Supplementary Information:

A natural CCR2 antagonist relieves tumor-associated macrophages mediated immunosuppression to produce a therapeutic effect for liver cancer

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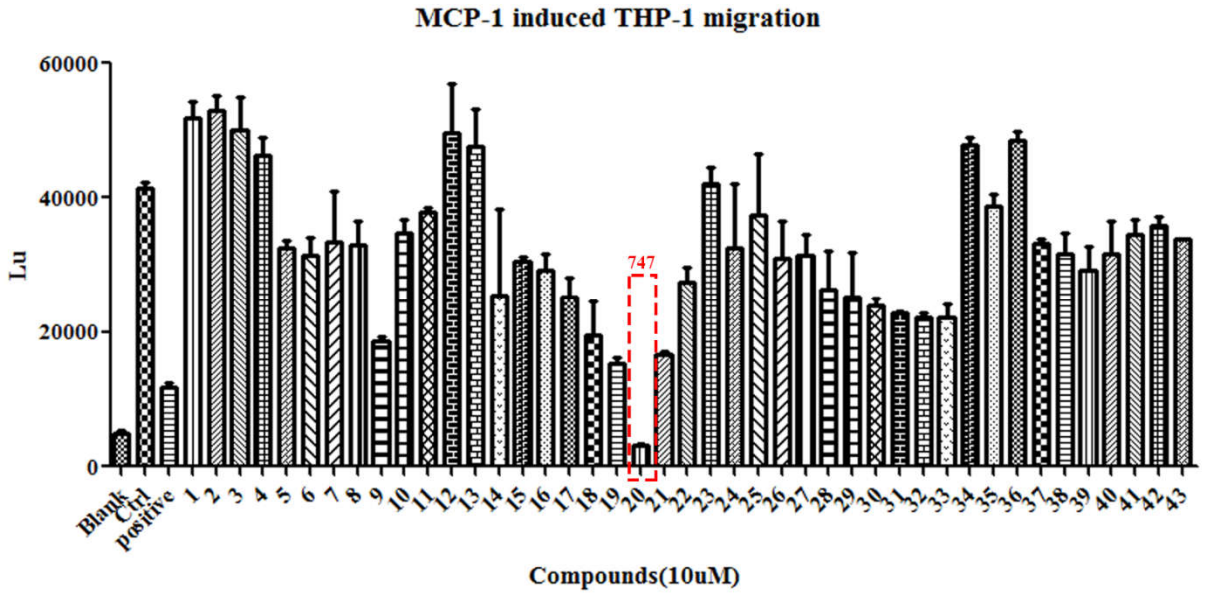

Figure S1. Screening results of CCR2 antagonist candidates based on MCP-1(hCCL2)-induced THP-1 chemotaxis.

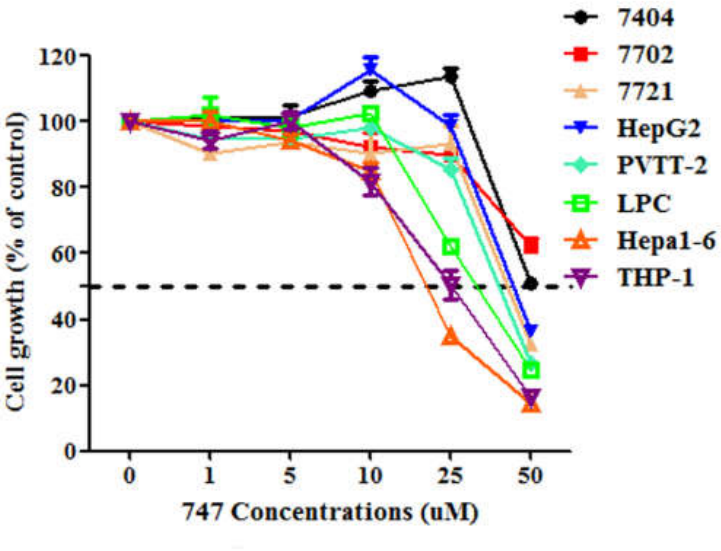

Figure S2. Growth of various cell lines after 48 h of exposure to 747.

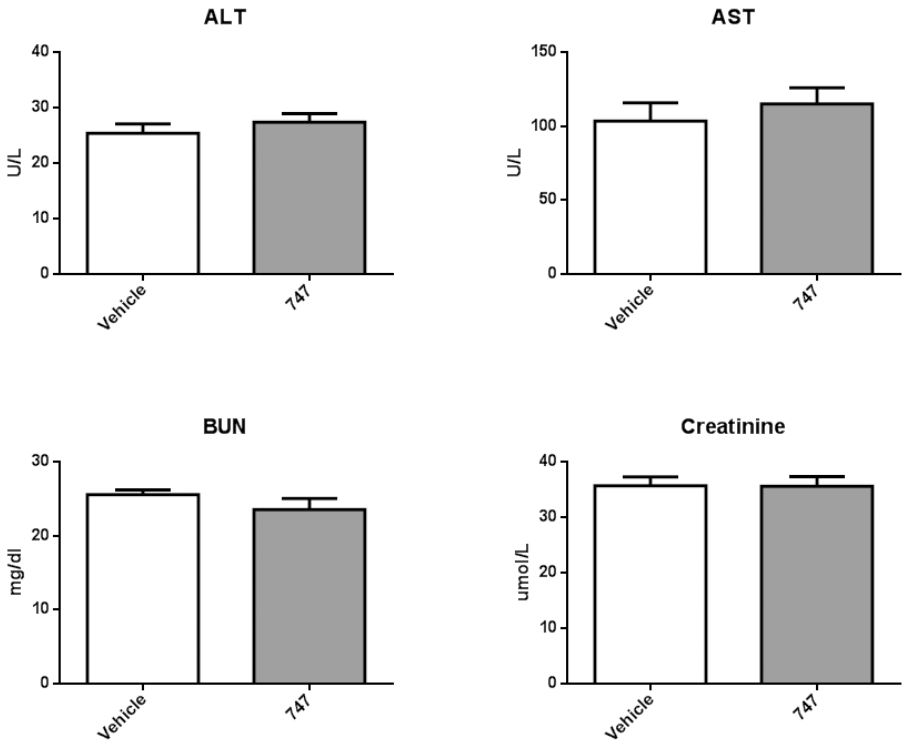

Figure S3. 747 shows no liver or kidney toxicity through ALT, AST, BUN(blood urea nitrogen), Creatinine in mice.

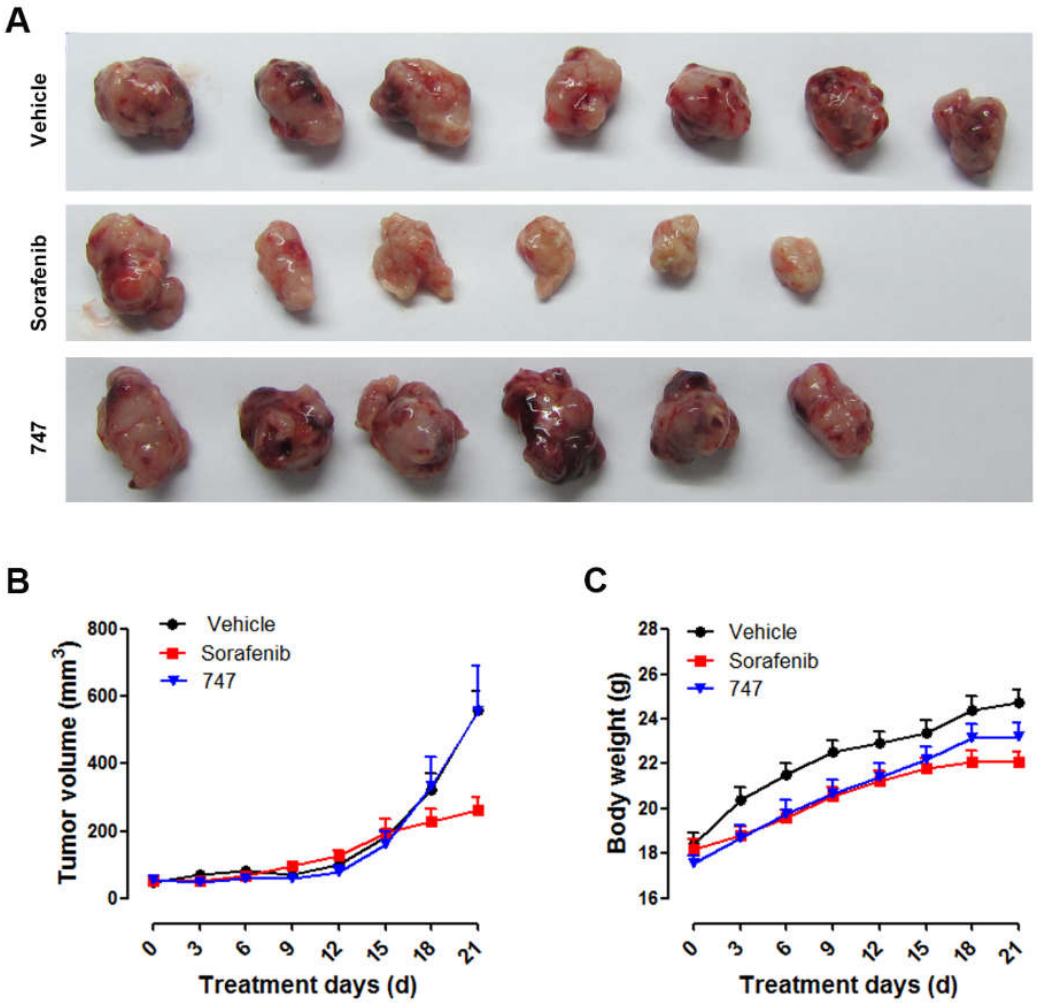

Figure S4. 747 shows no anti-tumor effect in T cell-deficient nude mice.

(A)Representative images of subcutaneous Hepa1-6 tumors in nude mice after 747 or sorafenib treatment. The tumors were measured (B), and body weights were was monitored during treatment (C).

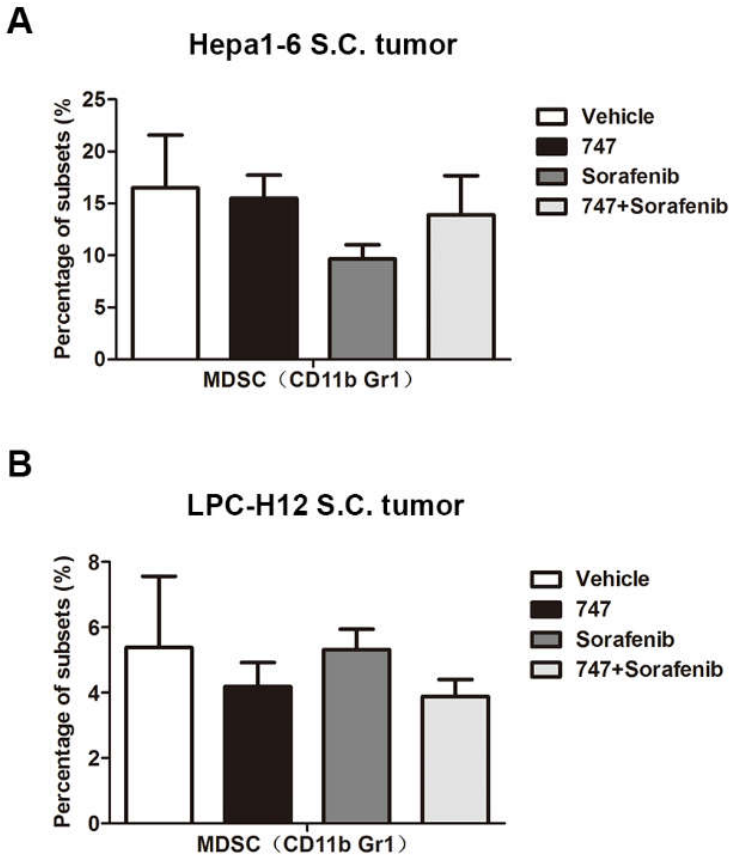

Figure S5. 747, sorafenib, or the combination had little effect on the proportion of MDSCs in Hepa1-6 subcutaneous tumors (A) or LPC-H12 subcutaneous tumors (B).

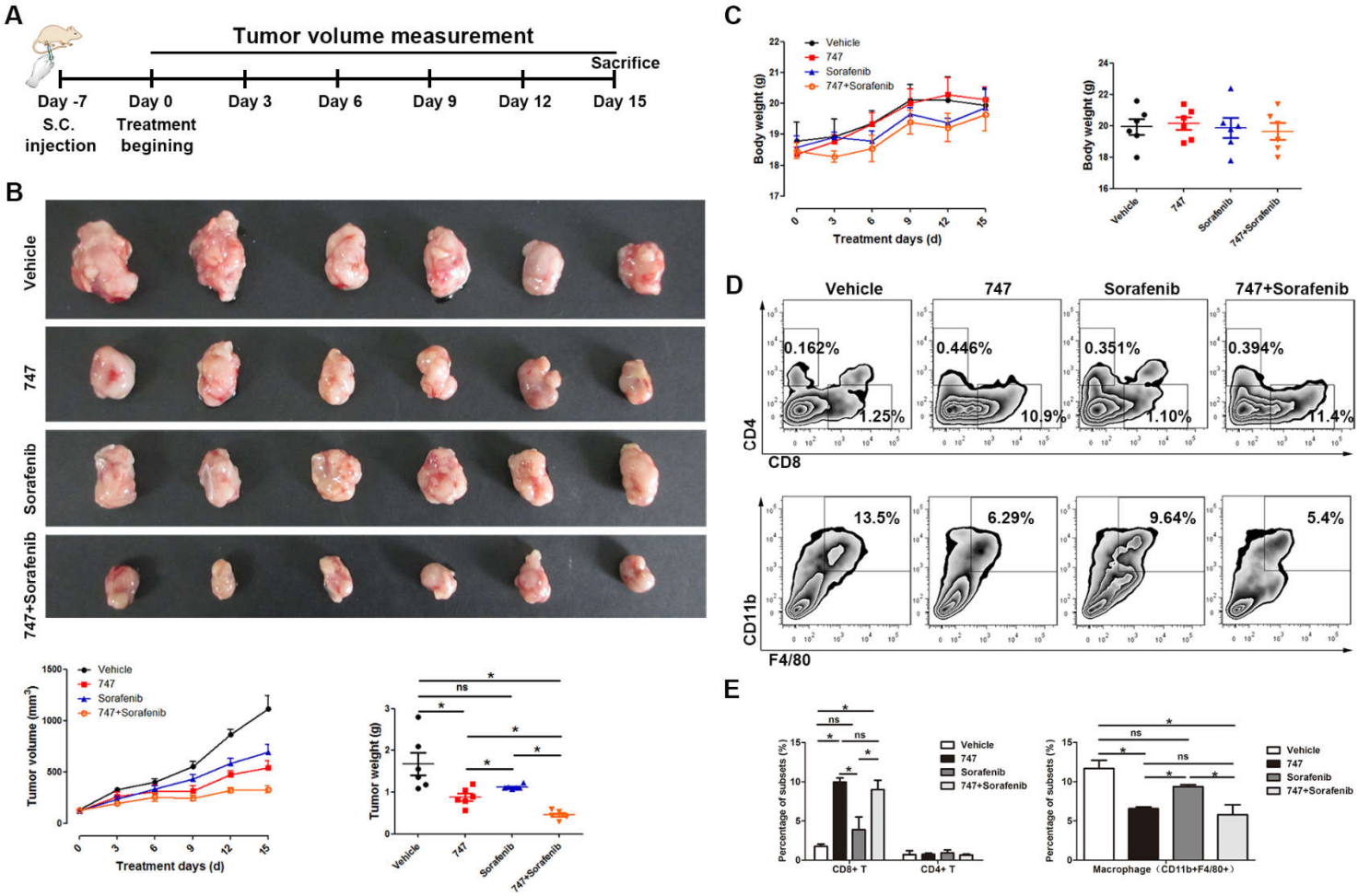

Figure S6. 747 combined with sorafenib enhances antitumor responses in LPC-H12 subcutaneous tumors.

(A) The schedule of 747 treatment and tumor measurement. (B) Representative photographs of subcutaneous liver tumors after treatment with 747, sorafenib, or the combination and effects on tumors as measured by tumor growth and weight. (C) Body weight changes of mice during treatment. (D, E) Proportions of TAMs, CD4 T cells, and CD8 T cells were quantified by FACS. Data are presented as means ± SEM. *p < 0.05.