

SUPPLEMENTARY DATA

Senescence and SASP in the Stromal Microenvironment of Breast Cancer: Dual Role in Progression and Therapeutic Options

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Table S1. Advantages and limitations of senescent cell detection platforms

Tool	Input data	Demonstrated application	Advantages	Limitations
SIT [157]	Gene signatures	Senescent cell identification in vivo; heterogeneity analysis	Simple deployment; works with transcriptomic data; reveals senescence subtypes	Fixed reference gene set; misses atypical senescence pathways; no protein or morphological data
SenMayo [158]	Gene signature	Tissue- and species-specific senescence	Portable; consensus-derived; applicable to human tissues	Transcript-level only; no spatial or protein information
DeepScience [159]	scRNA-seq + spatial transcriptomics	Senescent cell detection with spatial context	Preserves tissue localization; high biological resolution	Costly; technically demanding; limited accessibility
SenPred [160]	scRNA-seq (2D/3D fibroblast models)	Improved in vivo detection of deep senescence	Trained on well-defined senescence phenotype; includes 2D and 3D data	Trained only on dermal fibroblasts; transfer to other cell types unvalidated
SenSCOUT [161]	Single-cell imaging + protein biomarkers	Functional senescence subtyping in dermal fibroblasts	Integrates imaging, multiple markers, and ML; captures functional states	High experimental complexity; standardization challenges
SENCAN [164]	Cancer cell culture RNA data	Detection of therapy-induced senescence	Specific to therapy-induced senescence; translational relevance	Early in vitro validation only; limited to SENESclopedia datasets
scCamAge [162]	Single-cell images, shape, bioactivity	Cross-species senescence prediction (yeast → human fibroblasts)	Morphology-based; independent of transcriptomic noise	Cross-species generalizability uncertain; requires image standardization
SAMP-Score [163]	Morphology	Screening of pro-senescence compounds	High-throughput compatible; practical for compound screens	Narrow intended use; not a general-purpose in vivo classifier
SenNet [65]	Organ-based multi-modal data (consortium)	Organ-specific senescence hallmarks across lifespan	Broad, standardized reference framework; NIH-supported	Utility depends on ongoing data accumulation; not a standalone classifier

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Table S2. Senolytics and senomorphics.

Title	Targets	Nosology	Stage	Reference
ABT-199 (Venetoclax)	Bcl-2	Chronic lymphocytic leukemia, acute myeloid leukemia	Clinical trial	[337, 338]
		BC	Preclinical	[257]
			Clinical trial PALVEN (venetoclax+palbociclib+letrazole)	[256]
		Pancreatic adenocarcinoma	Preclinical	[239]
ABT-263 (Navitoclax)	Bcl-2, Bcl-w, Bcl-xL	Soft tissue sarcomas	Preclinical	[310]
		Leukemia, lymphoma	Clinical trial	[258]
		TNBC	Clinical trial (navitoclax+olaparib)	[259]
			Preclinical (galacto-conjugated navitoclax (nav-Gal)+CDK4/6 inhibitors)	[325]
			Preclinical (combination with doxorubicin)	[257]
		Cholangiocarcinoma	Preclinical	[263]
Nintedanib	Multikinase inhibitor	TNBC	Preclinical	[267]
Wogonin	CDK9	ER ⁺ and TNBC	Clinical trial, phase I	[268]
ABT-737	BCL-2, BCL-XL and BCL-W	BC	Preclinical	[28, 272]
Ruxolitinib	JAK2	BC	Preclinical	[278]
Metformin	NF-κB inhibitor	BC Head and neck squamous cell carcinoma	Preclinical	[281, 282]
Tocilizumab	IL-6	TNBC	Clinical trial, phase I/II	[285]
Rapamycin, “rapalogs”	mTOR	BC	Clinical trial	[339]