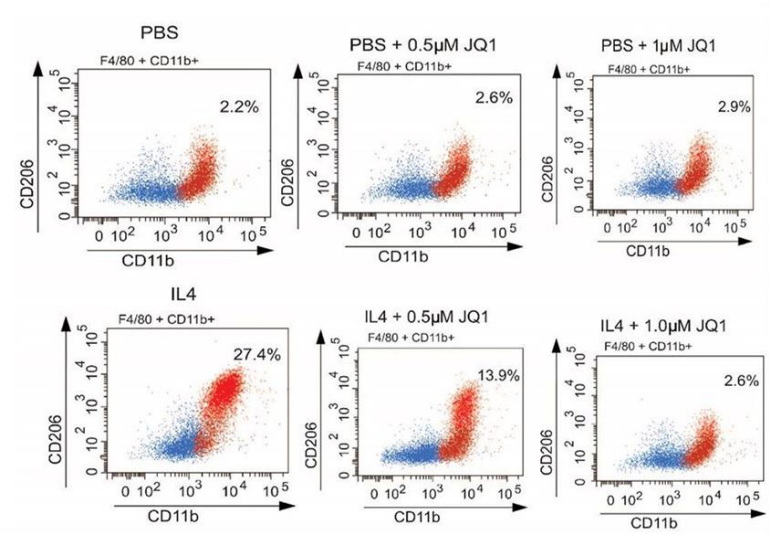
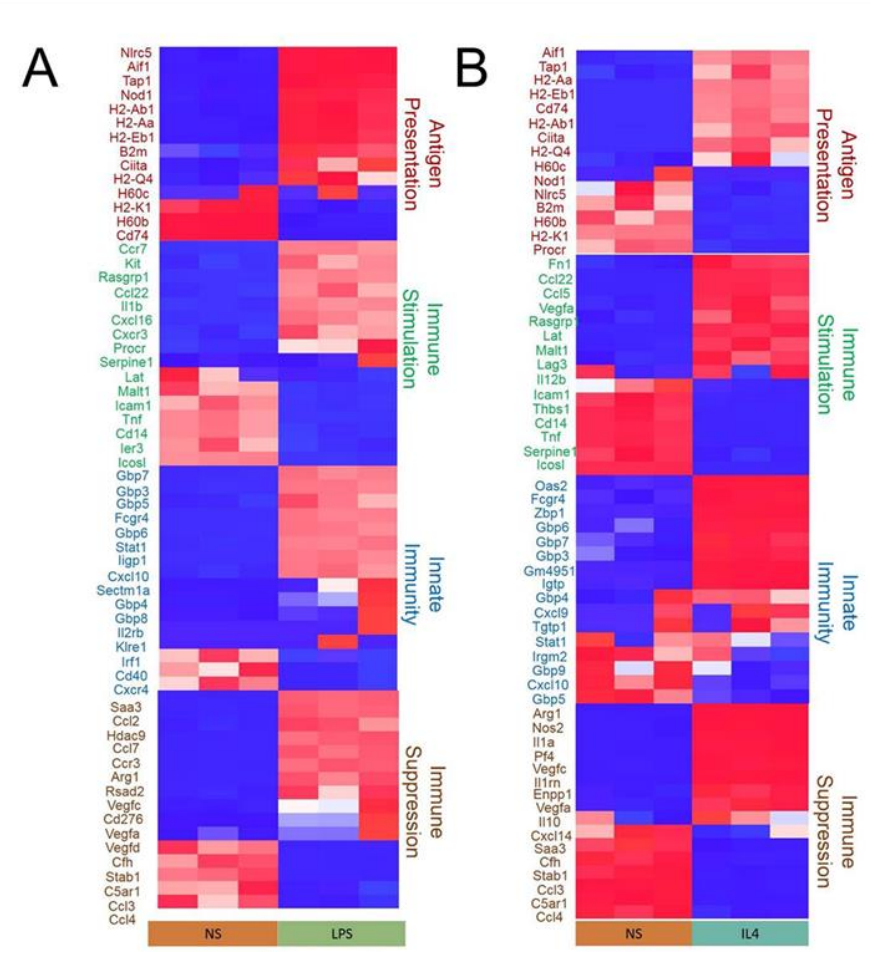
Supplementary Figures

Supplementary Fig. S1



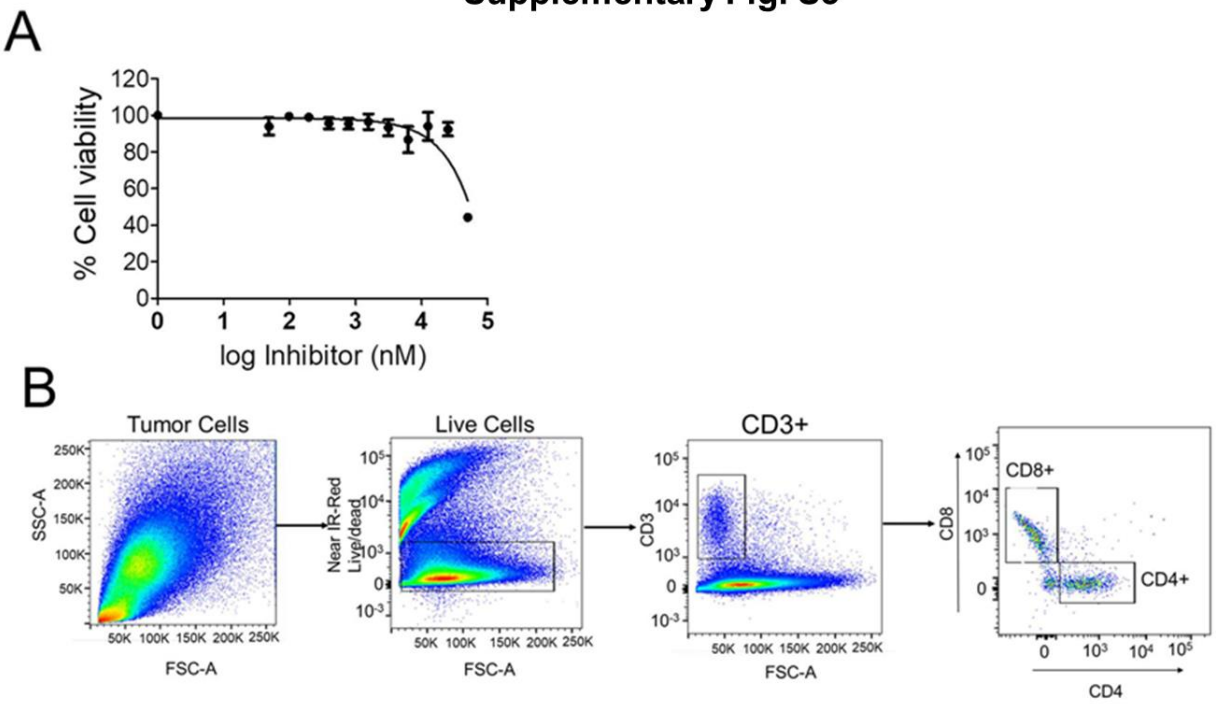
Supplementary Fig. S1. JQ1 blocks IL4 induced CD206 expression: FACS analysis of CD206+ macrophages in IL4 stimulated BMDMs treated with JQ1.

Supplementary Fig. S2



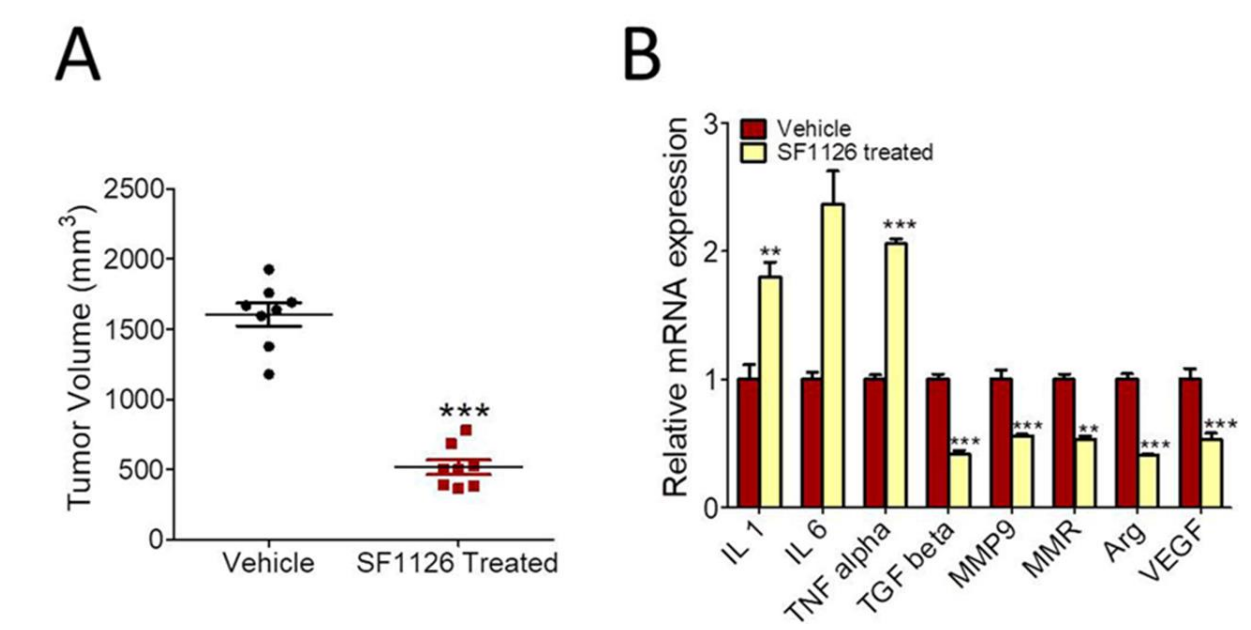
Supplementary Fig. S2. Differentially expressed genes in LPS-stimulated or IL4 stimulated BMDMs: **A-B.** BMDMs were stimulated with 100ng/ml LPS for 24 hrs or 20ng/ml of IL4 followed by RNA isolation and RNA-Seq. Heat map of log2 fold differences from sample wise mean expression for genes that were significantly differentially expressed (at an FDR of 0.05) in LPS stimulated (A) or IL4 stimulated (B) versus NS stimulated BMDMs.

Supplementary Fig. S3



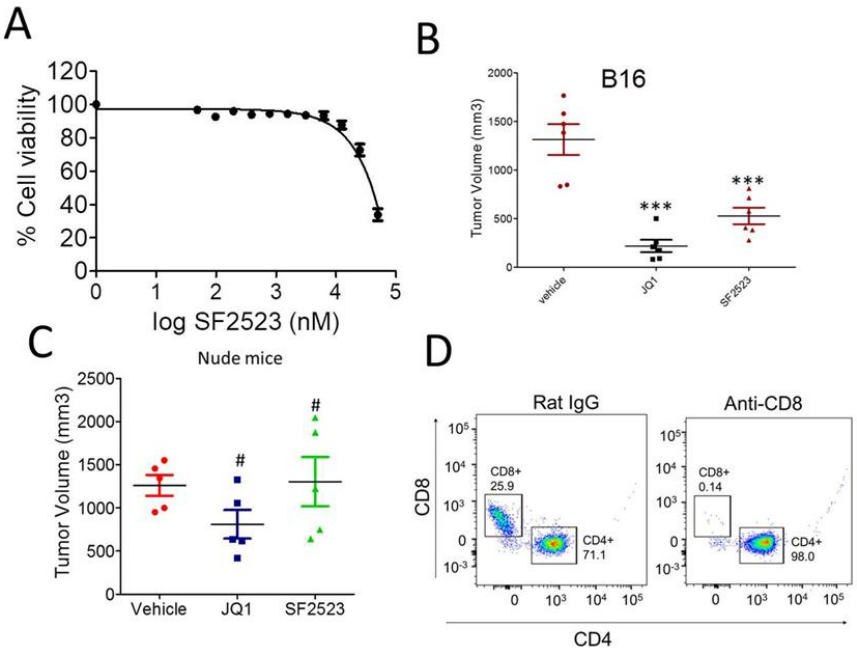
Supplementary Fig. S3. Effect of JQ1 on LLC tumor growth. A. Cell viability assay using Alamar Blue showing no direct effect of JQ1 on LLC cells. **B.** Gating strategy of CD4+ and CD8+ T cells.

Supplementary Fig. S4



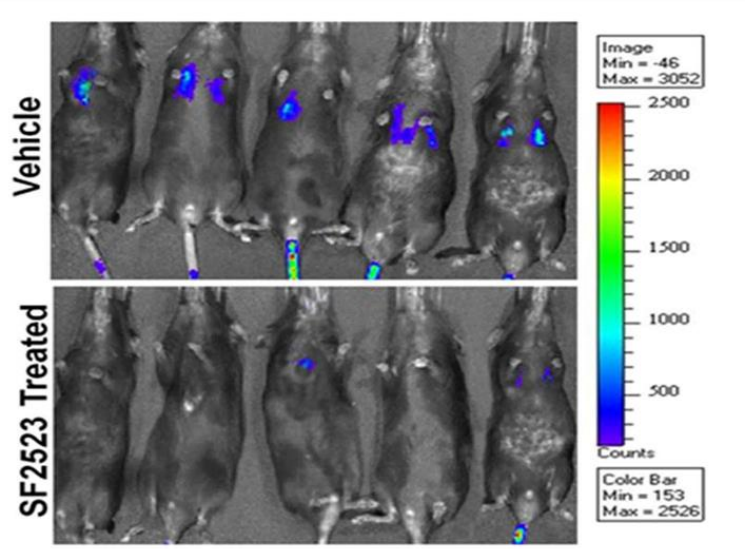
Supplementary Fig. S4. SF1126 blocks tumor growth and immunosuppressive macrophage polarization A. 1X10^5 LLC cells were injected into C57BL/6 mice and were treated with 40mg/kg SF1126 three times a week **B.** Quantitative PCR analysis of mRNA for immunosuppressive genes in the CD11b+ cells isolated from treated and untreated tumors described in A.

Supplementary Fig. S5



Supplementary Fig. S5. JQ1 and SF2523 reduce tumor growth due to its effect on macrophages. A. SF2523 does not affect cell viability of LLC cells *in vitro.* Dose response of the effect of SF2523 on *in vitro* LLC cell viability. **B**. Tumor volume of B16 tumors injected in C57/Bl6 mice and treated with 40mg/kg JQ1 or 40 mg/kg SF2523 **C.** Tumor volume of CT26 tumors injected in nude mice and treated with 40mg/kg JQ1 or 40 mg/kg SF2523. **D.** FACS data showing depletion of CD8 population in anti-CD8 treated tumors.

Supplementary Fig. S6



Supplementary Fig. S6. SF2523 inhibits B16 tumor metastasis A. Experimental metastasis of B16 melanoma cells in WT mice treated with or without SF2523 (n=5). B16 F10 luciferase cells (5×10^5 cells) were injected through the tail vein, and 40mg/kg SF2523 was administered every other day until lungs were removed after 15 days.The luciferase signal was monitored every third day on IVIS by injecting luciferin, until lungs were harvested (n=5).

Supplementary Tables

Gene	Forward primer	Reverse primer
IL-6	5'-TGTGGGATTTTCCCATGAGT-3'	5'-TGCCTTCACTTACTTGCAGAGA- 3'
Chi3l3	5'-CATTTGCCCTGCCTTTGG-3'	5'-TCTTTCATGGATATTGATTTCCTAAGAG-3'
Retnla	5'- TGCAATTCTTTGATGCTGTGTCT-3'	5'-TTGTGTCCCTTGGCTACATGAA-3'
Arg 1	5' –TGAACAGGCTGTATTAGCCAACA-3'	5'-AGCACCCTCAACCCAAAGTG-3'

Supplementary Table S1: Primers used for ChIP analysis

a.	**LPS Up (total = 7822)**	**LPS Down (total = 4340)**	**Not Significant in LPS**
LPS + JQ1 Up	221	3210	1266
LPS +JQ1 Down	6484	162	1259
b.			
LPS + SF2523 Up	1327	1432	1041
LPS + SF2523 Down	4183	1436	1925
c.	**IL4 Up (total = 8979)**	**IL4 Down (total = 4177)**	**Not Significant in IL4**
IL4 + JQ1 Up	224	3170	1002
IL4 + JQ1 Down	7470	116	1026
d.			
IL4 + SF2523 Up	1677	1416	1048
IL4 + SF2523 Down	3755	1052	1389

Supplementary Table S2: Contingency tables representing the effects on the number of shared over or under expressed genes of different exposures. The column headers (bolded) represent the genes up- or downregulated in macrophages solely exposed to LPS or IL4, agents known to induce macrophage polarization to M1 or M2 states, respectively. The row headers represent the genes up or downregulated in macrophages exposed to LPS or IL4 in addition to JQ1 and SF2523. The cells at each intersection represent the number of genes shared in common between the two groups; the column farthest to the right represents the

number of genes found to be significantly up- or downregulated solely in the macrophages exposed to 2 agents. Only the significantly up- or downregulated genes ($p \leq 0.05$) were counted for the table.