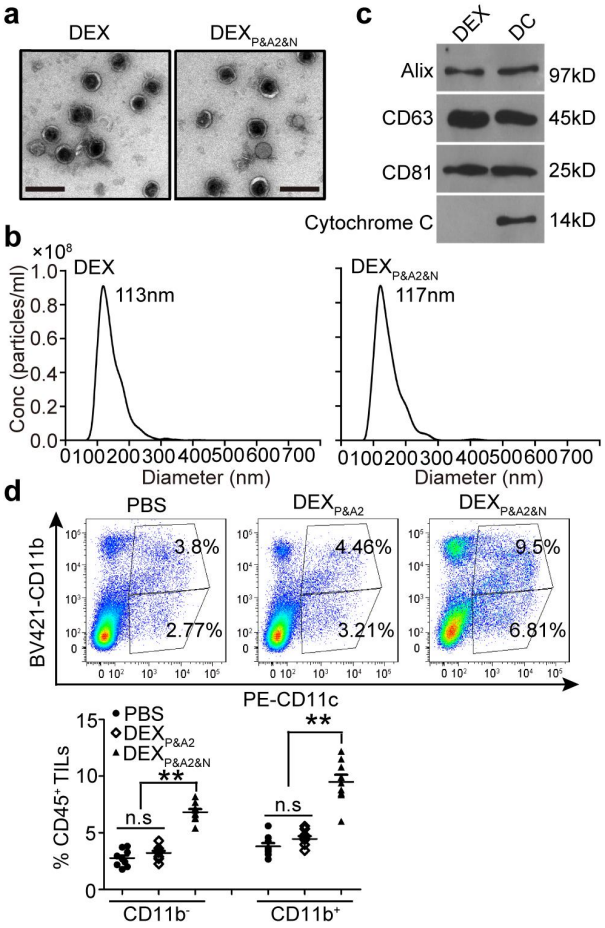
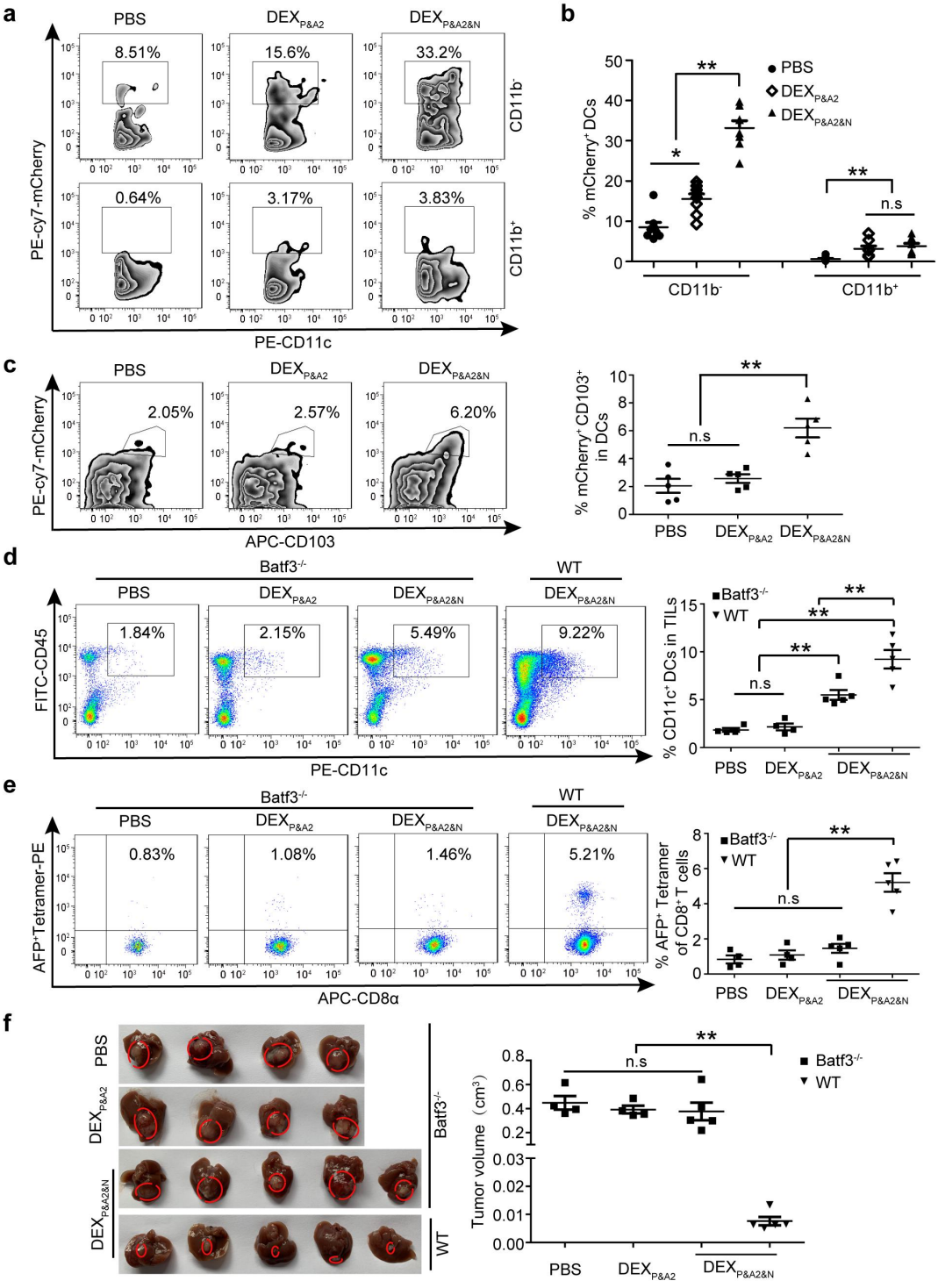
Supplementary Figures

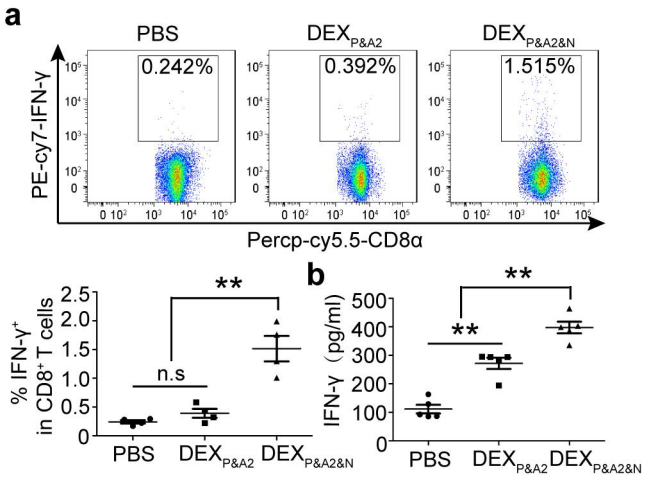


Supplementary Figure 1. Characterization and evaluation of $DEX_{P\&A2\&N}$ to recruit DCs to tumor of orthotopic mCherry-expressing HCC mice. (**a**) Representative transmission electron microscopic (TEM) images of DEX and $DEX_{P\&A2\&N}$ (scale bar= 200nm). P-P47; A2-AFP212; N-N1ND. DEX refers to DC-derived exosomes. (**b**) Size distribution of DEX and $DEX_{P\&A2\&N}$ with nanoparticle tracking analysis (NTA). (**c**) Western blot to examine the expression of exosomal biomarkers. Total protein (30 μg) was loaded for DEX and DC. (**d**) Flow cytometric and quantitative analysis of $CD11b^{+}CD11c^{+}$ and $CD11b^{-}CD11c^{+}$ DCs from tumor of orthotopic HCC mice treated with $DEX_{P\&A2}$ or $DEX_{P\&A2\&N}$ (n=9; One way-ANOVA post hoc Student-Newman -Keuls test). **p<0.001; n.s means not significant.

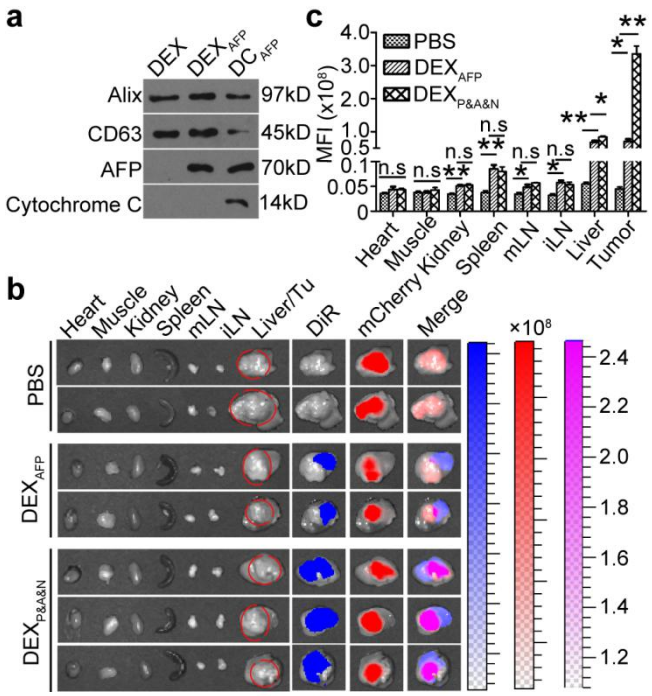


Supplementary Figure 2. Effects of $DEX_{P\&A2\&N}$-mediated DC cross-presentation and antitumor responses in orthotopic HCC mice. Flow cytometric (**a**) and quantitative analysis (**b**) of $mCherry^+CD11b^+CD11c^+$ or $mCherry^+CD11b^-CD11c^+$ DCs from tumor of orthotopic HCC mice treated with $DEX_{P\&A2}$ or $DEX_{P\&A2\&N}$ (n=8; One way-

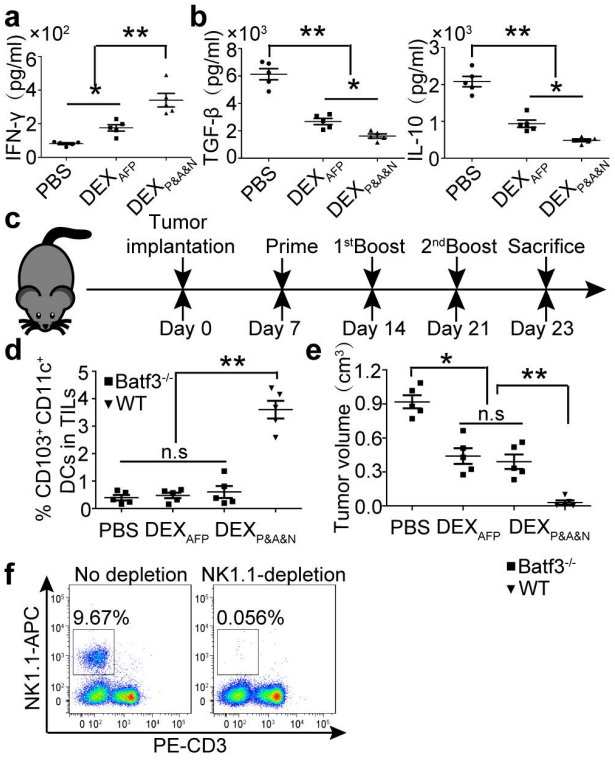
ANOVA post hoc Student-Newman-Keuls test). (**c**) Flow cytometric and quantitative analysis of $mCherry^{+}CD103^{+}CD11c^{+}$ DCs in splenocytes of orthotopic HCC mice treated with $DEX_{P\&A2}$ or $DEX_{P\&A2\&N}$ (n=5; One way-ANOVA post hoc Student-Newman-Keuls test). (**d**) Flow cytometric and quantitative analysis of $CD11c^{+}$ DCs from tumor- infiltrating lymphocytes (TILs) of orthotopic $Batf3^{-/-}$ HCC mice treated with PBS (n=4), $DEX_{P\&A2}$ (n=4) or $DEX_{P\&A2\&N}$ (n=5) and orthotopic wild-type (WT) HCC mice treated with $DEX_{P\&A2\&N}$ (n=5) (One way-ANOVA post hoc Student-Newman-Keuls test). (**e**) Flow cytometric and quantitative analysis of AFP^{+} tetramer T cells from tumor of orthotopic $Batf3^{-/-}$ HCC mice treated with PBS (n=4), $DEX_{P\&A2}$ (n=4) or $DEX_{P\&A2\&N}$ (n=5) and orthotopic WT HCC mice treated with $DEX_{P\&A2\&N}$ (n=5) (One way-ANOVA post hoc Student-Newman-Keuls test). (**f**) Representative tumor images and tumor volume of orthotopic $Batf3^{-/-}$ HCC mice treated with PBS (n=4) $DEX_{P\&A2}$ (n=4) or $DEX_{P\&A2\&N}$ (n=5) and orthotopic WT HCC mice treated with $DEX_{P\&A2\&N}$ (n=5) (One way-ANOVA post hoc Student-Newman-Keuls test). *$p<0.05$, **$p<0.001$; n.s means not significant.



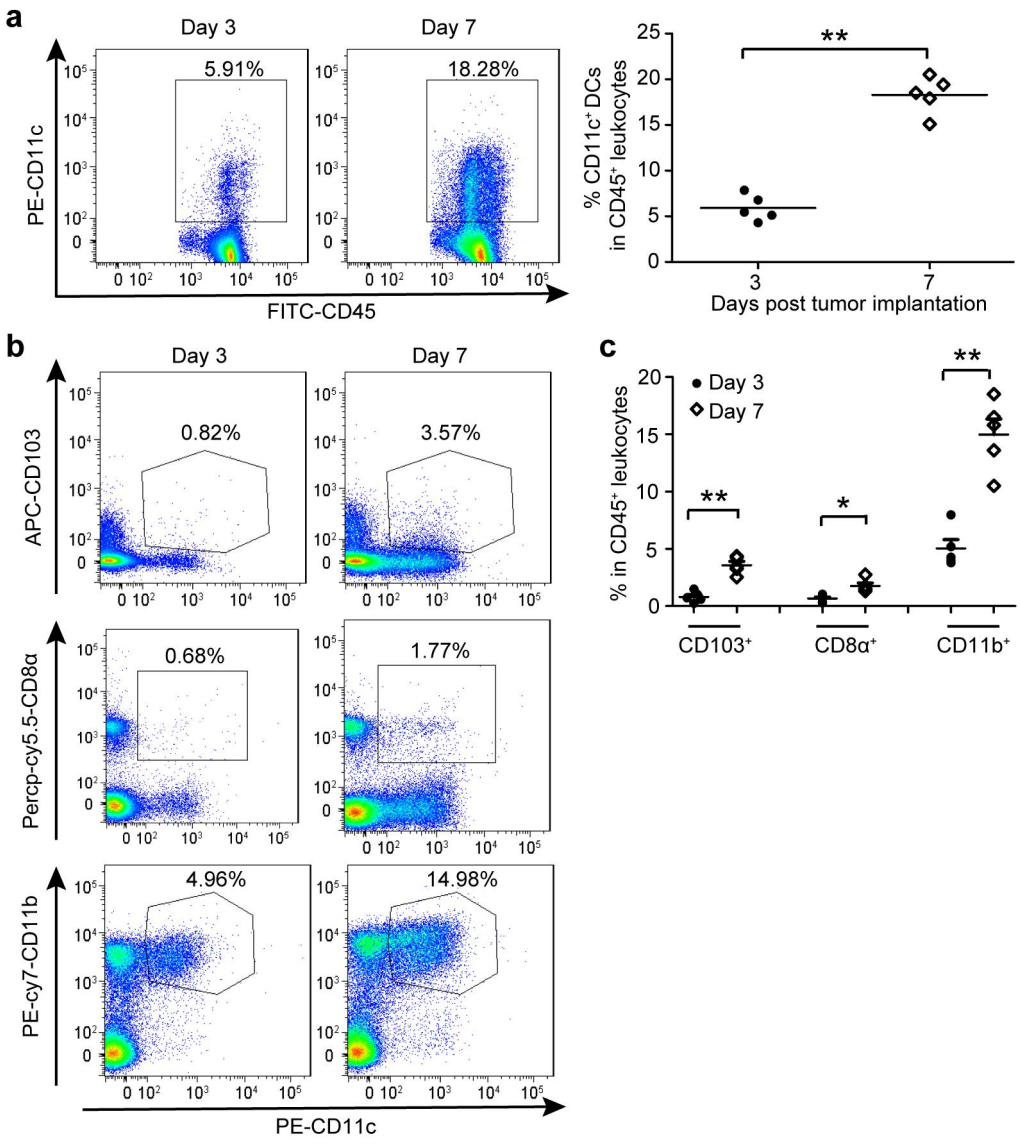
Supplementary Figure 3. Analysis of immune microenvironment of orthotopic HCC mice treated with $DEX_{P\&A2\&N}$. (**a**) Flow cytometric and quantitative analysis of IFN-γ^+CD8^+ T cells in blood of orthotopic HCC mice treated with $DEX_{P\&A2}$ or $DEX_{P\&A2\&N}$ (n=4; One way-ANOVA post hoc Student-Newman-Keuls test). (**b**) Measurement of IFN-γ in blood of orthotopic HCC mice treated with $DEX_{P\&A2}$ or $DEX_{P\&A2\&N}$ (n=5; One way-ANOVA post hoc Student-Newman-Keuls test). **p<0.001; n.s means not significant.



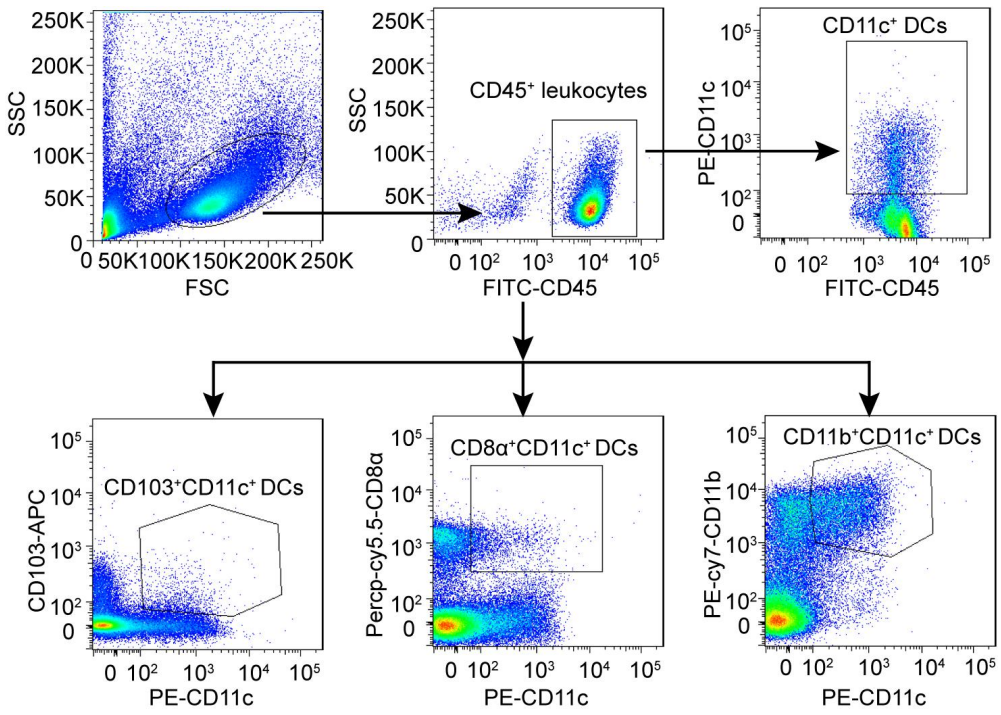
Supplementary Figure 4. Western blot analysis and tissue distribution of DEX_{AFP} and $DEX_{P\&A\&N}$. (**a**) Western blot to examine the expression of AFP on DEX. Total protein (30 μg) was loaded for DEX and DC. DEX refer to DC-derived exosomes. Tissue distribution (**b**) and quantitative analysis (**c**) of labeled $DEX_{P\&A\&N}$. DiR-labeled DEX_{AFP} or $DEX_{P\&A\&N}$ (80 μg/mouse) were injected into day-14 orthotopic HCC mice bearing mCherry-expressing tumors intravenously and tissues were harvested 2 h after injection (n=3; One way-ANOVA post hoc Student-Newman-Keuls test). mLN-mesenteric lymph node; iLN-inguinal lymph node. Tumor was circled. *p<0.05, **p<0.001; n.s means not significant.



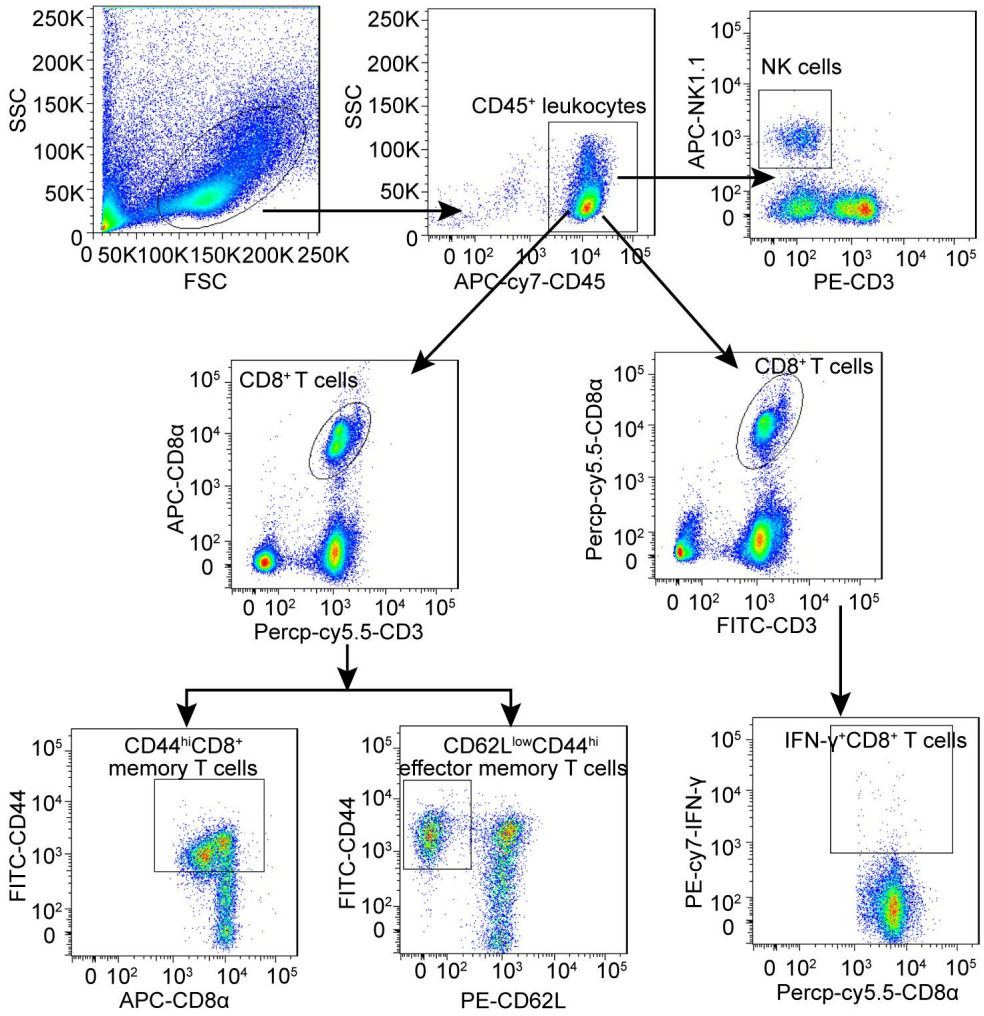
Supplementary Figure 5. Examination of tumor microenvironment in $DEX_{P\&A\&N}$-treated orthotopic HCC mice bearing large tumors and NK depletion. Measurement of IFN-γ (**a**) and TGF-β and IL-10 (**b**) in tumor of DEX_{AFP}- or $DEX_{P\&A\&N}$-treated orthotopic HCC mice bearing large established tumors (n=5). (**c**) Diagram for dosing regimen of $DEX_{P\&A\&N}$ in orthotopic $Batf3^{-/-}$ HCC mice. DEX_{AFP} or $DEX_{P\&A\&N}$ (80 μg/mouse) were intravenously injected into day-7 orthotopic $Batf3^{-/-}$ HCC mice weekly for 3 times and tissues were harvested 2 days after last injection. (**d**) Quantitative analysis of $CD103^{+}CD11c^{+}$ DCs from TILs of $DEX_{P\&A\&N}$-treated orthotopic $Batf3^{-/-}$ and wild-type (WT) HCC mice (n=5). (**e**) Measurement of tumor size in $DEX_{P\&A\&N}$-treated orthotopic $Batf3^{-/-}$ and WT HCC mice (n=5). (**f**) Flow cytometric analysis of NK cells in blood of orthotopic HCC mice on day 23 after tumor inoculation. *$p<0.05$, **$p<0.001$; n.s means not significant; One way-ANOVA post hoc Student-Newman-Keuls test was used.



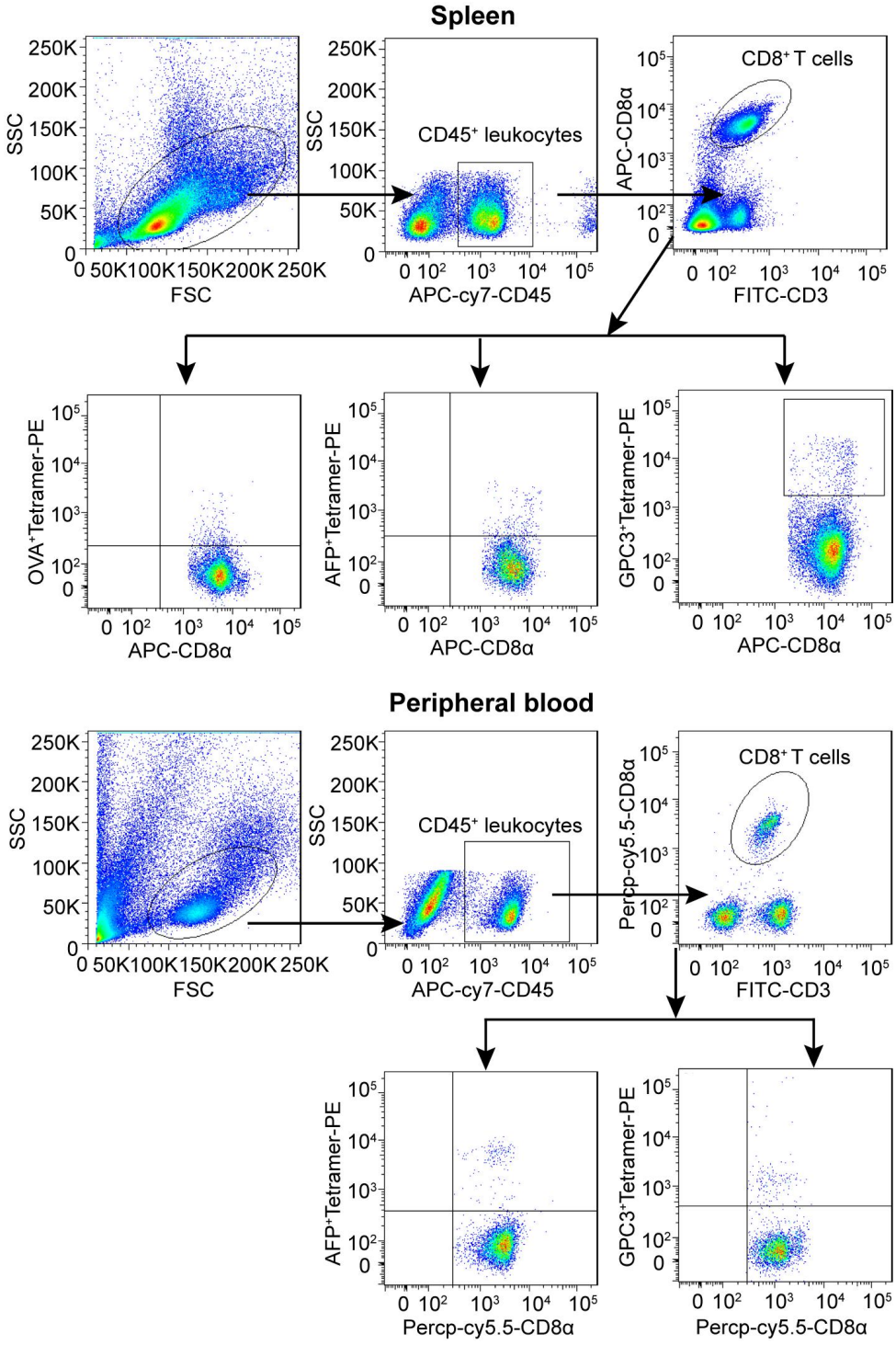
Supplementary Figure 6. Analysis of DCs in blood of orthotopic HCC mice treated with Flt3L. Flt3L (800 μg/kg/day) was injected into day-3 orthotopic HCC mice subcutaneously for 8 days consecutively and blood was collected at day 3 and day 7 after tumor inoculation. Flow cytometric and quantitative analysis of $CD11c^+$ (**a**) and $CD103^+CD11c^+$, $CD8\alpha^+CD11c^+$ and $CD11b^+CD11c^+$ (**b** and **c**) DCs in blood of orthotopic HCC mice on day 3 and 7 after tumor inoculation (n=5; two-tailed t test). *p<0.05, **p<0.001; n.s means not significant.



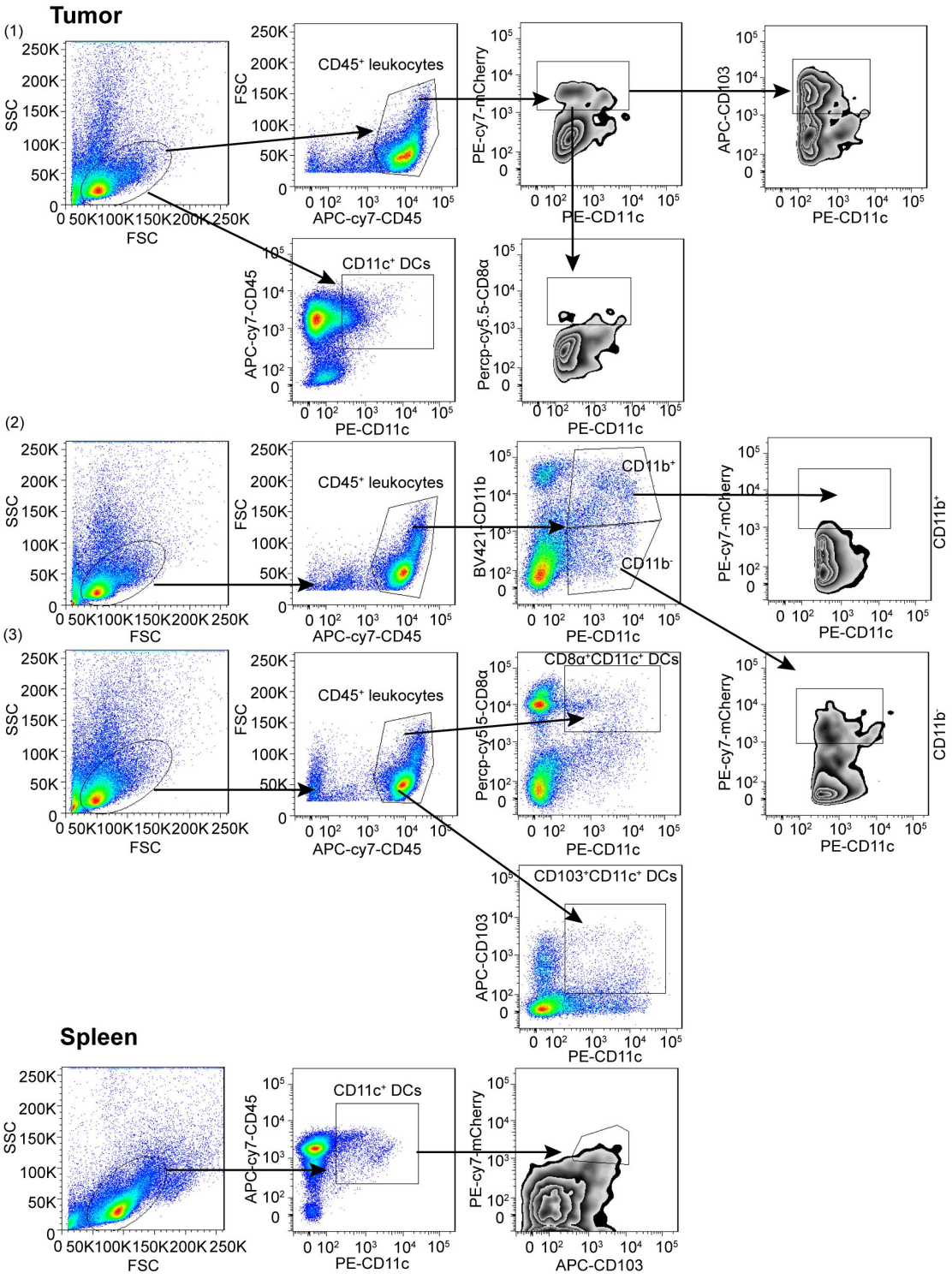
Supplementary Figure 7. Representative gating information for the flow cytometic analysis of different DC subsets in mouse peripheral blood.



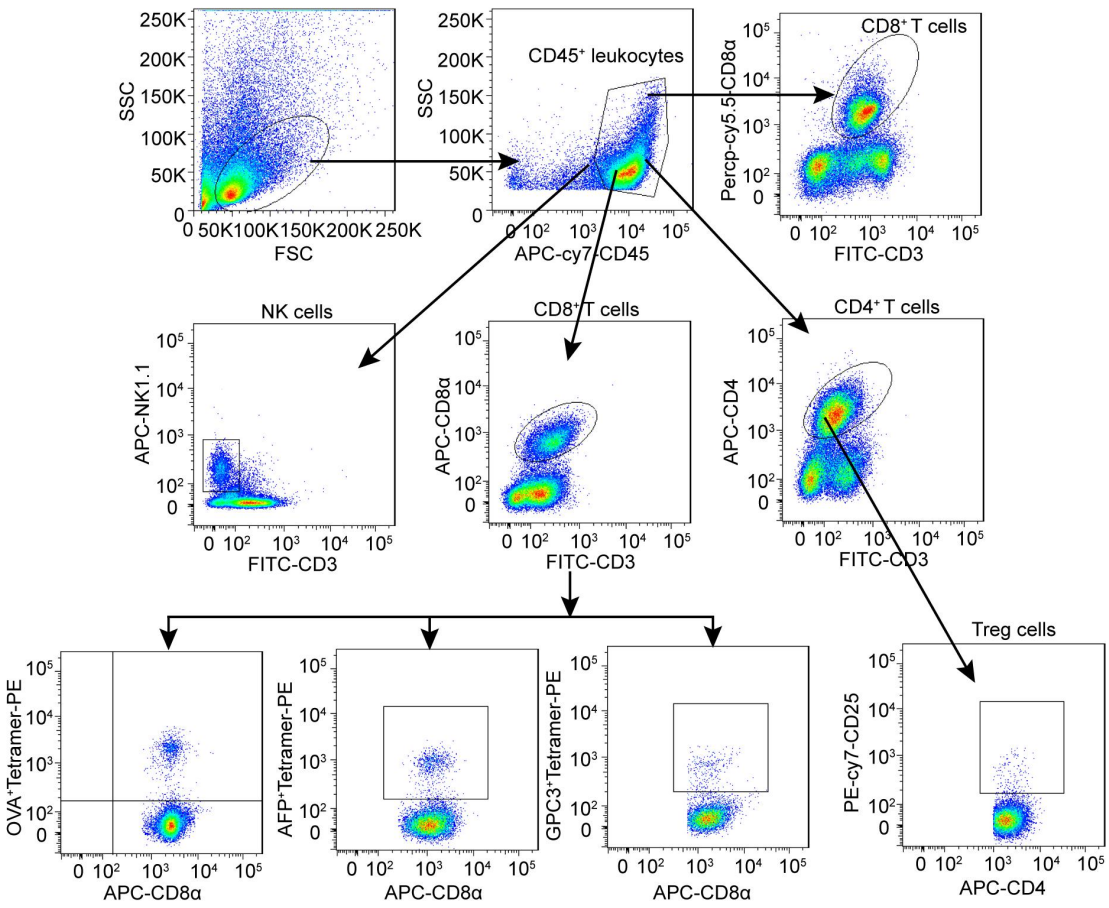
Supplementary Figure 8. Representative gating information for the flow cytometric analysis of different lymphocytes, effector and memory T cells in mouse peripheral blood.



Supplementary Figure 9. Representative gating information for the flow cytometric analysis of different antigen-specific T cells in mouse spleen and peripheral blood.



Supplementary Figure 10. Representative gating information for the flow cytometric analysis of different DC or mCherry+ DC subsets in tumor and spleen. (1)-(3) represents different DC or mCherry+ DC subsets in tumor.



Supplementary Figure 11. Representative gating information for the flow cytometric analysis of different lymphocytes, Tregs and antigen-specific T cells in tumor.