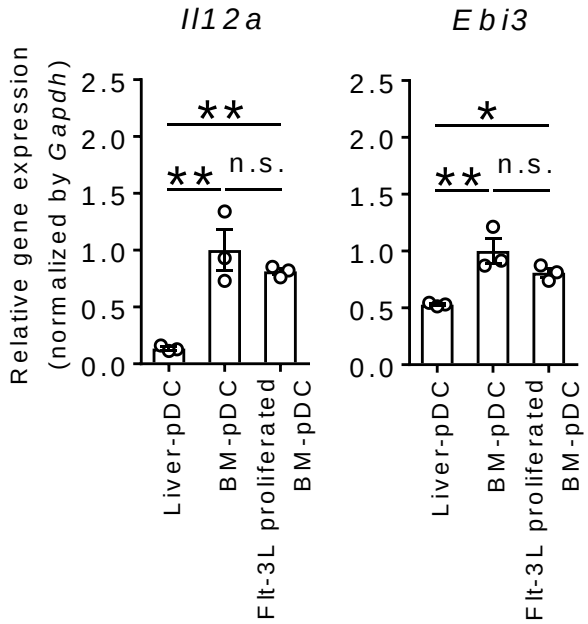
Supplemental Figure 8. Adoptive transfer of BM-pDCs ameliorates CCl4-induced liver inflammation and DDC-induced cholangitis.
(A) Study design. CCl4 (Wako, Osaka, Japan, 1 ml/kg) in corn oil or corn oil was injected intraperitoneally. One hour later, the mice were inoculated intravenously with BM-pDCs (2×10^6 cells/200 µL PBS) or 200 µL PBS alone. All mice were sacrificed and analyzed 20 h after the CCl4 injection. (B) Serum ALT levels and (C) Serum cytokine concentrations. Data represent the mean ± SEM (n=2 for the control group, n=4 for the CCl4 or CCl4+pDC group). (D) Study design. Mice were freely fed a 0.1% DDC (Sigma-Aldrich, Tokyo, Japan)-enriched or control diet for 7 days. 1 day and 4 days later, the mice were inoculated intravenously with BM-pDCs (2×10^6 cells/200 µL PBS) or 200 µL PBS alone. 7 days later, all mice were sacrificed and analyzed. (E) Serum ALT levels, (F) Serum bilirubin, and (G)Th1 ($CD45^+TCR\beta^+CD4^+IFN\gamma^+$) and Th17 ($CD45^+TCR\beta^+CD4^+IL\text{-}17A^+$) in liver CD4 T cells. Data represent the mean ± SEM (n=2 for the control group, n=4 for the DDC or DDC+pDC group). *p <0.05, **p <0.01 by Student's t test. Data are representative from two independent experiments.

Figure S8 Koda et. al.



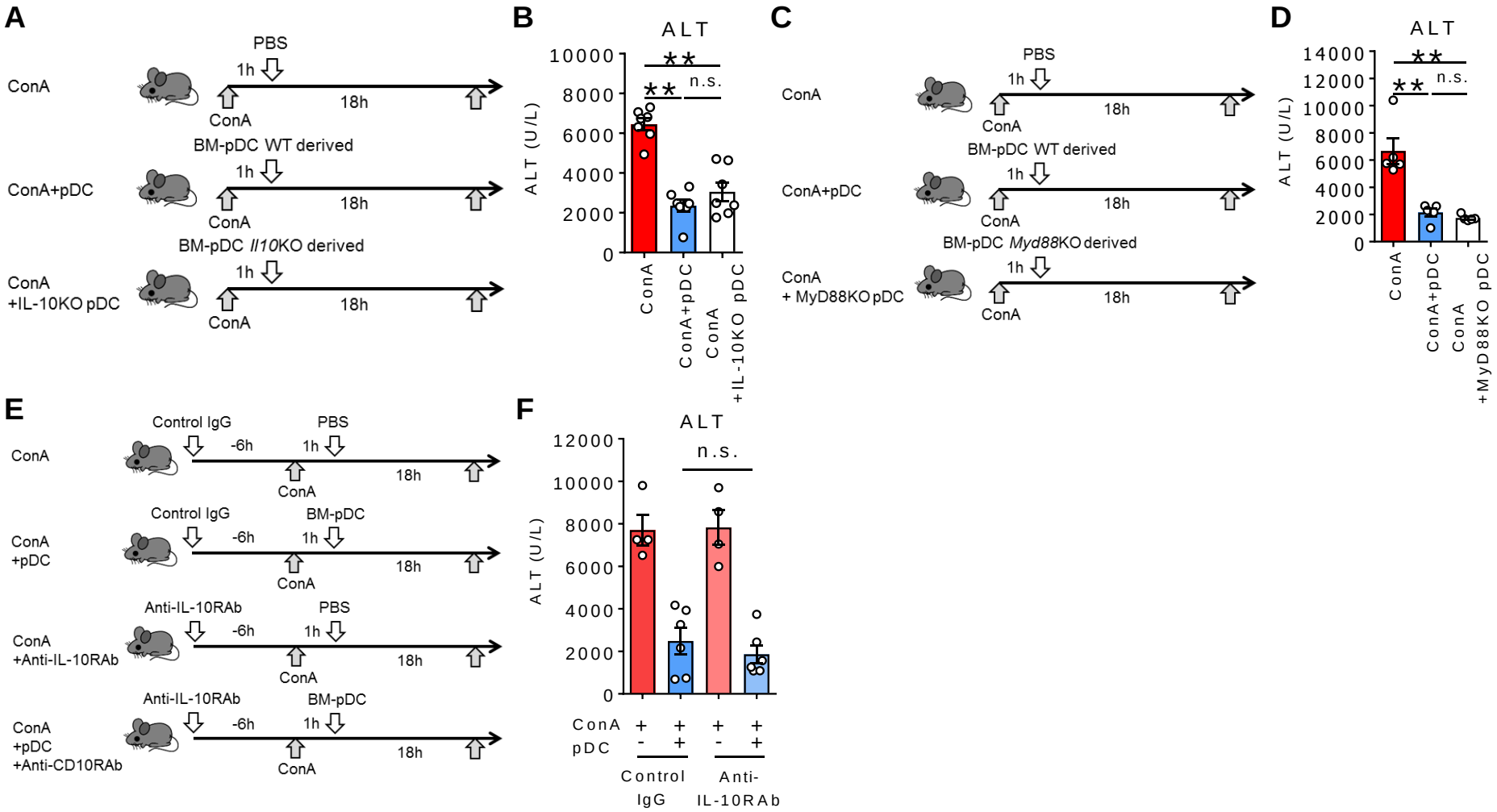
Supplemental Figure 9. Adoptive transfer of Tregs does not ameliorate ConA-induced liver inflammation.
(A) Study design. ConA (15 mg/kg) was intravenously injected into the tail vein of mice. One hour later, the mice were inoculated intravenously with splenic $CD4^+CD25^+$Tregs derived from Ly5.1 mice (2×10^6 cells/200 µL PBS) or 200 µL PBS alone. All mice were sacrificed and analyzed 18 h after the ConA injection. (B) Representative intracellular Foxp3 and CD25 staining of pre-transferred Tregs. (C) Serum ALT levels. Data represent the mean ± SEM (n=5 per group). (D) Representative CD45.1 and CD4 staining of liver mononuclear cells of Tregs (CD45.1) transferred mice. (E) Cell numbers of transferred pDCs and Tregs in liver during ConA-induced inflammation. (F) Study design. Splenic $CD4^+CD25^+$Tregs (2×10^6 cells/200 µL PBS), BM-pDCs (2×10^6 cells/200 µL PBS), or both pDCs and Tregs (2×10^6 cells and 2×10^6 cells/200 µL PBS) derived from Ly5.1 mice were intravenously inoculated to Ly5.2 mice. All mice were sacrificed and analyzed 18 h after the ConA injection. (G) Serum ALT levels. (H) Cell numbers of transferred Tregs in each condition. Data represent the mean ± SEM (n=4 per group). **p <0.01 by Student's t test. Data are representative (B and D) or combined (C, E, G, and H) from two independent experiments.

Figure S9 Koda et. al.



Supplemental Figure 10. Comparison of IL-35 gene expressions among liver pDCs, BM pDCs, and Flt-3L proliferated BM-pDCs. IL-35 genes (IL-12a and Ebi3) expression in natural liver pDCs, natural BM pDCs, and Flt-3L proliferated BM-pDCs. Data represent the mean ± SEM (n = 3 per group). *$p < 0.05$, **$p < 0.01$ by ANOVA with Tukey's multiple comparisons post-hoc test. Data are representative from two independent experiments.

Figure S10 Koda et. al.



Supplemental Figure 11. IL-10 production and TLR7/9 signaling do not participate in amelioration of ConA-induced inflammation by BM-pDCs.
(A) Study design. ConA (15 mg/kg) or PBS was intravenously injected into the tail vein of mice. One hour later, the mice were inoculated intravenously with WT or IL-10$^{-/-}$mice derived BM-pDCs (2 × 10^6 cells/200 µL PBS), or 200 µL PBS alone. (B) Serum ALT levels. Data represent the mean ± SEM (n=7 per group). **p <0.01 by ANOVA with Tukey's multiple comparisons post-hoc test. (C) Study design. ConA (15 mg/kg) or PBS was intravenously injected into the tail vein of mice. One hour later, the mice were inoculated intravenously with WT or MyD88$^{-/-}$mice derived BM-pDCs (2 × 10^6 cells/200 µL PBS), or 200 µL PBS alone. (D) Serum ALT levels. Data represent the mean ± SEM (n=5 per group). **p <0.01 by ANOVA with Tukey's multiple comparisons post-hoc test. (E) Study design. WT mice were treated with anti-IL-10R Ab (Biolgend, clone; 1B1.3a) or isotype control (500 µg/head) intraperitoneally 6 h prior to ConA or PBS injection. One hour later, the mice were intravenously inoculated with Flt-3L-proliferated BM-pDCs (2 × 10^6 cells/200 µL PBS) or 200 µL PBS alone. All mice were sacrificed and analyzed 18 h after the ConA injection. (F) Serum ALT levels. Data represent the mean ± SEM (n=4 or 6 per group). Data are combined from two independent experiments.

Figure S11 Koda et. al.