Supplementary Figure 1. Autophagy flux of CD8+ or CD4+ TILs, especially exhausted TILs is significantly impaired

A, Representative flow cytometric results of LC3-II from the PTCs (CD8+ or CD4+) and TILs (CD8+ or CD4+) treated with or without CQ and the corresponding statistical results were shown (n=3).

B, Representative flow cytometric results for LC3-II in PD1+ TILs (CD8+ or CD4+) and PD1- TILs (CD8+ or CD4+) with or without CQ treatment and the corresponding statistical results were shown (n=4).

C, Representative flow cytometric results for LC3-II in TIM3+ TILs (CD8+ or CD4+) and TIM3- TILs (CD8+ or CD4+) with or without CQ treatment and the corresponding statistical results were shown (n=4).

D, Representative flow cytometric results for LC3-II in LAG3+ TILs (CD8+ or CD4+) and LAG3- TILs (CD8+ or CD4+) with or without CQ treatment and the corresponding statistical results were shown (n=4).

E, Representative flow cytometric results for LC3-II in Ki67+ TILs and Ki67- TILs (CD8+ or CD4+) with or without CQ treatment and the corresponding statistical results were shown (n=4).

F, Representative flow cytometric results for LC3-II in IFN-γ+ TILs and IFN-γ- TILs (CD8+ or CD4+) with or without CQ treatment and the corresponding statistical results were shown (n=4).

Supplementary Figure 2. Spermidine enhances the autophagic flux in CD8+ or CD4+ TILs

A, Illustration of the lentiviral constructs encoding the autophagy gene LC3 in conjunction with mCherry and eGFP. Replacement of the LC3b glycine at amino acid 120 position with alanine is used as an autophagy incompetent construct.

B, Representative flow cytometry plot of autophagy flux in the indicated conditions by measuring the loss of GFP in mCherry TILs and the corresponding statistical results were shown (CD8+ or CD4+) (n=5).

Supplementary Figure 3. Dysfunction of CD8+ or CD4+ TILs are ameliorated by spermidine.

A-C, Representative flow cytometric plots of TILs (CD8+ or CD4+) expressing inhibitory immunoreceptors (PD1, TIM3, LAG3) with or without spermidine treatment was shown **(A)**. Statistical summary of proportions of PD1+, TIM3+ or LAG3+ TILs (CD8+ or CD4+) with or without spermidine treatment was shown **(B)**. Statistical summary of double positive (PD1+TIM3; PD1+LAG3; TIM3+LAG3) TILs (CD8+ or CD4+) with or without spermidine

treatment was shown **(C)**.

D-E, Representative flow cytometric plots showed proportions of Ki67+ TILs (CD8+ or CD4+) with or without spermidine treatment **(D).** Statistical summary of proportions of Ki67+ TILs (CD8+ or CD4+) with or without spermidine treatment was shown **(E)**.

Supplementary Figure 4. Restoration of autophagy flux improves CD107a expression of CD8+ or CD4+ TILs

A-B, Representative flow cytometric plots showed proportions of CD107a+ TILs (CD8+ or CD4+) and sTILs (CD8+ or CD4+) **(A)**. Statistical summary of proportions of CD107a+ TILs (CD8+ or CD4+) and sTILs (CD8+ or CD4+) with or without coculture with autologous tumor cells was shown (n=6) **(B)**.

Supplementary Figure 5. Spermidine enhances the in vivo antitumor effect of TILs.

A, The growth curves of tumors in the PDX mice infused with TILs, sTILs and saline (control) were shown (n=5).

B-F, Adoptively transferred TILs and sTILs in PDX tumors were analysed for expression of CD4 (**B**), CD8 (**C**), PD1 (**D**), TIM3 (**E**) and LAG3 (**F**) by flow cytometry at day 12 after tumor inoculation (n=3).

G, A statistical summary of counts of transferred T cells per g tumour was shown at day 20 after tumor implantation (n=3).