Supplementary Table S1. Summary of references categorized by 3D culture system used and field of cancer immunology investigated.

Spheroids	rapy Penetrance	
Reference #	10	
		Article Title
35	Liu et al.	MALDI-MSI of Immunotherapy: Mapping the EGFR-Targeting
		Antibody Cetuximab in 3D Colon-Cancer Cell Cultures.
36	Rodallec et al.	From 3D spheroids to tumor bearing mice: efficacy and distribution
		studies of trastuzumab-docetaxel immunoliposome in breast cancer.
Lymphocyte	e Infiltration	
38	Mark et al.	Cryopreservation impairs 3-D migration and cytotoxicity of natural
		killer cells.
39	Crourau et al.	Cocultures of human colorectal tumor spheroids with immune cells
		reveal the therapeutic potential of MICA/B and NKG2A targeting for
		cancer treatment
Tumor Doi	rmancy/Immunosup	pression
44	Liu et al.	Blockade of IDO-kynurenine-AhR metabolic circuitry abrogates IFN-
		γ -induced immunologic dormancy of tumor-repopulating cells.
45	Stüber et al.	Inhibition of TGF- β - Receptor signaling augments the antitumor
10	Stuber et ui.	function of ROR1-specific CAR T-cells against triple-negative breast
		cancer.
46	Raghavan et	Ovarian cancer stem cells and macrophages reciprocally interact
40	al.	
	dl.	through the WNT pathway to promote pro-tumoral and malignant
17	T/ / 1	phenotypes in 3D engineered microenvironments.
47	Kuen et al.	Pancreatic cancer cell/fibroblast co-culture induces M2 like
		macrophages that influence therapeutic response in a 3D model.
48	Chandrakesan	DCLK1-Isoform2 Alternative Splice Variant Promotes Pancreatic
	et al.	Tumor Immunosuppressive M2-Macrophage Polarization.
58	Rocha et al.	3D Cellular Architecture Affects MicroRNA and Protein Cargo of
		Extracellular Vesicles.
59	Thippabhotla	3D cell culture stimulates the secretion of in vivo like extracellular
	et al.	vesicles.
60	Muller et al.	Human tumor-derived exosomes (TEX) regulate Treg functions via
		cell surface signaling rather than uptake mechanisms.
Organoids		
Antigen Pre		
61	Chakrabarti et	Hedgehog signaling induces PD-L1 expression and tumor cell
	al.	proliferation in gastric cancer.
62	Dijkstra et al	Generation of Tumor-Reactive T Cells by Co-culture of Peripheral
	Dijkotra et ar	Blood Lymphocytes and Tumor Organoids.
Fihrohlast-(Cancer Interactions	Diota Lymphoty as and runior organolus.
65	Tsai et al.	Development of primary human pancreatic cancer organoids,
65	1 5ai Ct al.	matched stromal and immune cells and 3D tumor microenvironment
		matched stromar and immune cens and 5D tumor microenvironment models.
((Dhan 1 1	
66	Rhee et al.	Fibroblasts in three dimensional matrices: Cell migration and matrix
		remodeling.

67	Hanley et al.	Tumor resident stromal cells promote breast cancer invasion through
	5	regulation of the basal phenotype.
68	Oszvald et al.	Fibroblast-Derived Extracellular Vesicles Induce Colorectal Cancer
		Progression by Transmitting Amphiregulin.
69	Liu et al.	Cancer-Associated Fibroblasts Provide a Stromal Niche for Liver
		Cancer Organoids That Confers Trophic Effects and Therapy
		Resistance.
CAR Cell	Development	
18	Dillard et al.	Colorectal cysts as a validating tool for CAR therapy.
72	Leuci et al.	CSPG4-Specific CAR.CIK Lymphocytes as a Novel Therapy for the
		Treatment of Multiple Soft-Tissue Sarcoma Histotypes
73	Jacob et al.	A Patient-Derived Glioblastoma Organoid Model and Biobank
		Recapitulates Inter- and Intra-tumoral Heterogeneity.
75	Schnalzger et	3D model for CAR-mediated cytotoxicity using patient-derived
	al.	colorectal cancer organoids.
Personaliz	ed Immunotherapy Tes	
79	Votanopoulos	Model of Patient-Specific Immune-Enhanced Organoids for
	et al.	Immunotherapy Screening: Feasibility Study.
80	Neal et al.	Organoid Modeling of the Tumor Immune Microenvironment.
Microflu	idic Chips	
Immune C	Checkpoints	
81	Jenkins et al.	Ex vivo profiling of PD-1 blockade using organotypic tumor
		spheroids.
84	Diskin et al.	PD-L1 engagement on T cells promotes self-tolerance and suppression
		of neighboring macrophages and effector T cells in cancer.
85	Schmidt et al.	Assessment of Clinical Activity of PD-1 Checkpoint Inhibitor
		Combination Therapies Reported in Clinical Trials.
Migration	, Extravasation and An	giogenesis
88	Mascolo et al.	Nanoformulated Zoledronic Acid Boosts the V82 T Cell
		Immunotherapeutic Potential in Colorectal Cancer.
89	Aung et al.	An Engineered Tumor-on-a-Chip Device with Breast Cancer-Immune
		Cell Interactions for Assessing T-cell Recruitment.
90	Cui et al.	Hacking macrophage-associated immunosuppression for regulating
		glioblastoma angiogenesis.