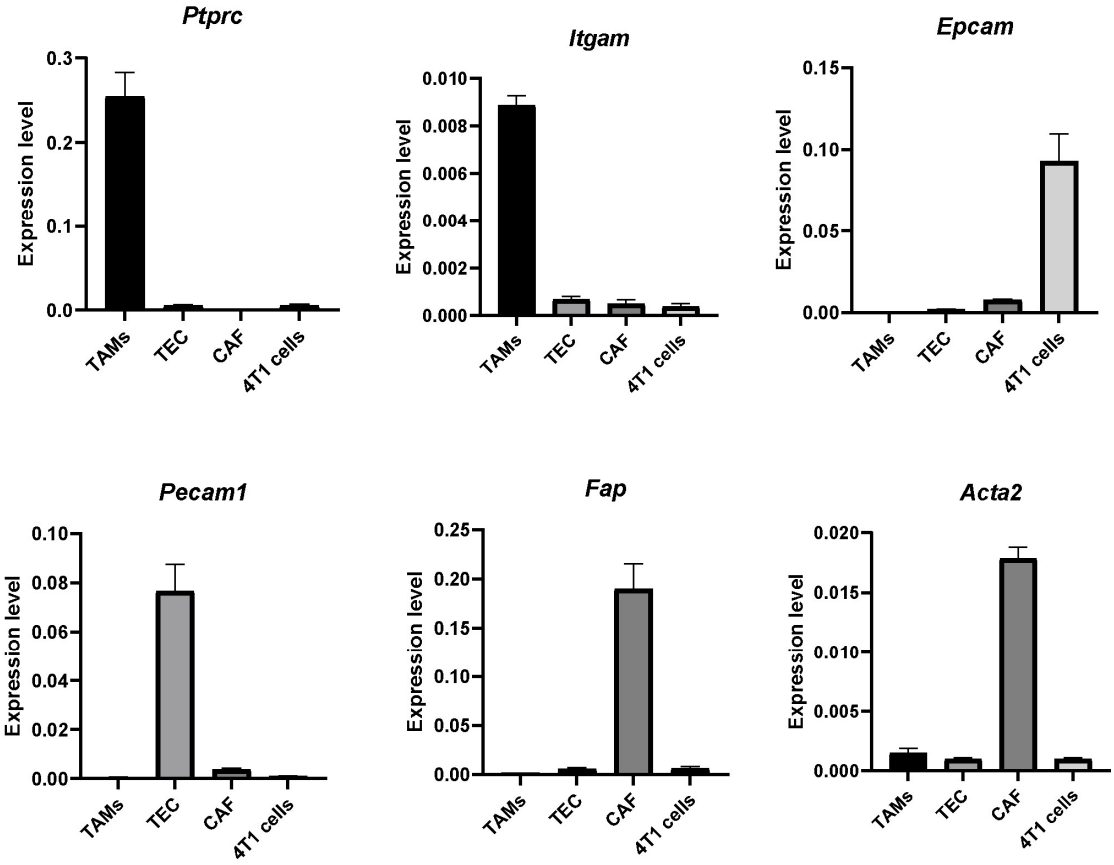
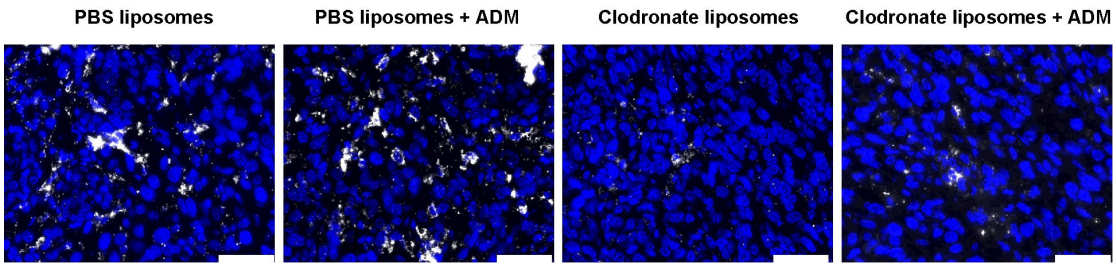
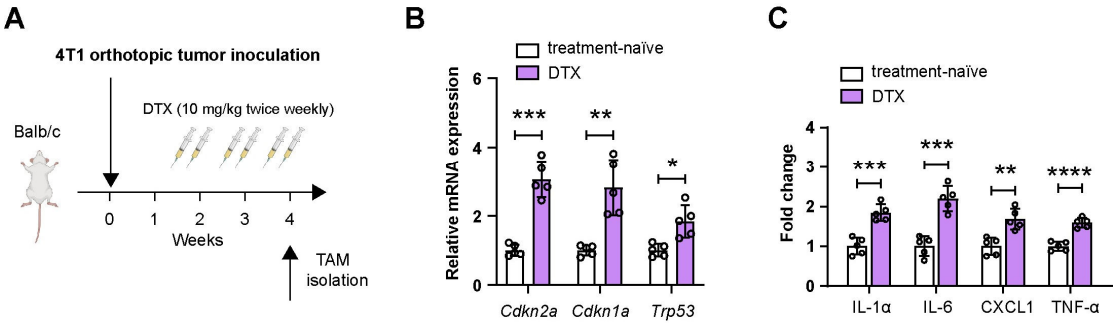
Supplementary information



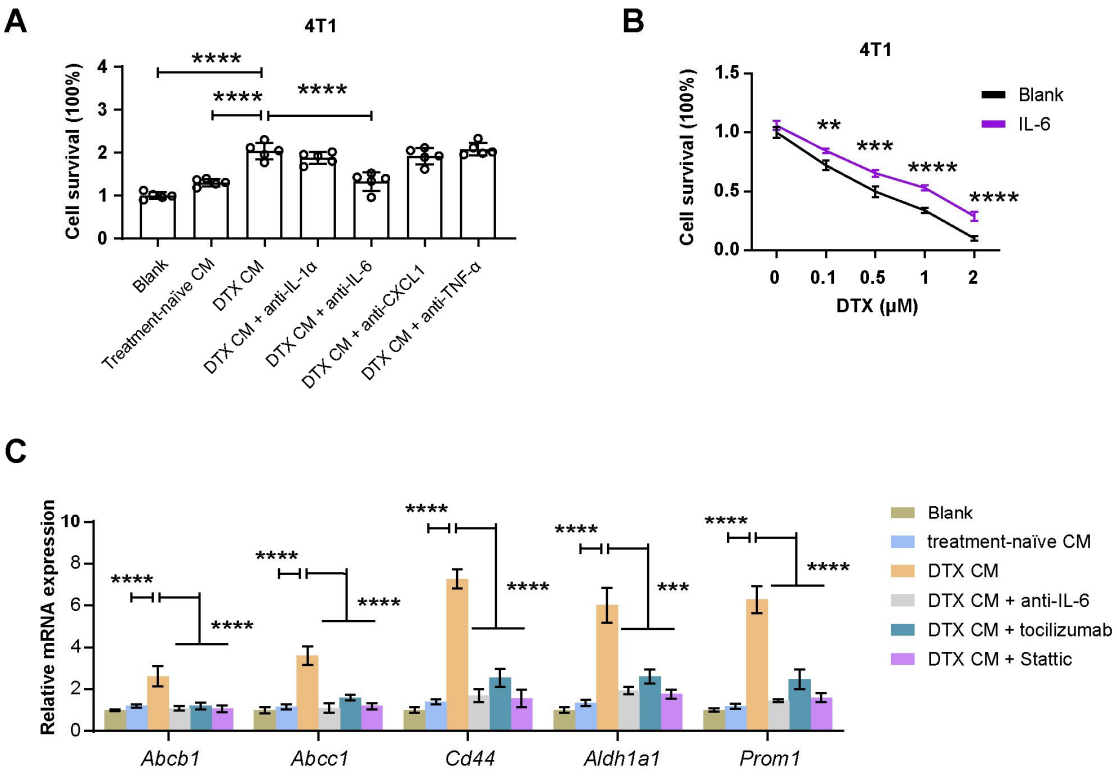
Supplementary Fig. 1. Verification of isolated TAMs, TEC, and CAFs. Real-time qPCR analysis showed the expression of *Ptprc*, *Itgam*, *Epcam*, *Pecam1*, *Fap*, and *Acta2* in TAMs, TEC, CAFs, and 4T1 cells.



Supplementary Fig. 2. Verification of macrophage deletion by clodronate liposomes. IF analysis of F4/80^{+} macrophages in the following groups: PBS-liposomes, ADM, Clodronate-liposome, or ADM + Clodronate-liposome. Scale bar, 50 μm.



Supplementary Fig. 3. Senescence-like TAMs are induced by DTX treatment. (A) Treatment schedule of DTX and isolation of TAM from orthotopic 4T1 tumor model. **(B)** Real-time qPCR analysis of senescence-related genes (*Cdkn2a*, *Cdkn1a*, and *Trp53*) in TAMs isolated from treatment-naïve and DTX-treated tumors (n = 5). **(C)** ELISA quantification of senescence-associated secretory phenotype (SASP) markers (IL-1α, IL-6, CXCL1, TNF-α) in conditioned media from TAMs isolated from orthotopic 4T1 tumors treated with control or DTX (n = 5). **P* < 0.05, ***P* < 0.01, ****P* < 0.001, *****P* < 0.0001.



Supplementary Fig. 4. IL-6-IL6R-STAT3 axis drives chemoresistance in TNBC.

(A) Viability of 4T1 tumor cells treated for 48 h with conditioned medium (CM) from TAMs isolated from PBS- or DTX-treated orthotopic 4T1 tumors, with/without neutralizing antibodies against SASP factors (IL-1α, IL-6, CXCL1, and TNF-α). Viability measured by CCK-8 assay (OD 450 nm). **(B)** CCK-8 assay showing the viability of 4T1 tumor cells upon treatment of DTX and recombinant IL-6 for 48 h. **(C)** Real-time qPCR analysis of drug resistance- and stemness-associated genes (*Abcb1*, *Abcc1*, *Cd44*, *Aldh1a1*, and *Prom1*) in TAMs isolated from indicted groups. ***P* < 0.01, ****P* < 0.001, and *****P* < 0.0001.

Supplementary Table 1. The primer sequences

Gene symbol	Forward (5'-3')	Reverse (5'-3')
Ptprc	ATATCGCGGTGTAAAACTCGTC	TAGGCTTAGGCGTTTCTGGAA
Itgam	ATGGACGCTGATGGCAATACC	TCCCCATTCACGTCTCCCA
Epcam	CGTGAGGACCTACTGGATCAT	GTCCACGTCGTCTTGTGTTTT
Pecam1	ACGCTGGTGCTCTATGCAAG	TCAGTTGCTGCCCATTCATCA
Fap	GCGACATACTACATCTACGACCT	AGATACTGAATTGGACGAGGGAG
Acta2	CCCAACTGGGACCACATGG	TACATGCGGGGGACATTGAAG
Cdkn2a	CGCAGGTTCTTGGTCACTGT	TGTTCACGAAAGCCAGAGCG
Cdkn1a	CCTGGTGATGTCCGACCTG	CCATGAGCGCATCGCAATC
Trp53	GGCAGACTTTTCGCCACAG	CAGGCACAAACACGAACCTC
Abcb1	TGATGGCTCCGATCCACTCT	TCCACAGAAAGAATCCTAAGGCA
Abcc1	AAGGGAGTCCAATCCTCGGG	GGAATCTCGAAACACGTCCAC
Cd44	TCGATTTGAATGTAACCTGCCG	ACCTGTCTGCTGCATAGCCTA
Aldh1a1	ATACTTGTCGGATTTAGGAGGCT	GGGCCTATCTTCCAAATGAACA
Prom1	GTTGAGACTGTGCCCATGAAA	GACGGGCTTGTCATAACAGGA
Actb	GGCTGTATTCCCCTCCATCG	CCAGTTGGTAACAATGCCATGT