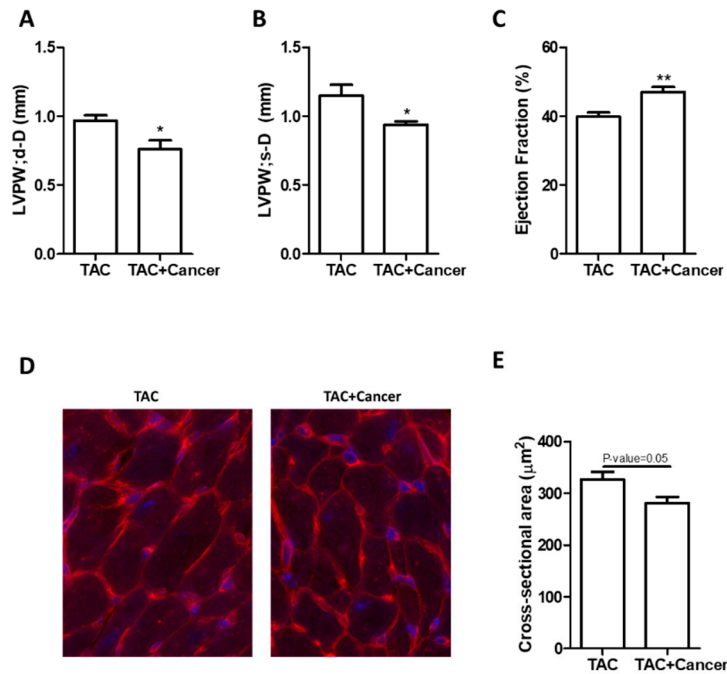


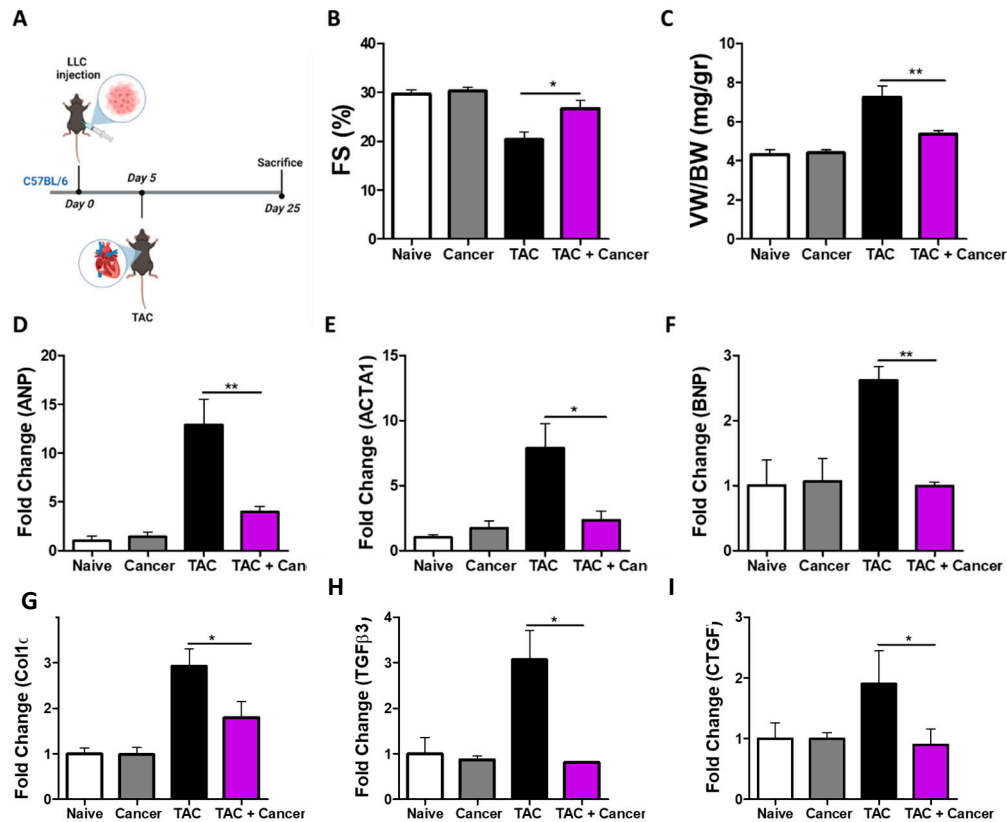
Supplementary material

Supplemental Figures:



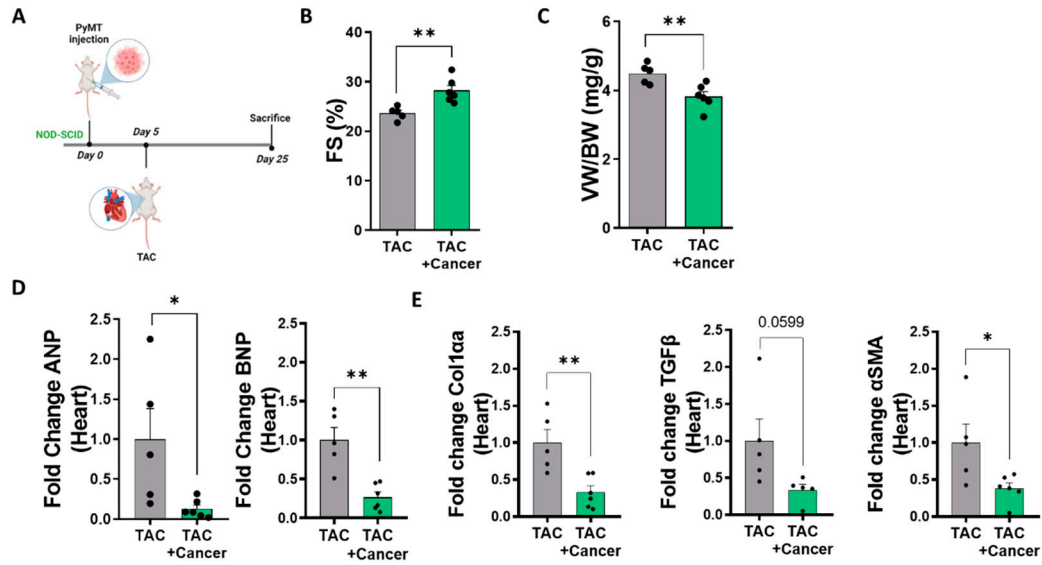
Supplemental Figure S1: Echocardiography parameters and cell size analysis.

A Left ventricular posterior wall thickness in diastole (mm). **B** Left ventricular posterior wall thickness in systole (mm). **C** Left ventricular ejection fraction (%). **D** Female mice were either injected with PyMT cancer cells or left untreated. Five days after, all mice underwent TAC surgery for 3 weeks and hearts were analyzed. Ventricles sections were stained with FETC-labeled wheat germ agglutinin and cell size was analyzed. Scale bar=50μm. **E**. Quantification of cell size from D represented as cross sectional area in μm². Results are presented as mean presented as mean ± SEM, student-t test. * $P < 0.05$, ** $P < 0.01$.



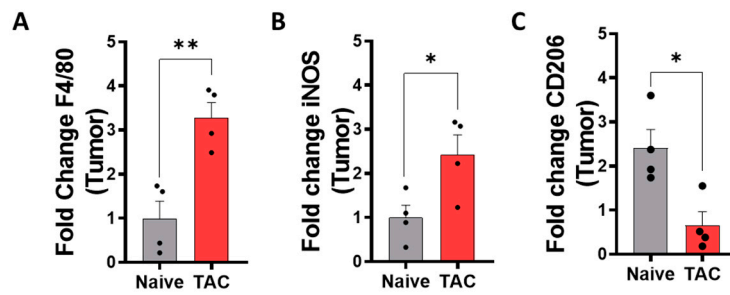
Supplemental Figure S2: LLC Tumor growth improves cardiac dysfunction following TAC in male mice.

A. Schematic diagram of the experimental timeline. The 4 experimental groups included are naïve mice, LLC-injected mice, TAC-operated either LL-bearing or non-bearing mice. **B.** Fractional shortening (FS) of the experimental cohorts, calculated from echocardiography data, at day 25. Calculated based on parameters in Supp. Table 5. **C.** Ventricular weight/body weight ratio (VW/BW) of the experimental cohorts at day 25. **D-I.** The mRNA levels of hypertrophic markers ANP and BNP and ACTA1 (D-F) and fibrosis markers collagen, TGFβ3, and CTGF (G-I) in the hearts of the experimental cohorts at day 25, measured using qRT-PCR, normalized to the GAPDH housekeeping gene. The results are presented as mean ± SEM, student-t test. * $P < 0.05$, ** $P < 0.01$. ($n = 5$ in all groups).



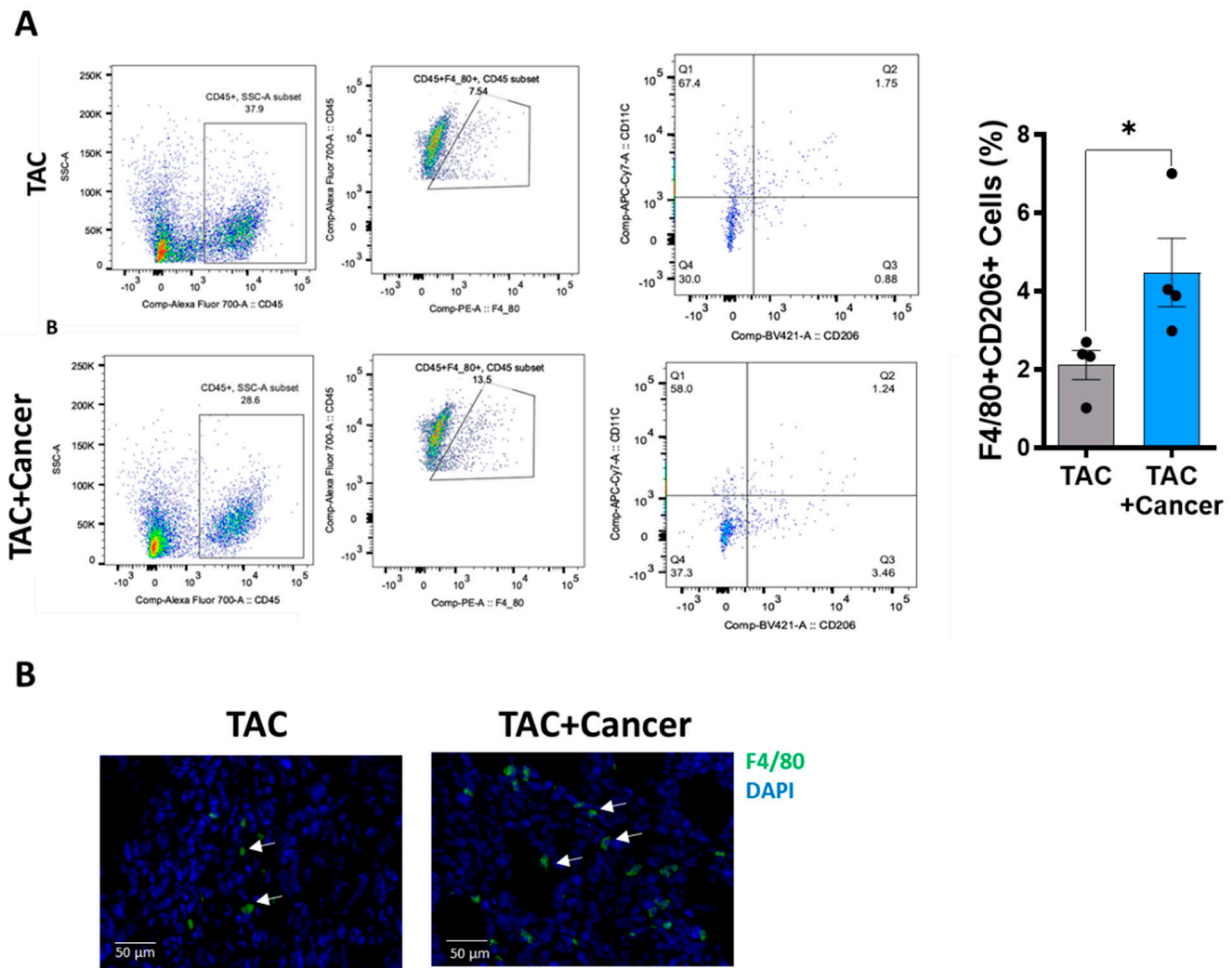
Supplemental Figure S3: Tumor growth's beneficial effect in NOD-SCID mice.

A. Schematic diagram of the experimental timeline. **B.** Fractional shortening (FS) of TAC-operated PyMT-bearing and non-cancer bearing mice, calculated from echocardiography data. Calculated based on parameters in Supp. Table 6. **C.** The ventricular weight/body weight ratio (VW/BW) of TAC-operated PyMT-bearing and non-cancer bearing mice. **D-E.** The mRNA levels of hypertrophic markers ANP and BNP (D) and fibrosis markers collagen, TGFβ3 and αSMA (E) in the hearts of TAC-operated PyMT-bearing and non-cancer bearing mice, measured using qRT-PCR, normalized to the GAPDH housekeeping gene. The results are presented as mean ± SEM, student-t test. * $P < 0.05$, ** $P < 0.01$. In B-E, each dot represents one mouse. ($n=5$ in all groups).



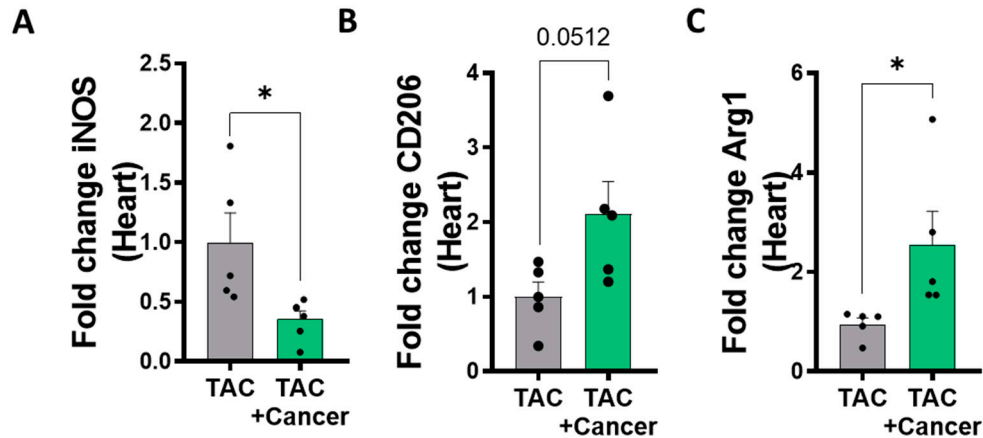
Supplemental Figure S4: M1 macrophage polarization in the tumor of TAC-operated mice.

A-C. Tumor mRNA levels of macrophage markers F4/80 (A), iNOS (B), CD206 (C), in the PyMT tumor of TAC-operated ($n=4$) and non-TAC-operated (naïve) ($n=4$) mice, measured using qRT-PCR, normalized to the Hsp90 housekeeping gene. The results are presented as mean \pm SEM, Student t -test. * $P < 0.05$, ** $P < 0.01$. Each dot represents one mouse.



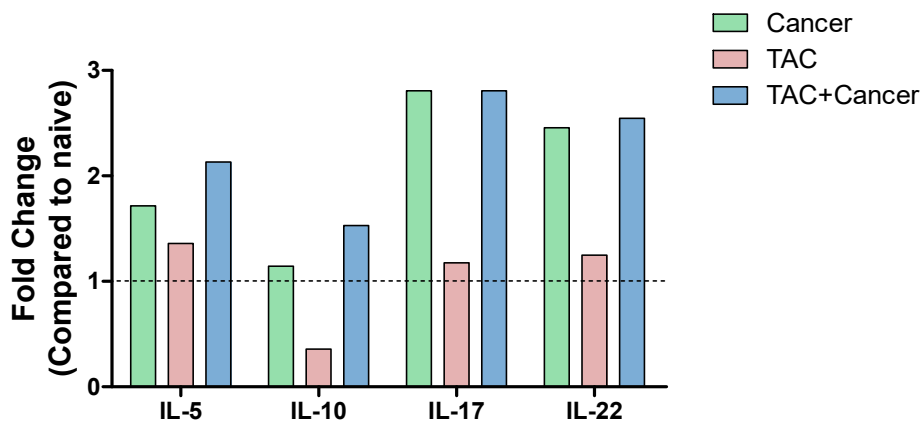
Supplemental Figure S5: Tumor growth induces cardiac macrophage polarization

A. Gating strategy (right) and CD45+F4/80+CD206+ cell count (%) (left) in TAC-operated (n=4) and TAC-operated PyMT-bearing (n=4) mice hearts using flow cytometry. Each dot represents one mouse. **B.** Representative heart sections of a TAC-operated PyMT-bearing and non-cancer-bearing mouse hearts stained with F4/80, arrows indicate to positive cells. Arrows indicate for F4/80 positive cells. The results are presented as mean \pm SEM, Student t-test. * $P < 0.05$.



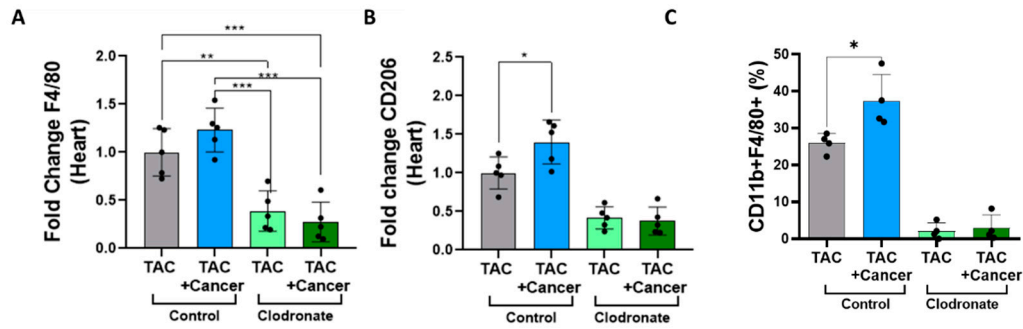
Supplemental Figure S6: M1-to-M2 polarization in NOD-SCID mice.

A-C. mRNA levels of macrophages markers iNOS (A), CD206 (B) and ARG1 (C) in the hearts of TAC-operated PyMT-bearing (n=5) and non-tumor-bearing (n=5) mice, measured using qRT-PCR, normalized to the GAPDH housekeeping gene. The results are presented as mean \pm SEM, Student t-test. * $P < 0.05$. Each dot represents one mouse.



Supplemental Figure S7: M2 polarizing cytokines are elevated in the serum of TAC-operated PyMT-bearing mice.

Blood serum of 4 groups: naïve, PyMT bearing (Cancer), TAC-operated PyMT-bearing (TAC+cancer) and non PyMT-bearing (TAC) was used to probe cytokine array. For each cytokine, serum level is presented as fold change relative to naïve mice's blood serum. (n=4 in all groups). Dashed line indicates to 1 Fold change.



Supplemental Figure S8: Efficiency of macrophage depletion by clodronate liposomes.

A-B. Expression levels of macrophage markers F4/80 (A) and CD206 (B) in the hearts of TAC-operated PyMT-bearing and non-tumor-bearing mice, measured using qRT-PCR, normalized to the HSP90 housekeeping gene. **C.** CD11b+F4/80+ cell count in the heart of TAC-operated PyMT-bearing and non-tumor-bearing, measured using flow cytometry. The results are presented as mean \pm SEM, Student *t*-test. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$. Each dot represents one mouse. ($n=5$ in all groups).

Gene	Forward	Reversed
Hsp90	TCGTCAGAGCTGATGATGAAGT	GCGTTTAACCCATCCAACCTGAAT
GAPDH	TTGCCATCAACGACCCCTTCAT	AGACTCCACGACATACTCAGCA
ANP	GCTTCCAGGCCATATTGGAG	GGGGGCATGACCTCATCTT
BNP	GAGGTCACCTCTATCCTCTGG	GCCATTTCTCTCCGACTTTTCTC
ACTA-1	GTGAGATTGTGCGCGACATC	GGCAACGGAAACGCTCATT
Coll α 1	CTGGCGGTTTCAGGTCCAAT	TTCCAGGCAATCCACGAGC
TGF β 3	CCTGGCCCTGCTGAACTTG	GACGTGGGTCATCACCGAT
CTgF	AGACCTGTGGGATGGGCAT	GCTTGGCGATTTTAGGTGTCC
α SMA	GTCCCAGACATCAGGGAGTAA	TCGGATACTTCAGCGTCAGGA
F4/80	CCCCAGTGTCTTACAGAGTG	GTGCCCAGAGTGGATGTCT
iNOS	GACATTACGACCCCTCCAC	GCACATGCAAGGAAGGGAAC
CD206	CTAACTGGGGTGCTGACGAG	GGCAGTTGAGGAGGTTTCAGT
Arg1	AATGAAGAGCTGGCTGGTGT	CTGGTTGTCAGGGGAGTGTT
CD163	CCTCCTCATTGTCTTCCTCCTGTG	CATCCGCCTTTGAATCCATCTCTTG
INF γ	ACAGCAAGGCGAAAAAGGATG	TGGTGGACCACTCGGATGA
IL-13	AACGGCAGCATGGTATGGAGTG	TGGGTCCTGTAGATGGCATTGC
CCL2	GTGATGGAGGGGGTCAGGA	GGGATGGGACAGCCTAAACT
TNF α	CCCTCACACTCAGATCATCTTCT	GCTACGACGTGGGCTACAG

Supplemental Table S1: Oligonucleotides sequence

	TAC	TAC+Cancer
LVID;d-D	4.34 ± 0.28	4.12 ± 0.38
LVID;s-D	3.34 ± 0.26	2.96 ± 0.33
FS	23.03 ± 3.16	28.14 ± 2.6

Supplemental Table S2: Echocardiography parameters of Figure 1B

	TAC	TAC+TVI
LVID;d-D	3.79± 0.59	3.72 ± 0.01
LVID;s-D	2.96 ± 0.53	2.64 ± 0.08
FS	22.29 ± 1.75	28.98 ± 2.08

Supplemental Table S3: Echocardiography parameters of Figure 3D

	Control		Clodronate	
	TAC	TAC+Cancer	TAC	TAC+Cancer
LVID;d-D	4.044 ± 0.36	3.94 ± 0.27	3.94 ± 0.24	3.93 ± 0.15
LVID;s-D	3.078 ± 0.27	2.8 ± 0.19	3.02 ± 0.25	2.96 ± 0.12
FS	23.83 ± 2.63	28.81 ± 1.72	23.35 ± 3.06	24.55 ± 2.62

Supplemental Table S4: Echocardiography parameters of Figure 5C

	TAC	TAC+Cancer
LVID;d-D	4.29 ± 0.29	4.14 ± 0.24
LVID;s-D	3.42 ± 0.3	3.04 ± 0.21
FS	20.36 ± 2.9	26.73 ± 2.74

Supplemental Table S5: Echocardiography parameters of Supp. Figure 1B

	TAC	TAC+Cancer
LVID;d-D	3.47 ± 0.33	3.25 ± 0.2
LVID;s-D	2.65 ± 0.28	2.32 ± 0.18
FS	23.83 ± 1.22	28.77 ± 2.15

Supplemental Table S6: Echocardiography parameters of Supp. Figure 2B