

Figure 1

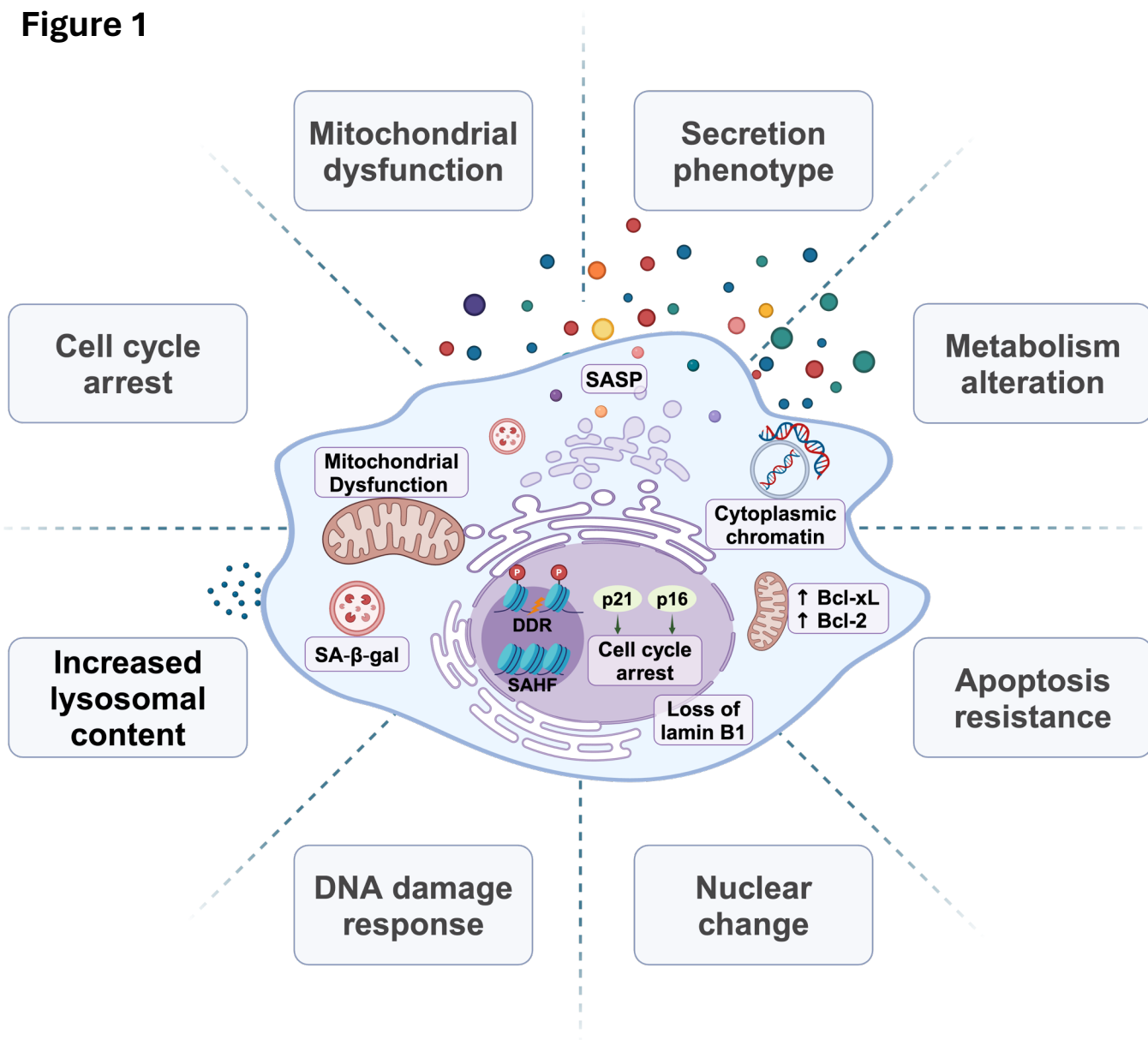


Figure 2

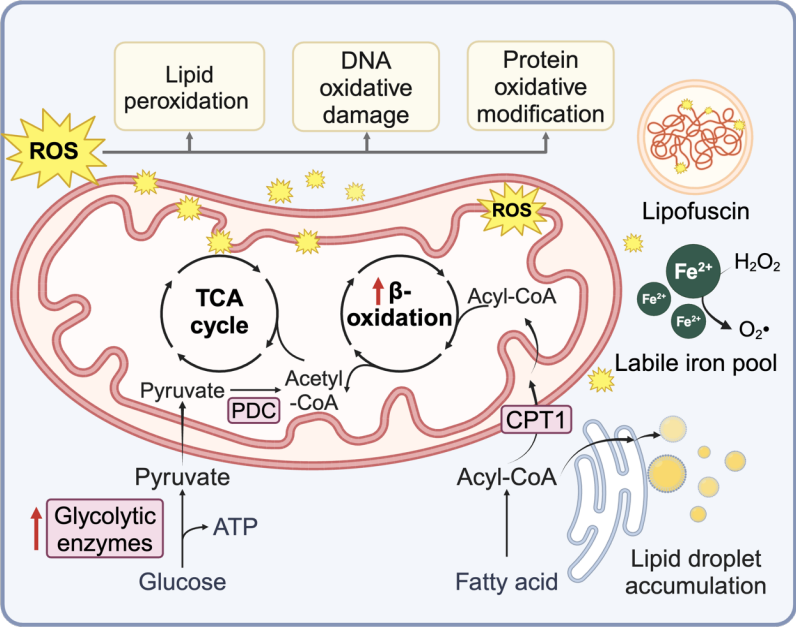


Figure 3

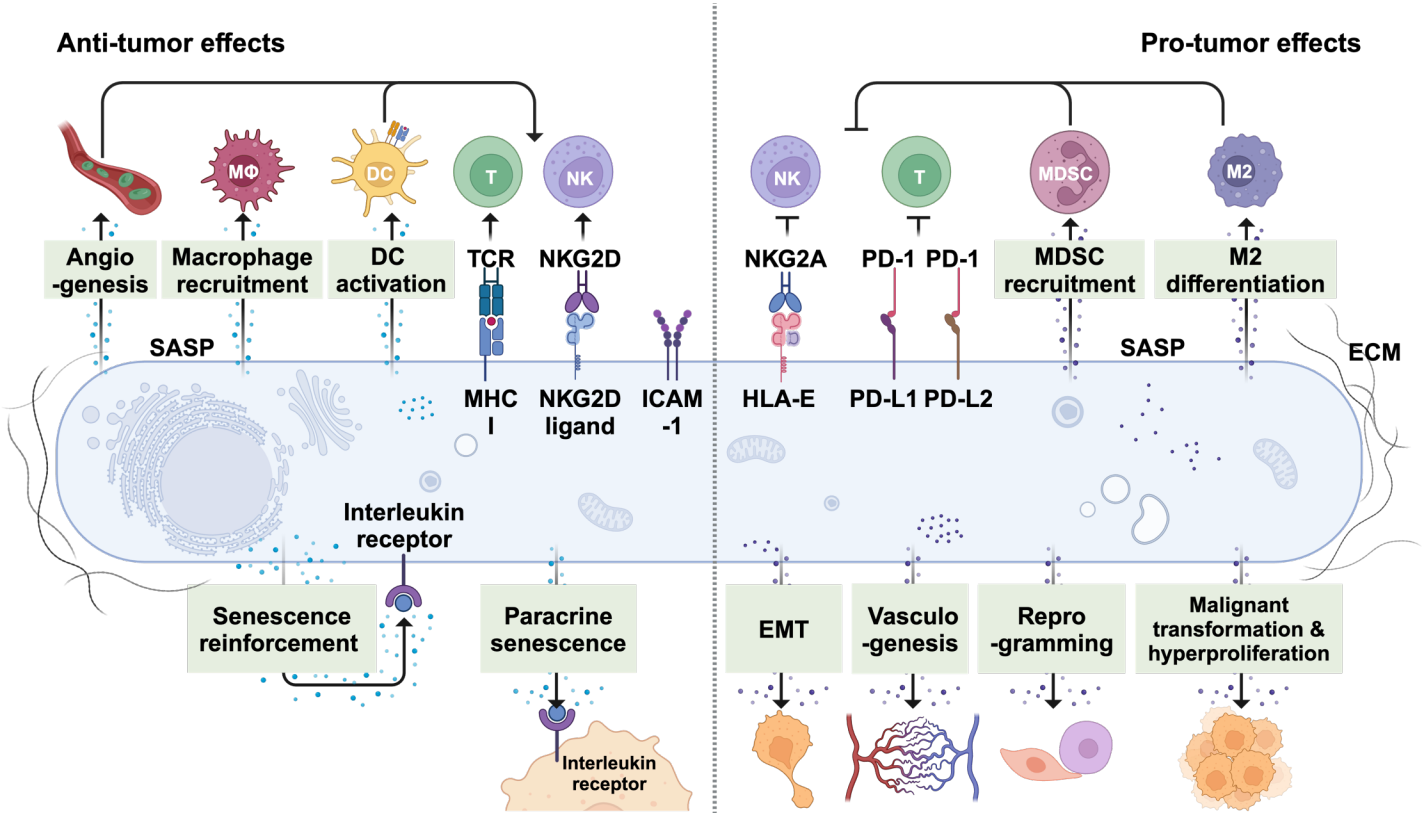


Table 1 Immunostimulatory senescent cells in cancer

Senescence Induction methods	Cancer type	Affected immune cell population	References (PMID)
H-Ras ^{G12V} and p53 reactivation	Liver cancer	PMN	17251933
Alisertib	Melanoma	PMN and Mφ	23180582
Carbon tetrachloride	Hepatocellular carcinoma	M1 Mφ	23562644
Temozolomide	Glioblastoma	Increased M1 Mφ and decreased MDSCs	36472478
IR	Lung cancer	M1 Mφ	33673859
Cyclophosphamide	B cell Lymphoma	NK cell	21979375
H-Ras ^{G12V}	Liver cancer	NK cell	24043758
Chemo agents	multiple myeloma	NK cell	19098271
Doxorubicin	multiple myeloma	NK cell	24913980
Trametinib + Palbociclib	KP lung cancer	NK cell	30573629
N-Ras ^{G12D}	Liver cancer	NK cell	27099234
Trametinib + Palbociclib + Tazemetostat	KPC PDAC model	NK and T cells	37142692
N-Ras ^{G12V}	Liver cancer	CD4 ⁺ T cells	25621566
IR	Osteosarcomas	NKT cells	24231354
Alisertib	Melanoma	CD8 ⁺ T cell	26719346
Dexamethasone	Lung adenocarcinoma	NK and T cell	36434273
Abemaciclib	mammary carcinoma	T cell	28813415
Cytarabine or Palbociclib	AML	T cells	10.1101/2022.11.17.515658

Doxorubicin	Melanoma	DCs and T cells	36302218
IR+veliparib	Multiple cancers	DCs, NK, and T cells	22334019, 36792123
N-Ras ^{G12D}	Liver cancer	Increased CD8 ⁺ T cells and decreased MDSCs	36302222
Doxorubicin	Metastatic breast cancer	CD8 ⁺ T cell	36384097
Trametinib + Palbociclib	PDAC KPC model	CD8 ⁺ T cells	32234521
Abemaciclib	Melanoma	T cells	30388455
AZD1152	Melanoma	T cells	33123754
Irinotecan + Cisplatin	ovarian cancer	DCs and T cells	33490922
IFN- γ	Multiple cancers	T cells	32165639

Table 2 Therapy induced senescence potentiates immunotherapy

Senescence induction methods	Cancer type	Immunotherapy agent	PMID (PMID)
Mitoxantrone	prostate cancer	α PD-1/PD-L1 Ab	31493351
Doxorubicin	melanoma	α PD-L2 Ab	BiorXiv
Alisertib	Melanoma	α CD137 Ab	26719346
Abemaciclib	mammary carcinoma	α PD-L1 Ab	28813415
IR + Veliparib	Multiple cancers	α PD-L1 Ab	36792123
Doxorubicin	Metastatic breast cancer	α PD-1 Ab	36384097
Trametinib + Palbociclib	PDAC (KPC model)	α PD-1 Ab	32234521
Abemaciclib	Melanoma	α CTLA4 Ab	30388455
AZD1152	Melanoma	α CTLA4 Ab	33123754
Irinotecan + Cisplatin	ovarian cancer	α PD-1 Ab	33490922

Table 3 Immunosuppressive senescent cells in cancer

Senescence Induction methods	Cancer type	Affected immune cell population	References (PMID)
Doxorubicin	Breast cancer	SASP p16-3MR mice	27979832
Docetaxel	PTEN loss prostate cancer	Increase Gr1 ⁺ MDSCs but decrease T and NK cells	25263564
p27 ^{Kip1}	Squamous cell carcinoma	Increase CD11b ⁺ Ly6G ^{Hi} MDSCs and Tregs	27272654
Palbociclib	Melanoma	Promote the recruitment of Gr1 ⁺ MDSCs	28039358
Pten-loss	PTEN loss prostate cancer	Increase MDSCs	25156255
N-Ras ^{G12V}	Liver cancer	Increase MDSCs	27728804
N-Ras ^{G12V}	Liver cancer	Reduce CD3 ⁺ T cells	27525720
IR	Lung metastases	Promote Ly6G ⁺ neutrophil recruitment	35221334
TGF- β	Lung cancer	Increase infiltration of immune-suppressive cell types	36821441
ROS	Colorectal Cancer	Enhance M2 macrophage polarization	33643790
Metabolites (DCA and LTA)	Hepatocellular carcinoma	Suppress CD8 ⁺ T cells	28202625
Mitoxantrone	Prostate cancer	Promote PD-L1 expression in tumors	31493351
Doxorubicin	Melanoma	PD-L2 ⁺ senescent cells dampen T cell activity and promote of CD11b ⁺ Gr1 ⁺ MDSC recruitment	38267628
H-Ras ^{G12V}	Glioblastoma	Decrease T cells and increase tumor promoting macrophages	36707509

Table 4 Senolytics in cancer

MOA	Senolytic agent	Senescence Induction methods	Cancer type	References (PMID)
Tyrosine kinase inhibitor + flavonoid derivative	Dasatinib and quercetin	Doxorubicin	Liver Cancer	30425964
Flavonoid derivative	Fisetin	Olaparib	Ovarian cancer	31186408
	GL-V9	Doxorubicin	Breast cancer	33617857
Bcl-2/Bcl-xL/Bcl-w inhibitor	ABT263	Doxorubicin or etoposide	Lung and breast cancer	32652830
	ABT263	SMARCB1 inhibition	Multiple cancer cell lines	29045843
	ABT263	Olaparib	Ovarian	31186408
	ABT263	Doxorubicin	Breast cancer	32457483
	ABT263	Radiation and temozolomide	Glioblastoma	35191501
	ABT737	K-Ras ^{G12V}	Pancreatic cancer	33649045
Bcl-xL degrader	PZ15227			32332723
Selective BCL-xL inhibitor	A1331852, A1155463	Radiation and temozolomide	Glioblastoma cell lines	35191501
Selective Bcl-2 inhibitor	ABT199	IR	Sarcoma cell lines	33494434
	ABT199	Palbociclib + fulvestrant	Breast cancer	32245900
MCL-1 inhibitor	S63845	Doxorubicin or etoposide	Breast cancer	32457483
	S63845	Docetaxel	Prostate cancer	35449130
Galacto-conjugation of ABT263	Nav-Gal	Cisplatin	A549 xenograft	32233024

	Nav-Gal	Palbociclib	Breast cancer lung metastasis	36566002
BET degrader	ARV825	High fat diet or doxorubicin	Liver cancer	32321921
Cardiac glycosides	Digoxin Digitoxin Proscillaridin A Ouabain	Therapy induced senescence	Multiple cancer types	31636264 31799499 34714358
mTOR inhibitor	AZD8055	CDC7 inhibitor XL413	Hepatocellular carcinoma	31578521
HDAC inhibitor	Panobinostat Decrease Bcl- xl	Taxol, cisplatin	NSCLC and HNSCC	28507307
Senolytic peptide	FOXO4 binding peptide ES2	BRAF inhibitor Dabrafenib	Melanoma	34689087
Senolytic CAR-T	urokinase-type plasminogen (uPAR)-specific CAR T cells)	Trametinib + Palbociclib	Lung cancer	32555459