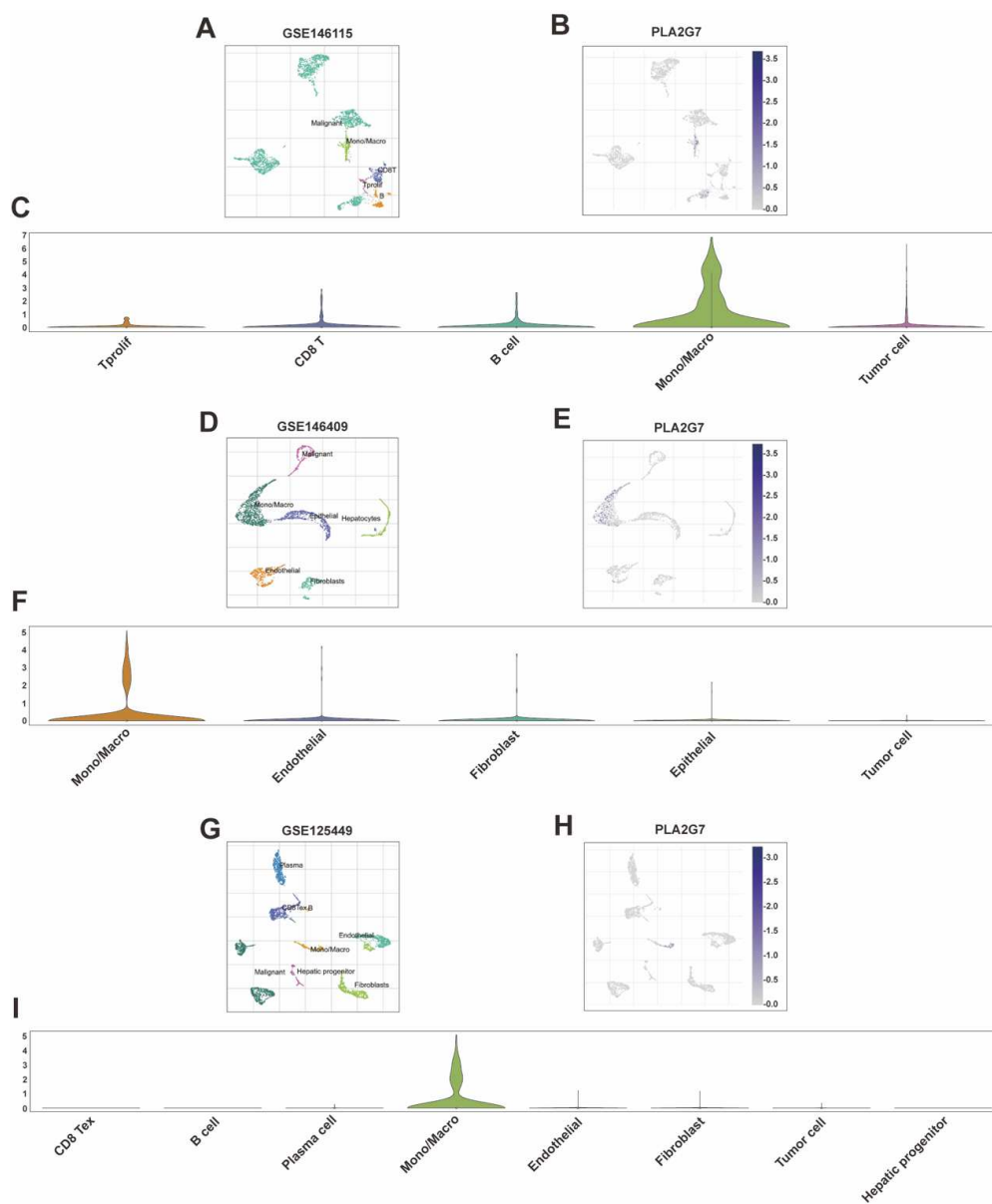
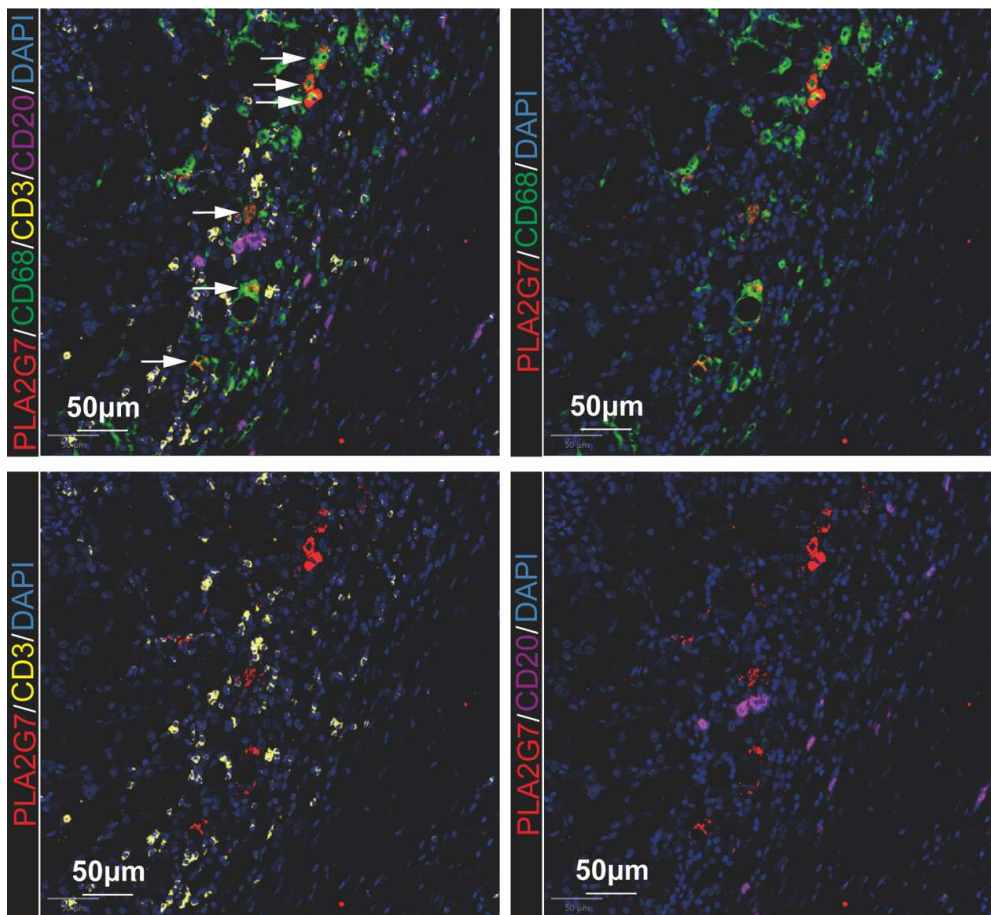


Supplementary Figures

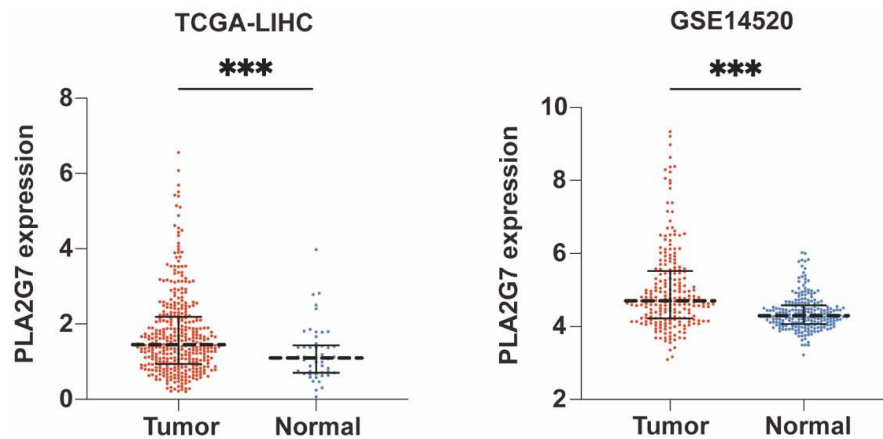
**Supplementary Figure 1. PLA2G7 is mainly expressed in macrophages in HCC. (A-C)**

Analysis of the single data from GSE146115 using the TISCH tool. t-SNE plots for distinct cell subsets (A). t-SNE plot of all single cells colored by the expression level of PLA2G7 (B). Violin plot displaying the expression levels of PLA2G7 in distinct cell subsets (C). (D-F) Analysis of the single data from GSE146409 using the TISCH tool. t-SNE plots for distinct cell subsets (D). t-

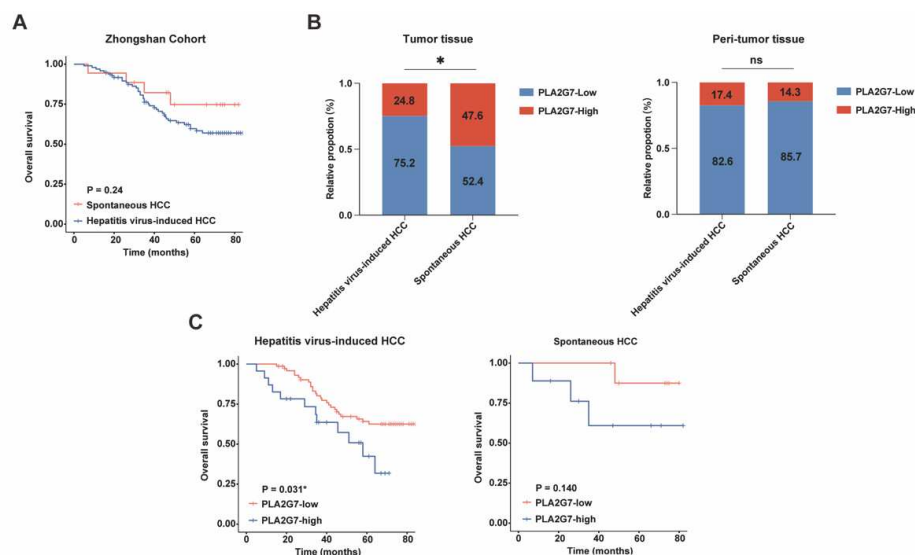
SNE plot of all single cells colored by the expression level of PLA2G7 (E). Violin plot displaying the expression levels of PLA2G7 in distinct cell subsets (F). (G-I) Analysis of the single data from GSE125449 using the TISCH tool. t-SNE plots for distinct cell subsets (G). t-SNE plot of all single cells colored by the expression level of PLA2G7 (H). Violin plot displaying the expression levels of PLA2G7 in distinct cell subsets (I). HCC: hepatocellular carcinoma; TISCH: Tumor Immune Single-cell Hu; t-SNE: t-Distributed Stochastic Neighbor Embedding.



Supplementary Figure 2. Multiplex immunofluorescence analysis for PLA2G7, CD68, CD3, and CD20 markers in human HCC tissues. Scale bar: 50 µm.

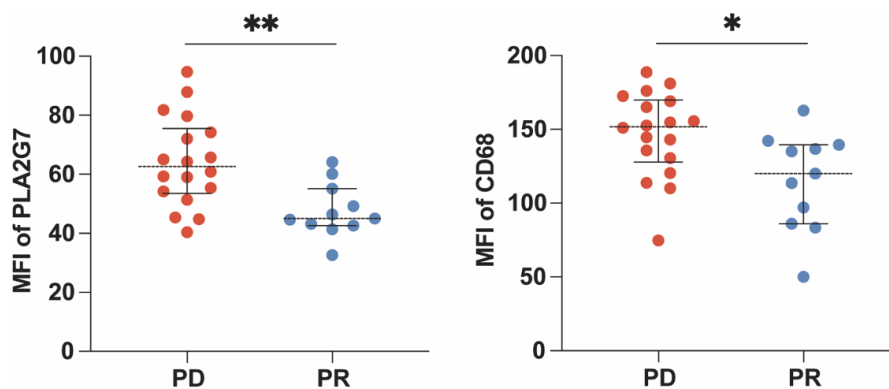


Supplementary Figure 3. The mRNA levels of PLA2G7 in HCC tissues versus peritumor tissues in TCGA-LIHC and GSE14520 cohorts. Statistical analysis was performed using the Mann-Whitney U test. Data was presented as median with IQR. *** $p < 0.001$. HCC: hepatocellular carcinoma; TCGA-LIHC, the cancer genome atlas liver hepatocellular carcinoma; IQR: interquartile range.



Supplementary Figure 4. Subgroup analysis on HCC patients with diverse oncogenic etiologies in the Zhongshan cohort. (A) OS curves comparing hepatitis virus-induced HCC and spontaneous HCC (n=115). (B) IHC expression pattern of PLA2G7 in tumor HCC (left panel) or

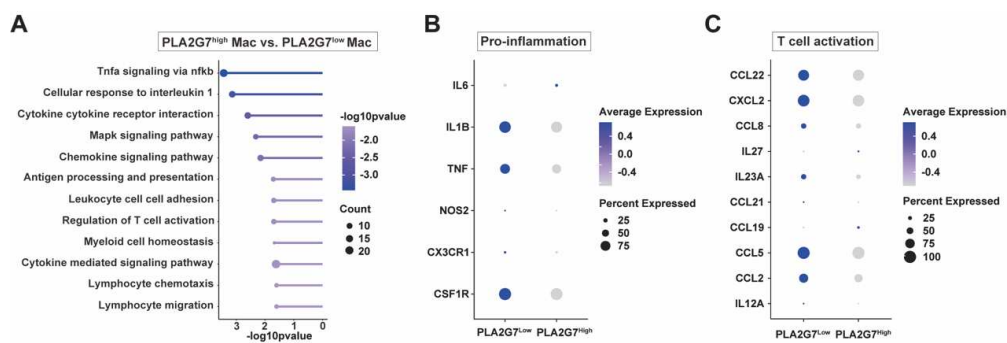
peritumor (right panel) tissues from hepatitis virus-induced HCC and spontaneous HCC (n=130). (C) OS curves for hepatitis virus-induced (n=97, left panel) or spontaneous (n=18, right panel) HCC patients stratified by low and high expression of PLA2G7. Statistical analysis was performed using the log-rank test in (A) and (C), and the Chi-square test in (B). ns, no significance; * $p < 0.05$. HCC: hepatocellular carcinoma; OS: overall survival; IHC: immunohistochemistry.



Supplementary Figure 5. The MFI of PLA2G7 and CD68 in tumor tissues from HCC

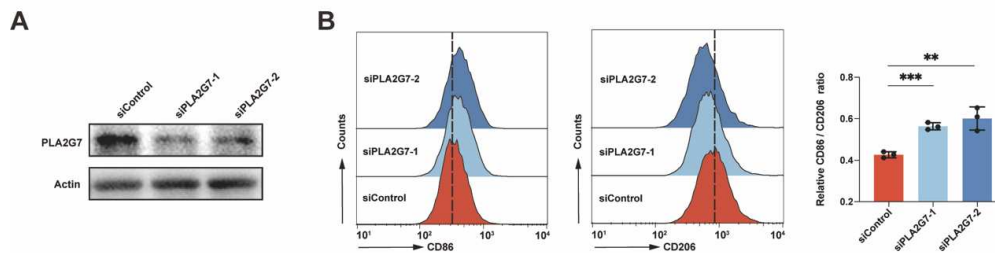
patients with PD and PR. Statistical analysis was performed using the Mann-Whitney U test.

Data was presented as median with IQR. * $P < 0.05$, ** $p < 0.01$. MFI: Mean Fluorescence Intensity; HCC: hepatocellular carcinoma; PD: progressive disease; PR: partial response; IQR: interquartile range.



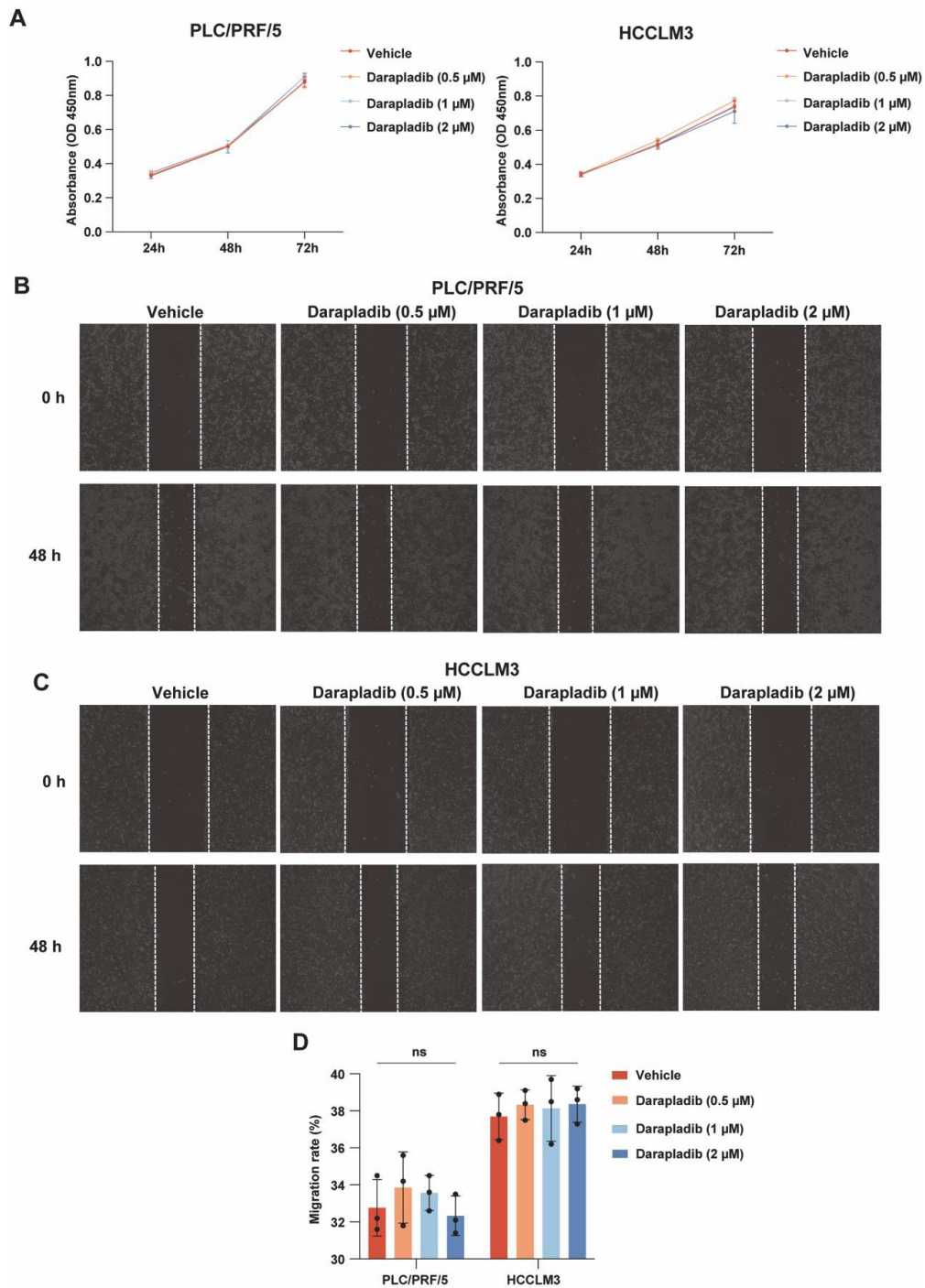
Supplementary Figure 6. PLA2G7 preserves the immunosuppressive phenotype in

macrophages. (A) GSEA enrichment analysis of PLA2G7^{high} vs. PLA2G7^{low} macrophages in Dataset 1. (B-C) Bubble plots showing the expression levels of representative marker genes for pro-inflammation and T cell activation in PLA2G7^{low} and PLA2G7^{high} macrophages. GSEA: Gene Set Enrichment Analysis.



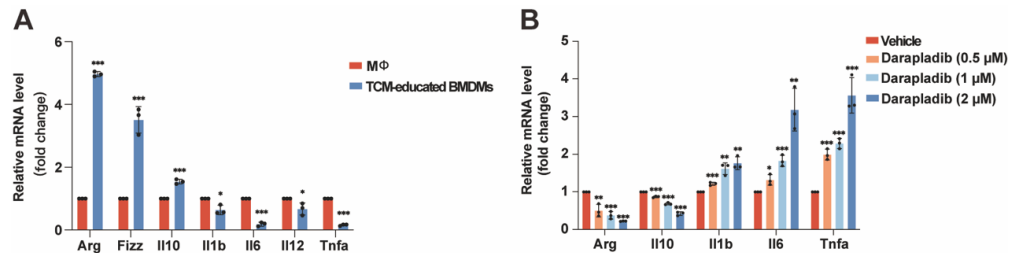
Supplementary Figure 7. Silencing PLA2G7 induces M1 polarization of human macrophages.

(A) Western blot analysis of PLA2G7 in TCM-educated THP-1-differentiated macrophages transfected with control siRNA or siRNA targeting PLA2G7. β -actin was used as loading control. (B) Flow cytometric analysis of CD86 and CD206 on TCM-education THP-1-differentiated macrophages transfected with control siRNA or siRNA targeting PLA2G7. Student's t-test. Data was presented as mean with SD. ** $p < 0.01$, *** $p < 0.001$. TCM: tumor-conditioned media; siRNA: small interfering RNA.

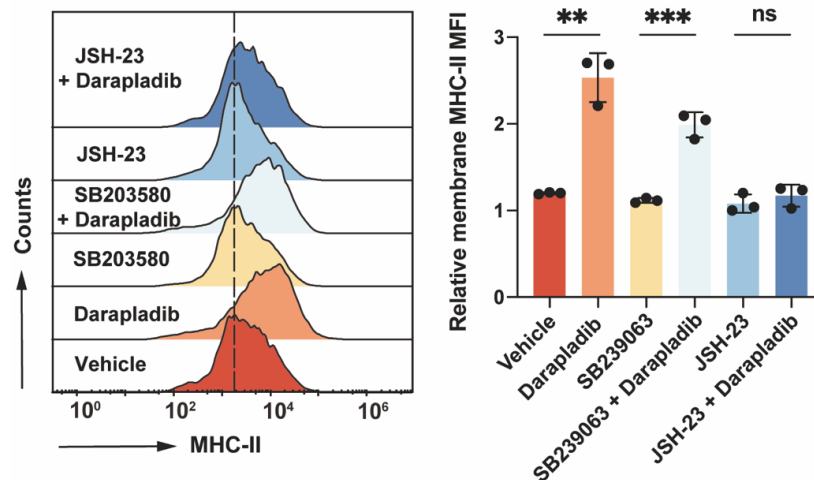


Supplementary Figure 8. Treatment with Darapladib did not impact the proliferation and migration of human HCC cells. (A) Cell proliferation in PLC/PRF/5 (left panel) and HCCLM3 (right panel) cells treated with various concentrations of Darapladib was assessed using a CCK-8 assay. (B-D) A wound healing migration assay was performed to evaluate the migration ability of

human HCC cells treated with various concentrations of Darapladib. One-way ANOVA with a post hoc LSD test. Data was presented as mean with SD. ns, no significance. HCC: hepatocellular carcinoma; SD: standard deviation.

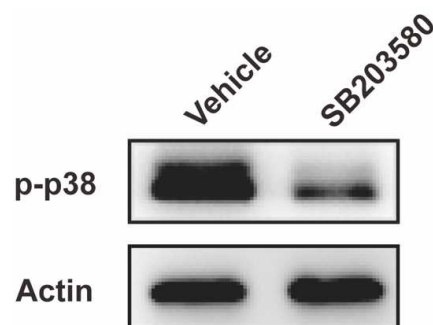


Supplementary Figure 9. qPCR analysis of the mRNA levels of immune-regulatory genes in BMDMs. (A) The mRNA levels of immune-regulatory genes in MΦ (untreated BMDMs) versus TCM-educated BMDMs. (B) The mRNA levels of immune-regulatory genes in TCM-educated BMDMs treated with either Darapladib (0.5 μM, 1 μM, and 2 μM) or vehicle. Statistical analysis was performed using the Student's t-test. Data was presented as mean with SD. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. BMDM: bone marrow-derived macrophage; TCM: tumor condition medium; SD: standard deviation.

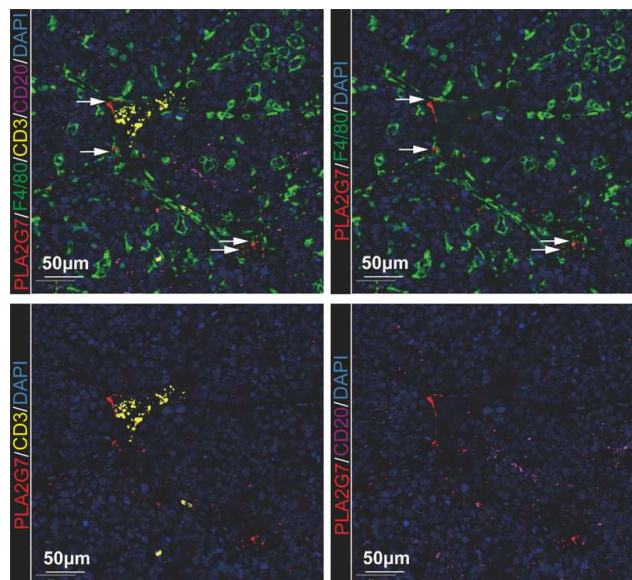


Supplementary Figure 10. Flow cytometric analysis of membrane MHC-II on TCM-educated

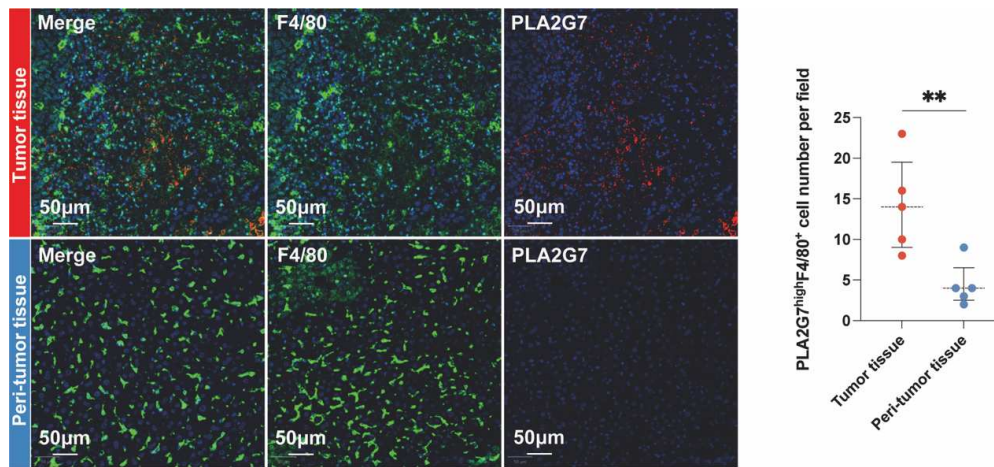
BMDMs. The cells were treated with either Darapladib (2 μ M), SB203580 (10 μ M), SB203580 (10 μ M) + Darapladib (2 μ M), JSH-23 (10 μ M), JSH-23 (10 μ M) + Darapladib (2 μ M), or vehicle. Representative flow cytometry data (left panel) and the statistical diagram (right panel) are shown. Student's t-test. Data was presented as mean with SD. ns, no significance; ** $p < 0.01$, *** $p < 0.001$. TCM: tumor condition medium; BMDM: bone marrow-derived macrophage; SD: standard deviation; MFI: mean fluorescence intensity.



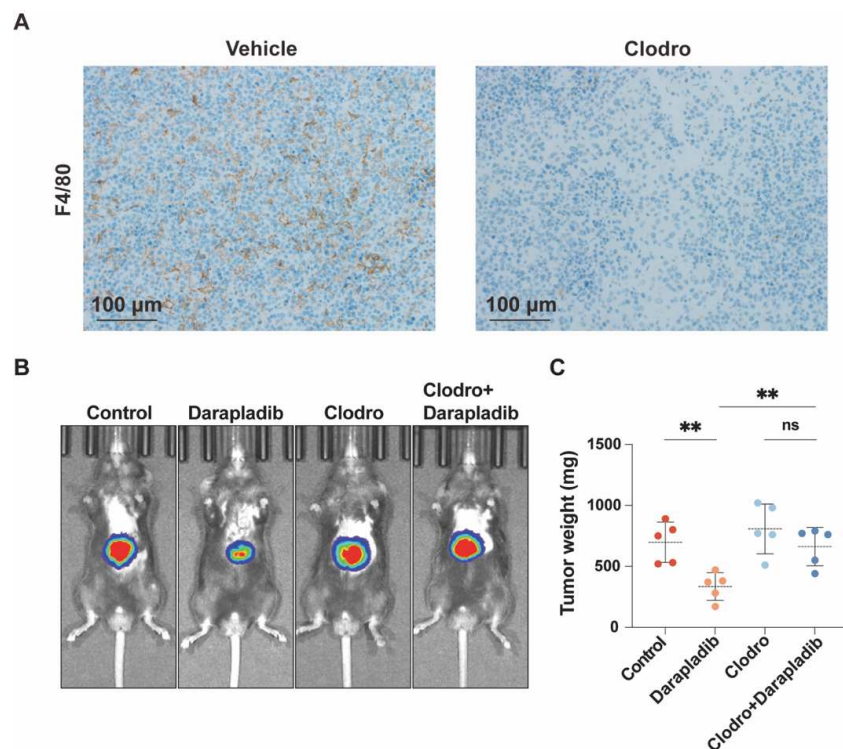
Supplementary Figure 11. Western blot analysis of p-p38 in macrophages treated with either SB203580 or vehicle.



Supplementary Figure 12. Multiplex immunofluorescence analysis for PLA2G7, F4/80, CD3, and CD20 markers in murine orthotopic HCC tissues. Scale bar: 50 μ m.



Supplementary Figure 13. Multiplex immunofluorescence analysis for PLA2G7 and F4/80 in tumor or peritumor tissues from murine orthotopic HCC. Representative images and statistical diagram illustrating PLA2G7^{high} F4/80⁺ cells are shown. Scale bar: 50 μm. Student's t-test. Data was presented as mean with SD. **p<0.01. HCC: hepatocellular carcinoma.



Supplementary Figure 14. Depletion of macrophages abolishes the anti-tumor effects of

Darapladib. (A) Representative IHC images depicting F4/80⁺ macrophages in murine HCC tumors treated with either vehicle or clodronate liposomes. Scale bar: 100 μ m. (B-C) Murine orthotopic HCC treated with either vehicle or Darapladib in control or macrophage-depleted mice. Representative bioluminescence images and statistical diagram illustrating tumor weights are presented (n=5, each). Student's t-test. Data was presented as mean with SD. ns, no significance; **p<0.01. IHC: immunohistochemistry; HCC: hepatocellular carcinoma; SD: standard deviation.

Supplementary Tables

Table S1. Primers used for quantitative real-time PCR in this study

Name	Forward Sequence (5' to 3')	Reverse Sequence (3' to 5')
β -actin	GGCTGTATTCCCCTCCATCG	CCAGTTGGTAACAATGCCATGT
Arg	CTCCAAGCCAAAGTCCTTAGAG	AGGAGCTGTCATTAGGGACATC
Fizz	CCAATCCAGCTAACTATCCCTCC	ACCCAGTAGCAGTCATCCCA
Il10	GCTCTTACTGACTGGCATGAG	CGCAGCTCTAGGAGCATGTG
Il1b	GCAACTGTTCTGAACTCAACT	ATCTTTTGGGGTCCGTCAACT
Il6	TAGTCCTTCCTACCCCAATTTCC	TTGGTCCTTAGCCACTCCTTC
Il12	TGGTTTGCCATCGTTTTGCTG	ACAGGTGAGGTTCACTGTTTCT
Tnf α	CCCTCACACTCAGATCATCTTCT	GCTACGACGTGGGCTACAG

Table S2. Antibodies used for Western blot analysis

Antibody	Catalogue number	Company
Anti-PLA2G7	#15526-1-AP	Proteintech
Anti-Phospho-Ikk α / β	#2697	Cell Signaling Technology
Anti-Ikk β	#2370	Cell Signaling Technology
Anti-Phospho-NF- κ B p65	#3033	Cell Signaling Technology
Anti-NF- κ B p65	#8242	Cell Signaling Technology
Anti-NF- κ B p50	#12540	Cell Signaling Technology
Anti-Phospho-p44/42 MAPK (Erk1/2)	#4370	Cell Signaling Technology
Anti-p44/42 MAPK (Erk1/2)	#4695	Cell Signaling Technology
Anti-Phospho-SAPK/JNK	#4668	Cell Signaling Technology
Anti-SAPK/JNK	#9252	Cell Signaling Technology
Anti-Phospho-p38 MAPK	#4511	Cell Signaling Technology
Anti-p38 MAPK	#8690	Cell Signaling Technology