Additional Table 1. Nanomaterials related to the immunosuppressive tumor microenvironment

Author, year	Material type	Material name	Cancer	Treatments	Impact
Honglin Huang, 2025[24]	Biomimetic gold nanoregulators	GNR-SNO@MMT	BC	NIR-II photothermal immunotherapy	Reducing the expression of HIF-1α and PD-L1, repolarizing TAMs to the M1 type, and increasing the infiltration of CTLs
Xin Ding, 2025[25]	Polydopamine nanoparticles	PDA-SAHA NPs	BC	PTT, HDAC inhibitors	Photothermal effect of PDA and inhibition of HDAC
Shenzhen Ren, 2025[26]	Carrier - free ultrasound - responsive polyphenol nanonetworks based on gossypol	GTC	BC	SDT	Conjugated with transferrin, ultrasound-activated GTC for ROS generation, inhibition of Bcl-2 protein expression, enhanced ICD, STING pathway activation, and promotion of dendritic cell maturation and T-cell infiltration
Xindi Qian, 2025[27]	Ultrasound-sensitive system	Dead APC-Tumor-N3-Lipo H	TNBC	SDT	Activating DC maturation, activating NK cells via the NKG2D-NKG2DL pathway, and activating T cells via MHC-I and co-stimulatory molecules
Yu Guo, 2025[28]	Immune hydrogel	Gel−MB−MT	TNBC	SDT	Releasing toluidine blue and 1-methyltryptophan upon ultrasound activation to induce ICD
Jing Liang, 2025[29]	Aza-Boron-Dipyrromethene-based sonosensitizer molecules and sulfur dioxide prodrug caged with 2,4-dinitrobenzenesulfonate	Aza-DNBS	HCC	SDT	Generating $\bullet^1O_2$, releasing SO_2, and triggering ICD
Marzia Conte, 2025[30]	Lipid-coated iron-doped zinc oxide nanoparticles, combined with fluorescent sonosensitizer IR780	Lipid-coated iron-doped zinc oxide nanoparticles, combined with fluorescent sonosensitizer IR780	PDAC	SDT	Generating ROS, reducing the viability of KPC cells, and inducing apoptosis

Pengfei Chen, 2025[31]	CSF1R/IL12-macrophage membrane-liposome hybrid nanovesicles	IL12/CSF1R-MM-IRC 18-LPS	GBM	PTT	Achieving membrane-targeted mild photothermal therapy, blocking the CSF1-CSF1R axis, enriching IL-12, and activating cytotoxic T Cells
Jing Meng, 2025[32]	Hematoporphyrin monomethyl ether-loaded nano-liposomes	HMME@Lip	OSCC	SDT	Generating ROS, activating Caspase-3, cleaving GSDME, inducing pyroptosis, releasing pro-inflammatory cytokines, recruiting CAR-NK cells, and enhancing immune responses
Huilan He, 2025[33]	Retinoic acid-loaded liposomal nanoparticles	LATRA	Colon cancer, BC	RT	Downregulating radiation-induced cancer stem cell markers, promoting DC maturation and polarizing macrophages to the M1 phenotype, and reducing immunosuppressive cells
Jialong Fan, 2025[34]	A complex of prussian blue nanoparticles based on glycyrrhetinic acid and attenuated salmonella	CS-6@CPB-S.lux	TNBC	PTT	Inducing ICD, inhibiting PD-L1 expression, and promoting dendritic cell maturation and T-cell infiltration
Andrés Ramos-Valle, 2025[35]	Oligonucleotides comprising 10 floxuridine units encapsulated in soluble silica nanoparticles	FdU10@SiO2	Malignant melanoma	Modulate immune responses	Eliminate melanoma cells and their support structures, and reduce tumor size after drug release
Feifei Liu, 2025[36]	Hyperbranched polymers and polyethylene glycol-conjugated polymer micelles	HBP	NSCLC	Modulate immune responses	Enhancing immune cell infiltration and cytokine secretion
YanFang, 2025[37]	PEG-modified iron-based single-atom nanozymes	P@Fe SAZ	Residual HCC tumor after iRFA	Low-intensity radiofrequency	Generating ROS, promoting polarization of TAMs to the M1 type, reducing infiltration of MDSCs and tregs, and activating DC maturation
Zonghao Liu, 2025[38]	Microwave-responsive engineered platelet microneedle patches	Fe3O4@MOF	BC, Melanoma	Leveraging the microwave thermal effect	Release drugs under microwave thermal stimulation, activate platelets to release platelet membrane particles, and enhance drug penetration
Yuanwei Wang, 2024[42]	Multifunctional nanoplatform	TCPH nanoparticles	BC	PDT, PTT	Generation of ROS and Heat, induction of ICD

Shipeng Ning, 2025[45]	Exosome-liposome hybrid nanoparticles based on TBTP-Bz and MSA-2	AMFL	TNBC	PTT	Utilizing photothermal effects to release the STING agonist MSA-2, activating the STING pathway, promoting type I interferon production, and enhancing dendritic cell maturation and T-cell activation
Shuying Chen, 2025[47]	Germanium disulfide nanosheets loaded with β-elemene	GeSNSs@ELE-Mφ	BC	SDT	Enhancing M1-type macrophage polarization and increasing the population of mature dendritic cells, $CD4^+$, and $CD8^+$ lymphocytes
Jianwen Song, 2024[48]	Molecular probes based on N-oxide structures	BN-O	BC	PDT, PTT	Promoting ICD and activating the STING pathway
Bangyi Zhou, 2025[49]	Zinc-Copper Bimetallic Nanoplatform	Cu-ZnO2@PDA	TNBC	Cuproptosis	Releasing copper and zinc ions as well as hydrogen peroxide, generating hydroxyl radicals, inducing irreversible cuproptosis, activating the cGAS-STING signaling pathway, and upregulating PD-L1 expression
Reyida Aishajiang, 2025[50]	Nanomedicine	DP-HBN/RA	TNBC	Ferroptosis	Generating ROS, leading to lipid peroxidation-induced ferroptosis, and activating the cGAS-STING signaling pathway
Zhaoyou Chu, 2025[51]	Zinc manganese sulfide and sparfloxacin-loaded microneedles (MNs)	ZMS/SP-HA	TNBC	Apoptosis	Inducing ROS generation, depleting GSH, inducing DAMP release, activating the cGAS-STING pathway, and leading to ECM degradation
Guanyu Jin, 2025[52]	A new type of polymeric immune hydrogel	OSA@CMCS	TNBC	Pyroptosis	Inducing pyroptosis of tumor cells and activating the STING pathway
Zhenhao Zhao, 2025[53]	Manganese-based virus-mimicking nanomedicine	Vir-HD@HM	Breast cancer brain metastasis	Apoptosis	Activating the cGAS-STING pathway and restoring the epigenetic silencing of PTEN
WeiYi Cheng, 2025[54]	Bimetallic sulfide MnZnSX nanorods loaded with arsenic-based prodrugs	As-MnZnSX NRs	HCC	Activating the STING pathway	Activating the cGAS-STING signaling pathway, inducing TBK1 phosphorylation and IRF3 activation, and promoting DC maturation
Li Liu, 2025[55]	Manganese dioxide nanoparticles coated with platinum (IV) backbone polymer drugs	DHP/MnO2NP	Lung cancer	Modulate immune responses	Releasing cisplatin and Mn^{2+}, activating the STING pathway, inducing DNA damage, and upregulating the expression of pro-inflammatory cytokines

Yanming Xia, 2025[56]	Ternary STING-activating nanoparticles coordinated by cGAMP, Mn^{3+}	CMTP	Colon cancer, BC	Modulate immune responses	Porphyrin disassembles into Mn^{2+} and TCPP in a high-glutathione environment, triggering mitochondrial DNA leakage, enhancing cGAMP enzyme activity, and releasing cGAMP, synergistically activating the STING signaling pathway, and promoting DC maturation and T cell activation
Yibin Liu, 2025[57]	CXCR4-targeted immune-modulating nanomedicine	CXNP-CeBM	BC	PDT	Inhibiting CXCR4-mediated signaling pathways, reducing tumor fibrosis, initiating ICD, and releasing HMGB1 and calreticulin
Hai Xu, 2025[58]	Nanomedicine loaded with anti-PD-1 antibody and MDK-siRNA	aPD-1-MDK-siRNA@NP	HCC	Modulate immune responses	Blocking the PD - 1/PD - L1 axis, modulating TAMs and MDSCs, and inhibiting M2 - Type polarization and polyamine metabolism
Duo Wang, 2025[59]	Nanomedicine containing anti-PD-L1, spermine, and shikonin	SPS-NPs	HCC	Inhibiting glycolysis	Inhibiting pyruvate kinase M2 and reversing the immunosuppressive microenvironment caused by incomplete radiofrequency ablation
Huanling Guo, 2025[60]	Lenvatinib liposomes wrapped with macrophage membranes overexpressing PD-1	PML@Len	HCC	Modulate immune responses	Blocking PD-L1 and releasing lenvatinib to inhibit angiogenesis
JunHyuck Lee, 2025[61]	Cell-penetrating peptide-conjugated anti-PD-L1 peptide nanoparticles	CPPD1	Colorectal cancer	PDT	Blocking the PD-L1 immune checkpoint, generating ROS, and inducing ICD
Sheng Wang, 2025[62]	Bispecific antibodies	JS-201	Lung cancer	RT	Inhibit ECM and angiogenesis, and in combination with RT, induce the abscopal effect. They also inhibit the TGF-β/Smad pathway and reduce the release of neutrophil extracellular traps
Xiaoting Shan, 2025[63]	Computer-aided design of self-assembled nanoparticles	VHEB	BC	Inducing ICD	Reducing the proportion of M2-Type TAMs and TGF-β secretion, inducing ICD, inhibiting the NF-κB pathway, reducing IL-6 secretion, and enhancing PD-L1 checkpoint blockade

CaoDai Phung, 2025[64]	Red blood cell-derived exosomes loaded with ASO and RIG-I agonist	Red blood cell-derived exosomes loaded with ASO and RIG-I agonist	Colorectal cancer	Modulate immune responses	Inhibiting KRAS mutation, activating the RIG-I signaling pathway, and inducing ICD
Wanxian Lin, 2025[65]	Nanoparticles coated with phosphatidylcholine	PCNP	GBM	Modulate immune responses	Targeting the adenosine A2A receptor, blocking the adenosinergic axis, and inducing ICD
Shuangshuang Ji, 2025[66]	Nanoparticles composed of GSH -GSH-responsive R848-HSA conjugate and membrane-active peptide iPep	iP-RS NPs	BC	Oncosis	Inducing oncosis in tumor cells, releasing DAMPs, promoting DC maturation and M1-type macrophage polarization, and degrading the fibrotic matrix surrounding the tumor
Yizhang Tang, 2025[67]	Bismuth(V) nanoplatforms	$NaBiVO_3$-PEG	Colon cancer, BC	Modulate immune responses	Undergoing accelerated hydrolysis by H^+ to generate •OH and $•^1O_2$, releasing sodium ions to trigger pyroptosis and activating immune responses
Hongbo Yan, 2025[68]	ROS-responsive pyroptosis nanoinitiators	NP/(DAC+DOX)	Colon cancer, BC	Modulate immune responses	Activating caspase-3 via DOX and upregulating GSDME expression through DAC induces pyroptosis in tumor cells, releases inflammatory factors, promotes dendritic cell maturation, enhances T cell infiltration, and reduces the proportion of myeloid-derived suppressor cells
Jing Xian, 2025[69]	Hydrogel embedded with ELE nanomedicine	ELE@LPNPs@Gel	BC	Modulate immune responses	Maintaining the effective concentration of the drug and prolonging the duration of action
Giulia Rodella, 2025[72]	Hyaluronic acid-doxorubicin and hyaluronic acid-gemcitabine	HA-DOX and HA-GEM	GBM	Chemotherapy	Enhancing ICD and depleting MDSCs
Li Yu, 2025[73]	Tumor-cell-derived microparticles co-loaded with sorafenib and gold nanoparticles	MPSF@AuNP	HCC	Modulate immune responses	Enhancing radiation dose deposition via AuNPs, improving drug targeting, and increasing drug uptake
Naeun Park, 2025[74]	PEG2K-Ce6-modified zinc oxide nanoparticles	PZnONPs	Liver injury repair	Modulate immune responses	Releasing Zn^{2+} and ROS, enhancing the proliferation and activation of stem cells, modulating the polarization of Treg and Th17 cells, and the balance of M2 and M1 macrophages

Gilbert Aaron Lee, 2025[75]	Cholesterol-PEG-superparamagnetic iron oxide-IL-19 antibody nanoparticles	CHOL-PEG-SPIO-IL-19	GBM	PTT	Blocking immunosuppressive signaling pathways, promoting T-cell activation, and inhibiting the immunosuppressive functions of TAMs
JianGang Zhang, 2025[76]	Reuterin encapsulated in covalent organic frameworks	COF-Reuterin	Melanoma	Modulate immune responses	Inducing trained immunity of TAMs via reuterin, stabilizing HIF-1α through the AHR-ROS-HIF-1α signaling pathway, enhancing glycerophospholipid metabolism, and increasing arachidonic acid levels
Marcela Filipová, 2025[77]	The sugar polymer N-(2-hydroxypropyl) methacrylamide	The sugar polymer N-(2-hydroxypropyl) methacrylamide	Various solid tumors	Modulate immune responses	Specifically binds to and inhibits Galectin-3, allowing IFNγ to function properly and promoting the polarization of M1-type macrophages
Yajing Guo, 2025[78]	Bifunctional peptide nanofibers composed of the S100A9-targeting peptide H6 and the self-assembling peptide Q11	H6-Q11	Lung metastasis of melanoma TNBC	Modulate immune responses	Target the S100A8/A9-NCF1 axis, reshape the tumor microenvironment, reduce the infiltration of immunosuppressive cells, and decrease the number of lung metastatic foci
Huisong Hao, 2025[79]	Biomimetic nanopoint igniters based on magnesium peroxide	D/M-MP@LM	BC	Inducing ICD	Inducing ICD, generating peroxynitrite ($ONOO^-$), activating MMPs, degrading ECM, and promoting T-Cell infiltration
Zhengwei Song, 2025[80]	Neutrophil membrane - hybrid liposomes	NLASF	BC	PDT	Generation of ROS, induction of EMT
Xuan Sha, 2025[81]	Glycyrrhizic acid-loaded nanoplatform	GA-DMOS@FeOOH	BC	Ferroptosis	Depleting GSH, promoting LPO accumulation, inducing ferroptosis, and inhibiting HMGB1 release
Chu Li, 2025[82]	Iron-doped dopamine-modified hollow mesoporous manganese dioxide nanoprobes release the ferroptosis inducer RSL3	MnO2R@FePDAc	OSCC	PDT	Releasing ferroptosis inducer RSL3 and mimicking multiple enzyme activities to enhance ROS generation and GSH consumption, inducing “explosive” ferroptosis
Jing Liu, 2025[83]	Two-dimensional nanoscale covalent organic frameworks	Td-Pc	PDAC, TNBC	SDT	Targeting the mitochondria of tumor cells, generate ROS, induce immunogenic pyroptosis, and upregulate PD-L1 expression

Jiaxing Wang, 2025[84]	Nano-vesicles	Nano-vesicles (NVs) formed by self-assembly of triterpenoid drug precursor (TP-PEG-SS) with ginsenoside Rg3 and lecithin	Pancreatic cancer	Modulate immune responses	Targeting mitochondria, promoting M1-type macrophage polarization via glucose transporter GLUT-1, and triggering apoptosis
Peijie Zhou, 2025[85]	Acid-responsive nanopreparations of Wee1 inhibitors	LN-MK1775	cervical cancer, BC, Colorectal cancer	Modulate immune responses	Promoting cancer cell ferroptosis via mitochondrial ROS and iron ion-dependent pathways, and inducing the abscopal effect
Li He, 2025[86]	Nano-dots constructed via the alloying strategy of arsenene and vanene	Arsenene-Vanadene	TNBC	Apoptosis, ferroptosis	Generating highly toxic trivalent arsenic to induce tumor cell apoptosis, indirectly promoting ferroptosis, and releasing DAMPs
Jianhao Chen, 2025[87]	FAP-targeted dimeric radiopharmaceutical	177Lu-DOTA-2P(FAPI)$_2$	Colorectal cancer	Modulate immune responses	Inducing DNA double-strand breaks, upregulating PD-L1 expression, increasing the infiltration of $CD8^+$ T cells and mature antitumor neutrophils, and reducing tregs
Yingli Luo, 2025[88]	Nanopreparations containing metal sulfide FeS and the GSDMD plasmid	NPFeS/GD	TNBC	Ferroptosis	Inducing immunogenic PANoptosis and ferroptosis, and inhibiting IDO1 activity
Xu Zhang, 2025[89]	Polymeric drug nanoregulators	PCDM NPs	TNBC	Apoptosis, ferroptosis	Inducing ferroptosis and apoptosis, enhancing ICD, and inhibiting tryptophan metabolism
Roberta Cillaria, 2025[90]	Sulfur-Doped Carbon Nanodots Conjugated with IDO Inhibitor (Indoximod)	CDs-IND	TNBC	Inhibiting IDO	Reducing IDO expression, recruiting NK cells, NKT cells, and T cells, and decreasing the number of immunosuppressive cells

Li Liao, 2025[91]	Dual-regulating biomimetic nanocomposites	IMMGP	TNBC	PDT	Generating ROS, inducing ICD, depleting GSH, downregulating IDO expression, and inhibiting urocanic acid metabolism
Fu Wang, 2025[92]	Hyaluronic acid/PEG-imine cross-linked siRNA Nanoplatform	HPssPT(HA/PEIss@siPtpn2)	HCC	siRNA technology	Silencing protein tyrosine phosphatase non-receptor type 2, enhancing the IFN-γ signaling pathway, increasing phosphorylation of JAK1 and STAT1, and promoting polarization of TAMs to the M1 type
Shuyao Lang, 2025[93]	Peptide-based nanoparticles loaded with siRNA	c-Rel siRNA	Melanoma	siRNA technology	siRNA silencing the c-Rel gene, reducing the number and immunosuppressive functions of MDSCs, and enhancing the response of $CD8^+$ T Cells

BC, breast cancer; TNBC, triple-negative breast cancer; HCC, hepatocellular carcinoma; PDAC, pancreatic ductal adenocarcinoma; CRC, colorectal cancer; GBM, glioblastoma; NSCLC, non-small cell lung cancer; OSCC, oral squamous cell carcinoma; PDT, photodynamic therapy; PTT, photothermal therapy; SDT, sonodynamic therapy; RT, radiotherapy; HIF-1α, hypoxia-inducible factor 1α; cGAS-STING, cyclic GMP-AMP synthase-stimulator of interferon genes; NK, natural killer cell; NKG2D, natural killer group 2 member D; MHC-I, major histocompatibility complex class I; PTEN, phosphatase and tensin homolog; NKT, natural killer T cell; TAMs, tumor-associated macrophages; MDSCs, myeloid-derived suppressor cells; Tregs, regulatory T cells; DCs, dendritic cells; CTLs, cytotoxic T lymphocytes; ICD, immunogenic cell death; ROS, reactive oxygen species; EMT, epithelial-mesenchymal transition; HDAC, histone deacetylase; PDA, polydopamine; DAMPs, damage-associated molecular patterns; IDO-1, indoleamine-2,3-dioxygenase 1; GSH, glutathione; ECM, extracellular matrix; TGF-β, transforming growth factor-β; CXCR, C-X-C motif chemokine receptor; HMGB1, high mobility group box 1; MMPs, matrix metalloproteinases; TBK1, TANK-binding kinase 1; IRF3, interferon regulatory factor 3; JAK1, janus kinase 1; STAT1, signal transducer and activator of transcription 1; GLUT-1, glucose transporter 1; KPC, klebsiella pneumoniae carbapenemase; LPO, lipid peroxides; PD-L1, programmed death-ligand 1; IFN-γ, interferon-γ; KRAS, kirsten rat sarcoma viral oncogene homolog; RIG-I, retinoic acid-inducible gene I; A2A, adenosine A2A receptor; CSF1, colony stimulating factor 1; AHR, aryl hydrocarbon receptor; iRFA, incomplete radiofrequency ablation; GSDME, gasdermin E; CAR, chimeric antigen receptor; TCPP, tetrakis(4-carboxyphenyl)porphyrin; cGAMP, cyclic GMP-AMP; DAC, decitabine.

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Additional Table 2. Nanomaterials related to the metabolic tumor microenvironment

Author, year	Material type	Material name	Cancer	Treatments	Impact
Lihua Chen, 2025[97]	Metal-organic framework materials loaded with bufalin and indocyanine green, encapsulating metal-phenolic networks, and modified with hyaluronic acid	ZIAMH	HCC	PTT, CDT, glycolysis	Intervene in glycolysis, oxidative phosphorylation, and the TCA cycle, achieving energy deprivation, generating •OH, and downregulating the expression of genes related to oxidative phosphorylation
Kejun Dong, 2025[98]	Zinc oxide nanoparticles loaded with doxorubicin and DNA nanosponge composites	ZnOov@DS-DOX	Ovarian cancer	Glycolysis	Targeting HIF-1α mRNA, inhibiting cellular glycolysis, enhancing mitochondrial respiration, increasing ROS levels, disrupting the redox system, and inducing ferroptosis
Huiling Zhou, 2025[99]	Multivalent targeting chimeras	multi-TACs	Melanoma	Glycolysis	Target PD-L1 on the tumor cell membrane, inducing its internalization and degradation of PD-L1, thereby reducing immune evasion
QiaoMei Zhou, 2025[100]	A GSH-responsive biomimetic hybrid nanozyme system	M@GOx/Fe-HMON	HCC	Glycolysis	Generates •OH via the Fenton reaction of glucose oxidase and iron ions, inducing ferroptosis; and in glucose-deprived regions, it induces thiosulfate death by exacerbating glucose deprivation, consuming NADPH, and disrupting cysteine metabolism
Jennifer Fernandez Alarcon, 2024[101]	Glycosylated gold nanoparticles	Man-GNPs	Liver metastatic colorectal cancer	Glycolysis	Targeting liver macrophages, modulating their polarization state, and achieving antitumor activity
Rui Liu, 2025[102]	A multi-layered cascaded responsive nanoplatform	GHB NPs	Melanoma	SDT, glutamine metabolism, glycolysis	Utilizes γ-glutamyl transpeptidase to degrade hyaluronic acid in the tumor extracellular matrix, reduces the expression of glycolysis-related proteins under ultrasound stimulation,

					and leads to mitochondrial damage and blockade of the lactate shuttle by modulating the β-catenin/c-Myc pathway
Jingyi Wang, 2025[103]	Small extracellular vesicles (sEVs) secreted by cancer stem cells (CSCs)	sEVs	Non-small cell lung cancer	Glycolysis	After receptor cells take up sEVs derived from CSCs, they exhibit metabolic reprogramming, slowed cell cycle progression, and enhanced chemoresistance
Yuehua Wang, 2025[104]	Nanoinhibitors	2-DG/BP MRs	HCC	RT, glycolysis, glutamine metabolism	Generate ROS, inhibit glucose metabolism and glutamine metabolism, and doubly block the energy supply of tumor cells
Jun Ma, 2025[105]	A photothermal controllable regulator based on hollow mesoporous Prussian blue nanoparticles and phase-change material 1-tetradecanol	B/T-HM	Melanoma	PTT, glycolysis	Inhibits the glycolytic pathway of tumor cells (especially hexokinase 2), reduces lactate production, and decreases the expression of immunosuppressive factors
Guimei Chen, 2024[107]	Carrier-free photodynamic bioregulator	CASN	TNBC	PDT, LA metabolism	Modulating LA metabolism, enhancing the antitumor efficacy of ICB
Chunhui Wang, 2025[108]	Nanoreactor	MCGH NSs	TNBC	Cascade starvation-chemodynamic therapy, sugar metabolism	Release of Mn^{2+} and chloroquine, catalyzing glucose oxidation to generate H_2O_2 for starvation therapy and CDT, while simultaneously inhibiting autophagy to enhance therapeutic efficacy
Xiaoxiao Chen, 2025[109]	Platelet membrane-coated superparamagnetic iron oxide nanoparticles, LOX, and the ferroptosis inducer erastin	PM@ESL NPs	HCC	LA metabolism	Generate hydrogen peroxide and •OH to enhance ferroptosis while consuming lactate, modulating the acidic environment, and enhancing immune cell function
LinPing Zhao, 2025[110]	Self-delivered ternary bioregulator	TerBio	CRC	PDT, LA metabolism	Reprograms the tumor microenvironment by inhibiting the TGF-β signaling pathway and lactate efflux, and synergizes with PDT immunotherapy
Yajing Guo,	Self-assembled	LCCS	TNBC, CRC	LA metabolism	Consumes LA via LOX to produce hydrogen peroxide, further catalyzes the generation of

2025[111]	nanomedicine composed of lactate oxidase, catalase, chlorophyll e6, and sorafenib				oxygen, produces ROS under laser irradiation, inhibits the VEGF signaling pathway, promotes tumor vascular normalization, induces ICD, activates DCs, and enhances CD8+ T-cell infiltration
FeiTing Hsu, 2025[112]	Glycopolymer-like nanoparticles	CG NPs	GBM, pancreatic cancer	LA metabolism	Modulate the STAT3/NF-κB signaling pathway, promote the conversion of M2-type TAMs to M1-type, inhibit the function of MCT4, reduce lactate efflux, release DAMPs, activate DCs, and enhance the activity of CTLs
Yongjian Zhang, 2025[113]	Heavy-atom-free near-infrared-activated photosensitizer	Cy-BF@PEV	TNBC	PTT, PDT, LA metabolism	Inducing ICD, and in combination with lithium carbonate, converting LA into an energy source for CD8+ T cells to enhance the efficacy of photodynamic immunotherapy
Junliang Dong, 2025[114]	Nanoporous metal-organic frameworks	DCCMH	HCC	CT, CDT, LA metabolism	Generate •OH, inhibit lactate efflux to lower intracellular pH, and upregulate tyrosine kinase activity
Senfeng Zhao, 2025[115]	Carbon-doped copper nitride nanozyme	Cu3N-CNEs	TNBC	LA metabolism	Enhancing LOX activity, catalyzing the oxidation of LA to pyruvate, while simultaneously inhibiting pyruvate entry into the mitochondrial respiratory chain, thereby reprogramming lactate homeostasis
Chenchen Tang, 2025[116]	Lactate oxidase and manganese porphyrin encapsulated in nanoliposomes	ML@Lip	TNBC	SDT, LA metabolism	Consumption of LA via LOX, promoting the polarization of TAMs towards the M1 phenotype, inducing tumor cell apoptosis and ICD, releasing DAMPs, activating DCs and T cells, while simultaneously generating oxygen to enhance the efficacy of SDT
Qian Xie, 2025[117]	pH-responsive gold nanorods@cuprous oxide core-shell plasmonic hybrid nanorods	ACNRs	Melanoma	PTT, glycolysis	Inhibit the glycolytic pathway, reduce the production of lactate and ATP, and release copper ions to induce cell death
Mingliang Ning, 2025[118]	Biomimetic nanomedicines that consume glucose	GMA-LP NPs	HCC	Glycolysis	Reduce lactate production, catalyze the generation of oxygen from hydrogen peroxide, induce DNA damage, activate the STING signaling pathway, and promote the maturation of DCs and T-cell infiltration

Edoardo D'Angelo, 2025[119]	M1 macrophage-derived lipid nanovesicles	M1-LNVs	CRC	Glycolysis	Integrate membrane proteins into the lipid bilayer via microfluidic technology to achieve targeted delivery and drug release to tumor cells
ZiZhan Li, 2025[122]	Copper-based metal-organic frameworks loaded with orlistat	ORL@Cu-MOF	OSCC	Lipid metabolism	Respond and release under the stimulation of GSH in the TME, inducing copper death and inhibiting fatty acid metabolism, targeting mitochondria to induce the production of ROS, inhibiting the expression of fatty acid synthase, and suppressing lipid uptake and lipid droplet formation
Yunfei Yi, 2025[123]	siRNA micelle complexes	MH@siGLS1	CRC	siRNA technology, PDT, glutamine metabolism	Targets and inhibits glutaminase 1 via siRNA to reprogram the glutamine metabolism of tumor cells, endothelial cells, and TAMs, achieving tumor vascular normalization and macrophage polarization, and inducing ICD
Jinling Zheng, 2025[124]	6-Diazo-5-oxo-l-norleucine grafted onto TiO_2-Au Janus nanoparticles	TiO2-Au@DON	TNBC	Glutamine metabolism	Highly active Type I and Type II ROS, antagonizing glutamine, reprogramming metabolic pathways to inhibit NADPH and tumor redox balance, and inducing ICD
Zesheng Li, 2025[125]	Adenosine deaminase and chlorophyll e6 encapsulated in liposomes modified with T-cell membranes	ADA/Ce6@tLipo	TNBC	Adenosine metabolism	Generation of ROS upon ultrasound activation, induction of ICD, release and conversion of ATP into immunosuppressive adenosine, conversion of adenosine to inosine, and reversal of adenosine-mediated immunosuppression
Hongrui Fan, 2025[126]	Cascaded targeting nanoparticles	B-PDEA@CPA	PDAC	Adenosine metabolism	Downregulate CD39, modulate adenosine metabolism, and achieve enhanced delivery of chemotherapeutic drugs

PDT, photodynamic therapy; PTT, photothermal therapy; CT, chemotherapy; CDT, chemodynamic therapy; SDT, sonodynamic therapy; RT, radiotherapy; TNBC, triple-negative breast cancer; BC, breast cancer; HCC, hepatocellular carcinoma; PDAC, pancreatic ductal adenocarcinoma; CRC, colorectal cancer; GBM, glioblastoma; NSCLC, non-small cell lung cancer; OSCC, oral squamous cell carcinoma; CTLs, cytotoxic T lymphocytes; LA, lactic acid; ICB, immune checkpoint blockade; ICD, immunogenic cell death; H_2O_2, hydrogen peroxide; •OH, hydroxyl radical; LOX, lactate oxidase; TAMs, tumor-associated macrophages; DAMPs, damage-associated molecular patterns; NADPH, nicotinamide adenine dinucleotide phosphate - reduced form; ATP, adenosine triphosphate; TCA, tricarboxylic acid cycle; cGAS-STING, cyclic GMP-AMP synthase - stimulator of interferon genes; TGF-β, transforming growth factor-β; HIF-1α, hypoxia-inducible factor 1α; DCs, dendritic cells; ROS, reactive oxygen species; GSH, glutathione; PD-L1, programmed death-ligand 1; MRI, magnetic resonance imaging; STAT3, signal transducer and activator of transcription 3; NF-κB, nuclear factor kappa-light-chain-enhancer of activated B cells; MCT4, monocarboxylate transporter 4; CTLs, cytotoxic T lymphocytes; VEGF, vascular endothelial growth factor.

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Additional Table 3. Nanomaterials related to the acidic tumor microenvironment

Author, year	Material type	Material name	Cancer	Treatments	Impact
Bing Ren, 2025[130]	Cu_2MoS_4@DTC@polydopamine @nitric oxide donor@folic acid	CDPNF NPs	BC	PDT	It releases dithiocarbamate and Cu^{2+} to form the highly cytotoxic $Cu(DTC)_2$ complex. Meanwhile, under NIR light irradiation, it releases NO and $\bullet O_2^-$, generating peroxynitrite ($ONOO^-$) to promote cell apoptosis
Haoran Chen, 2025[131]	Lanthanide-doped nanoparticles@calcium phosphate/manganese-doxorubicin	LnNP-Ce6@CaP/Mn-DOX	BC	PDT	Responsive release of Mn^{2+} and doxorubicin, enhancement of the T1-weighted MRI signal, and induction of ICD
Yurong Liu, 2025[132]	The pH-activated NIR cyanine dye LET-15 nanoprobe	nLET-15	BC	PDT	It is activated in the acidic TME, transitioning from a ring-closed conformation to a ring-open structure, restoring the classic cyanine framework. This results in strong NIR absorption and fluorescence emission. Under laser irradiation, it generates ROS and $\bullet^1O_2$, thereby reducing side effects
Baoru Fang, 2025[133]	The phosphomolybdic blue nano-photothermal agent	PMB	BC	PTT	Has a good photothermal conversion efficiency, can maintain a strong tumor ablation effect when passing through a 2 mm thick tumor tissue homogenate under the irradiation of a 1064 nm laser
Qianyun Lu, 2024[134]	Titanium-doped cerium vanadate nanorods loaded with polypyrrole	CeVO4-Ti@PPy	BC	PTT	Exhibit multiple enzyme-like activities, enhance the generation of •OH, and combine photothermal effects with oxidative stress to augment catalytic tumor necrosis
Haiqin Liao, 2025[135]	The nanosystem curcumin/MnO_2@PLGA@4T1 cell membrane	CMP@4T1m	BC	SDT	Generates ROS and •OH under ultrasound irradiation, induces ICD, activates T-cell responses, and polarizes tumor-promoting M2-type TAMs to M1-type. It also oxidizes GSH to GSSG and reacts with H_2O_2 and H^+ to produce

					oxygen, thereby alleviating hypoxia
Yihui Zhai, 2024[136]	Doxorubicin-loaded ferritin cores and nanovesicles displaying IL15/IL15 receptor α complexes	DoxFILN	TNBC	Modulate immune responses	Target the transferrin receptor on cancer cells, release doxorubicin to induce ICD, and simultaneously recognize and activate the IL15 receptor β/γc heterodimer. This process promotes the proliferation and activation of CTLs and NK cells through the STAT5-mediated signaling pathway
Yosra S. Mahmoud, 2025[137]	LPS-PEC nanoparticles	DOX@LPS-PEC	TNBC	Modulate oxidative stress	Target TLR4 and are combined with DOX for chemotherapy drug delivery, simultaneously inhibiting the Sirtuin 2 inhibitor and the secretion of IL6 by TAMs, thereby reducing inflammatory factors in the TME
Yingpei Yao, 2024[138]	$MnCO_3$–Au nanoparticles loaded with AuNPs (gold nanoparticles)	$MnCO_3$–Au nanoparticles loaded with AuNPs	BC	Modulate immune responses	Exhibit glucose oxidase-like activity, catalyzing the oxidation of glucose to produce gluconic acid and H_2O_2. They also promote the catalytic generation of ROS from H_2O_2, activate the cGAS-STING pathway, and enhance T-cell infiltration
Chenxin Liu, 2025[139]	Nanoparticles	DOX@CM@M	BC	Modulate immune responses	Catalyze the conversion of cholesterol to H_2O_2, reduce cholesterol levels, increase the accumulation of chemotherapeutic drugs, catalyze the generation of ROS, activate the cGAS-STING pathway, and induce tumor cell death
YungHsin Huang, 2025[140]	Polymer-based nanoparticles made of polycaprolactone for encapsulating doxorubicin	DOX@pB-pM NPs	BC	Modulate immune responses	Targeting the mannose receptor to enhance cellular uptake and endocytosis, thereby improving drug efficacy and reducing side effects
Sichen Li, 2025[141]	Glyco-based triple hydrophilic block copolymers	PGG2/Pt	HCC	Modulate oxidative stress	Targeting the asialoglycoprotein receptor on hepatocytes to achieve targeted delivery, while releasing cisplatin and reducing systemic toxicity
Bo Li, 2024[142]	γ-glutamyl transpeptidase-activated nanoprobes	BEAGA/ApoE-PDHD	Glioma	SDT	With good blood-brain barrier penetration, the nanoprobes can enhance ultrasound-induced drug release, activate DCs, and achieve SDT and immune activation
Myriam El Moutaoukil, 2025[143]	Bifunctionalized gold nanoparticles	BIOT-NFL-DOX AuNPs	GBM	Modulate oxidative stress	Specifically bind to the microtubule network of GBM cells, release DOX, and induce apoptosis and oxidative stress

Kan Li, 2025[144]	A nano-delivery system	PTX@NPs-aPD1-IL	Lung cancer	Modulate immune responses	Releases anti-PD-1 antibodies through the hydrolysis of pH-sensitive imine bonds, thereby blocking the PD-1/PD-L1 signaling pathway. Simultaneously, it releases paclitaxel, inducing tumor cell apoptosis and triggering ICD, which in turn activates the maturation of DCs and T cell activation
Wei Zhou, 2025[145]	Nanoparticles	HA-PTS@PCN	Lung squamous cell carcinoma	PDT	Release ROS under 660 nm laser irradiation to exert PDT effects.
Zhe Liu, 2025[146]	Chitosan nanogels doped with gold nanoparticles	CTS/TPP/PAA@AuNPs	OSCC	Modulate oxidative stress	Responsively releasing drugs in tumors can be used as a contrast agent for CT imaging, and enable CT imaging-guided tumor chemotherapy, thereby improving drug delivery efficiency
Menglin Zhu, 2025[147]	Nanoparticles	FX-11@PEG-Ce6	Gastric cancer	PDT	Inducing ICD through PDT, promoting the maturation of DCs, improving the acidic TME, enhancing the infiltration of CD8+ T cells, and increasing the levels of TNF-α, IFN-γ, and granzyme B in the tumor
Xiaoyang Gao, 2025[148]	Nanocomposites	ATG@MnCa	Cervical cancer	CDT	Targeting tumor cells with transferrin, achieving dynamic shielding with calcium manganese carbonate, enhancing CDT through upregulation of NOX4 and glucose oxidase, generating •OH, and activating the cGAS-STING signaling pathway
Haojie Liu, 2025[149]	A carrier for the chemotherapeutic agent DOX and the bispecific antibody YM101 targeting TGF-β and PD-L1	DOX@MPs-YM101	HCC, BC	Modulate immune responses	Reprograms CAFs, reduces the tumor ECM, induces ICD, and activates $CD8^+$ T cell-mediated antitumor immune responses
Jiansen Li, 2025[150]	Platinum single-atom nanozyme-decorated hairpin tetrahedral DNA nanostructures	PCFP@H-TDN	BC	PDT	Possessing CAT-like activity, it catalyzes the decomposition of endogenous H_2O_2 to generate O_2, alleviates hypoxia, blocks the PD-1/PD-L1 recognition pathway, and silences PD-L1 protein expression. Under 660 nm laser irradiation, it induces ICD, releases DAMPs, and activates the maturation of DCs

Chuan Wu, 2025[151]	Multifunctional nanocubes	Mn-ER-Cy	Various types of tumors	PTT, PDT	Target the endoplasmic reticulum of tumor cells, generate ROS through a Fenton reaction, induce endoplasmic reticulum stress, activate the NLRP3 inflammasome, and induce pyroptosis
Fang Wang, 2025[152]	Nanochemotherapeutic agents,	HmPB(DOX)	Various types of tumors	Modulate oxidative stress	Reduce DOX-induced oxidative stress and alleviate cardiotoxicity through the Nrf2/Keap1 signaling pathway, scavenge DOX-induced ROS, mitigate oxidative stress, and promote tumor cell apoptosis.
Bin Sun, 2025[153]	The nano-platform is composed of polyacrylic acid/mesoporous calcium phosphate/mesoporous copper phosphate	PAA/mCaP/mCuP NSs	Various types of tumors	PDT, cuproptosis	Releases Cu^{2+} in response to both pH and near-infrared light. This process induces cuproptosis and generates a photothermal effect, while simultaneously inducing mitochondrial damage through Ca^{2+} overload
Jiamin Qin, 2025[154]	Curcumin and indocyanine green co-loaded nanoparticles based on dynamic covalent boronate esters	LIP-C/I	Various types of tumors	PTT, CT	Enhance selective cytotoxicity against tumor cells through photothermal effects and drug release.
Zhiliang Gao, 2025[155]	pH-sheddable PEG-modified peptide nanoparticles	PLL/PGA@CPEG NPs	Various types of tumors	Modulate immune responses	Enhance cellular uptake and induce cytotoxicity, and possess good biocompatibility and drug loading capacity
Naikuan Fu, 2024[156]	PEGylated bortezomib nano-prodrug	mPEG-CA-BTZ	Multiple myeloma and mantle cell lymphoma	Apoptosis	Inhibits the activity of the 26S proteasome, leading to cell cycle arrest and apoptosis. It has good stability, biocompatibility, and drug loading capacity, and reduces non-specific toxicity
M. Tamilarasi Muniandy, 2025[157]	Ultra-low molecular weight chitosan-oleic acid-folic acid-cisplatin conjugates	UCS-OA-FA-CPT	Lung cancer	Modulate immune responses	Enhance the water solubility of chitosan through oleic acid modification, use folic acid as a targeting ligand to increase drug accumulation, and improve the release efficiency of cisplatin in the form of a conjugate
Zirui Ye, 2025[158]	Polydopamine-coated ferromagnetic vortex domain iron oxide nanorings	FVIO@PDA	HCC	Magnetic therapy	Respond to acidity and magnetic fields, regulate the expression of Tregs and PD-L1, trigger the release of DAMPs, and modulate the cytokine profile by reducing the secretion of the immunosuppressive cytokine IL-10 while increasing the secretion of pro-inflammatory cytokines IFN-γ and TNF-α

Jiayi Hu, 2025[159]	A nanoplatform	GNPs@AuNPs-PPy@Que	Various types of tumors	PDT, CDT, CT	Generates ROS to induce tumor cell death, has pH/NIR dual-responsive drug release capabilities under NIR light irradiation, and achieves tumor-targeted drug delivery through the enhanced permeability and retention effect
Zheng Li, 2025[160]	The nanoparticles composed of ARV-825 and PEG-ICG induce cell apoptosis and ICD by degrading the BRD4 protein	ARV@PEG-ICG	BC	PDT	By degrading the BRD4 protein, inhibiting the production of nitric oxide synthase, generating ROS under laser irradiation, downregulating the expression of Bcl-xL, inducing PARP cleavage, promoting cell apoptosis, inducing ICD, and facilitating the maturation of DCs and the activation of T cells
Wei Ni, 2025[161]	ZIF-8 functionalized nanoparticles loaded with indocyanine green and DOX	ZID@RM	HCC	PDT, PTT	Generate ROS under the dual regulation of acidity and infrared light, inducing pyroptosis in tumor cells and promoting the release of DAMPs, thereby enhancing the chemotherapeutic efficacy of doxorubicin
Xiuli Zhang, 2025[162]	Bio - mineralized nanoparticles of manganese ions, hydroxyapatite, and risedronate	MnHARis	TNBC	Modulate immune responses	Promote cell apoptosis via the p38-MAPK signaling pathway, induce ICD, increase calcium ion levels, and enhance the antigen-presenting capacity of tumor-infiltrating T cells and DCs
Jingwen Liu, 2025[163]	Tirazamin/ hollow mesoporous organosilica nanoparticles/iron oxide@Glucose oxidase	TPZ/HMOS/IO@GOx	BC	Modulate oxidative stress	Catalyzes the conversion of glucose into H_2O_2 and gluconic acid, consumes O_2, increases acidity, induces the Fenton reaction, generates ROS, Fe^{2+}, and GSSG, thereby enhancing oxidative stress in tumor cells
Jingjing Wang, 2025[164]	Poly (lactic-co-glycolic acid) @ultrasmall ferrous sulfide-glucose oxidase	PLGA@ultra-small FeS-GOx	BC	Ferroptosis	Induces vasodilation via H_2S and undergoes acid-responsive degradation, releasing Fe^{2+}, H_2S, and glucose oxidase to modulate the TME, leading to increased acidity, upregulation of H_2O_2, downregulation of GSH, and downregulation of adenosine triphosphate, resulting in the accumulation of substantial LPO and the induction of ferroptosis
Ruiqi Yan, 2025[165]	Copper death nanoprodrug	Lipo@CP@DQ NPs	TNBC	Cuproptosis	Releases copper ions, H_2O_2, and the prodrug DQ under acidic conditions, induces copper death, generates •OH, forms the anticancer compound $Cu(DTC)_2$, and depletes GSH, thereby synergistically integrating copper death, in situ chemotherapy, and oxidative stress

Miaomiao Ding, 2025[166]	Nanoparticles	BDPB/Pt/Fe@P[5]	BC	PTT, CDT	Catalyzing the production of $•O_2^-$ and •OH, promoting the Fenton reaction, converting "cold tumors" into "hot tumors" through the ICD effect, and activating T-cell functions
Xiangyu Meng, 2024[167]	Cerium oxide@copper peroxide@doxorubicin-lasoglitide @hyaluronic acid	CeO2@CuO2@DOX-RSL3 @HA	BC	Cuproptosis	It has CAT and POD mimetic activities, converts H_2O_2 into O_2 and •OH, inhibits the expression of glutathione peroxidase 4, depletes GSH, leads to lipid peroxidation, induces ferroptosis, induces oligomerization of dihydrolipoamide S-acetyltransferase, downregulates iron-sulfur cluster proteins, and induces copper death
HsinTing Tsai, 2025[168]	The supramolecular assembly nanoparticles containing iron, tannic acid, and zoledronic acid, which are surface-modified with fucoidan	FTZ@Fu SANs	Various types of tumors	Ferroptosis	Release zoledronic acid in the acidic TME, induce ferroptosis, and enhance ICD
Zhenxin Wang, 2025[169]	Copper-based nano-inducers	CST NPs （Cu2-xSe@DSPE-PEG-TPP ）	Osteosarcoma	Modulate immune responses	Inhibit the activity of glucose-6-phosphate dehydrogenase, reduce the production of NADPH, leading to decreased synthesis of GSH, generate a large amount of ROS, release tumor-associated antigens and DAMPs, induce ICD, and promote the maturation of DCs and activation of cytotoxic T cells
Shasha Zhao, 2025[170]	Cancer cell membrane-coated manganese-doped hollow mesoporous silica nanoparticles with isoniazid and benzothiazole sulfinate	CCM@MIB	BC	Modulate oxidative stress	Generation of highly toxic levels of •OH and $•O_2^-$, depletion of GSH, and inhibition of the activities of superoxide dismutase and glutathione peroxidase 4
Mengke Fan, 2025[171]	Copper–manganese composite nanomaterials, surface-modified with hyaluronic acid	CMCNs@HA	BC	Cuproptosis	Decompose to produce H_2O_2, catalyze the conversion of H_2O_2 to O_2, and in combination with GSH depletion and hypoxia alleviation, enhance copper-induced cell death and activate the cGAS-STING pathway
Le Xin,	Copper-doped polydopamine	PC NPs	BC	Cuproptosis	Cu^{2+} is reduced to Cu^+ in the presence of GSH, leading to GSH depletion,

2025[172]	nanoparticles, encapsulated with platelet cell membranes				ROS generation, and subsequent cell death
Gaizhen Kuang, 2025[173]	Stimuli-responsive dual-drug polymer nanoparticles	DDPoly NPs	Various types of tumors	Apoptosis	Enhance the expression of phosphorylated Akt by inhibiting the expression of protein phosphatase 2A, blocking DNA repair, and augmenting platinum (II)-induced apoptosis.
Qingyuan Deng, 2025[174]	Carbonic anhydrase IX (CAIX) inhibitor-conjugated hydroxyethyl starch-based nanoparticles	CHHD-Cu NPs	HCC	Modulate oxidative stress	By targeting CAIX, lower the intracellular pH, and release DOX and Cu^{2+} in the acidic environment to eliminate cancer stem cells
Min Lin, 2025[175]	Polypeptoid assembly cofactor-assisted ursolic acid helix	Polypeptoid assembly cofactor-assisted ursolic acid helix	HCC	Modulate oxidative stress	By undergoing acid-responsive transformation into virus-like structures, and triggering drug release through oxidative stress, leading to mitochondrial damage and apoptosis.
Ludwig Erik Aguilar, 2025[176]	Gold nanoparticles surface-modified with poly-caffeic acid, bortezomib, and folic acid	AuNP-PCA-BTZ-Fol	Various types of tumors	Modulate oxidative stress	Induce ROS generation in mitochondria, damage intracellular proteins and DNA, inhibit proteasome activity, prevent cells from repairing damaged proteins, and enhance apoptosis
Yilu Zheng, 2025[177]	An acid-triggered bilayer protective shell nanoplatform	CaO2@ZIF8:CUR@PAA	Osteosarcoma	Modulate immune responses	Causes intracellular calcium ion overload, leading to mitochondrial dysfunction and apoptosis, generates a large amount of ROS, triggers ICD through oxidative stress, and promotes the polarization of TAMs toward the M1 phenotype
XueHao Zhang, 2025[178]	Adaptive peptide nano-assembly materials	FeFKC	Various types of tumors	Modulate oxidative stress	Catalyze the generation of •OH from H_2O_2 in an acidic environment, escape from lysosomes, and target mitochondria to induce tumor cell death
Wenjing Xie, 2025[179]	DNA-templated manganese carbonate nanoparticles	DtMnP	BC	siRNA technology	Acting as cofactors for DNAzymes, catalyze the specific cleavage of target mRNA to achieve gene silencing, generate •OH, and enhance the efficacy of CDT
Zhifang Wang, 2025[180]	MgF_2@L-Arg nanoparticles	ML NPs	BC	SDT	Selectively protonate amino groups, generating spatial charge asymmetry, which promotes the sustained diffusion and penetration of the nanoparticles. They also reduce the expression of HIF-1α and HSP 70, induce ICD, and bind

					to the costimulatory molecule LFA-1 on the surface of tumor cells, thereby enhancing the specific cytotoxicity of $CD8^+$ T cells
Xu Zhang, 2025[181]	The engineered oncolytic bacterium YB1, carrying acid/enzyme-triggered detachable nanoparticles	YB1−HCNs	Bladder tumors	SPDT	Under continuous irradiation by laser and ultrasound, it can respectively generate Type II and Type I ROS for highly efficient sonophotodynamic therapy and optimized spatial distribution of the drug
Ziqi Guo, 2025[182]	pH-responsive lipid nanoparticles	lip@si-YTHDF2	HCC	siRNA technology	Target the delivery of siRNA to inhibit YTHDF2 expression, while stabilizing MYC mRNA through m6A modification, reducing the secretion of immunosuppressive cytokines, and enhancing the immunosuppressive activity of MDSCs

PDT, photodynamic therapy; PTT, photothermal therapy; SDT, sonodynamic therapy; SPDT, sonophotodynamic therapy; CDT, chemodynamic therapy; CT, chemotherapy; BC, breast cancer; TNBC, triple-negative breast cancer; HCC, hepatocellular carcinoma; GBM, glioblastoma; OSCC, oral squamous cell carcinoma; GSH, glutathione; GSSG, glutathione disulfide; H_2O_2, hydrogen peroxide; O_2, oxygen; NO, nitric oxide; ROS, reactive oxygen species; CAT, catalase; POD, peroxidase; •OH, hydroxyl radical; $•O_2^-$, superoxide anion; $•^1O_2$, singlet oxygen; LPO, lipid peroxidation; ICD, immunogenic cell death; cGAS-STING, cyclic GMP-AMP synthase (cGAS) - stimulator of interferon genes (STING) pathway; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; PARP, poly(ADP-ribose) polymerase; Bcl-xL, B-cell lymphoma-extra-large; TLR4, toll-like receptor 4; BRD4, bromodomain-containing protein 4; NIR, near-infrared light; TAMs, tumor-associated macrophages; DC, dendritic cells; CTLs, cytotoxic T lymphocytes; NK cells, natural killer cells; TAFs/CAFs, cancer-associated fibroblasts; Tregs, regulatory T cells; DAMPs, damage-associated molecular patterns; MDSCs, myeloid-derived suppressor cells; MRI, magnetic resonance imaging; DOX, doxorubicin; HIF-1α, hypoxia-inducible factor 1-alpha; HSP 70, heat shock protein 70; LFA-1, lymphocyte function-associated antigen 1; IFN-γ, interferon-gamma; TNF-α, tumor necrosis factor-alpha; TGF-β, transforming growth factor-beta; YTHDF2, YTH domain family protein 2; m6A, N^6-methyladenosine; MYC, v-myc avian myelocytomatosis viral oncogene homolog; NLRP3, nucleotide-binding domain, leucine-rich repeat containing family, pyrin domain containing 3; NADPH, nicotinamide adenine dinucleotide phosphate - reduced form; NOX4, NADPH oxidase 4; Nrf2, nuclear factor (erythroid-derived 2)-like 2; Keap1, kelch-like ECH-associated protein 1; MAPK, mitogen-activated protein kinase; Akt,protein kinase B (PKB) signaling pathway; BBB, blood-brain barrier; PTX, paclitaxel; ECM, extracellular matrix; CAT, catalase.

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Additional Table 4. Nanomaterials related to the hypoxic tumor microenvironment

Author, year	Material type	Material name	Cancer	Treatments	Impact
Jie Yu, 2025[185]	Hypoxia-tolerant polymer prodrugs of photosensitizers	Hypoxia-tolerant polymeric photosensitizer prodrug (HTPSNiclo)	BC	PDT	Specifically release niclosamide in the TME, inhibit the phosphorylation of STAT3, reduce the expression of HIF-1α, and enhance the activation of immune cells and the production of immunostimulatory cytokines
Lingzhijie Kong, 2025[186]	Gold nanorods/silica/hyaluronic acid/doxorubicin	Au@SiO2-HA-DOX	BC	PTT	Responsive to pH and ROS stimuli, achieve controlled drug release, target the CD44 receptors on the surface of tumor cells, enhance drug uptake in tumor cells, and exhibit good photothermal stability and sustained temperature increase under NIR irradiation
Dalu Xie, 2025[187]	Organic nanoparticles	2TT-oC6B NPs	BC	PTT	Convert light energy into thermal energy via 808 nm laser irradiation, inhibit the DNA repair process, modulate the cell cycle, induce cell apoptosis and ICD, release DAMPs, activate the immune system, and promote the maturation of DCs and infiltration of T cells
Yinjia Cheng, 2025[188]	A hydrogenated black titanium-based core-shell structured nanocarrier, surface-modified with hyaluronic acid	BT@M/T@T(Cu)GH	BC	SDT, CDT, CT	Capable of generating •OH and $•^1O_2$, while consuming GSH, catalyzing the oxidation of glucose to produce gluconic acid and H_2O_2, and inducing tumor starvation

Xingheng Wang, 2025[189]	Iron-based phthalocyanine network	p-PcFe	BC	SDT	Efficiently catalyzes the generation of ROS under ultrasound irradiation, induces the maturation of DCs and the polarization of macrophages by releasing tumor-associated antigens, DAMPs, and pro-inflammatory cytokines, thereby enhancing the infiltration of tumor-specific effector T cells
Xudong Li, 2025[190]	A nanotheranostic system based on chitosan modified with BODIPY dye	CsBPNs	BC	PTT	Exhibits hypoxia-responsive fluorescence and photothermal effects. It achieves synergistic therapeutic effects through the combined application of PTT and drugs
Jinglin Zou, 2025[191]	A siloxane-based nanomedicine co-loaded with zinc protoporphyrin and quercetin	ZnPP@FQOS	PDAC	PDT	Quercetin reshapes CAFs and reduces antioxidant stress. Meanwhile, zinc protoporphyrin generates $\bullet^1O_2$ under laser irradiation, enhancing the efficacy of PDT and inducing ICD
Simin Xi, 2025[192]	Nanoparticles assembled from the multifunctional photosensitizer TTNH, which is covalently linked by 2-cyanothiazole and N, N-diphenyl-4-(thiophen-2 -yl) aniline	TTNH NPs	CRC	PDT, PTT	Generate $\bullet O_2^-$ under 808 nm laser irradiation. They also exhibit high photothermal conversion efficiency, achieving synergistic therapy of PDT and PTT
Lu Zhang, 2025[193]	Reactive oxygen species-responsive polymer micelles containing paclitaxel and honokiol	RC-PH-Ms	Ovarian cancer	Modulate immune responses	Paclitaxel and honokiol work together to promote the transformation of TAMs from the M2 phenotype to the M1 phenotype, thereby inhibiting tumor growth, invasion, and metastasis, reducing angiogenesis, and decreasing tumor recurrence.

Qian Li, 2025[194]	Neuroblastoma-targeted π-conjugated organic polymer nanostructures	COPTPcFe	Neuroblastoma	Regulate oxidative stress	Mimic the activity of natural peroxidase, efficiently generate ROS by utilizing local H_2O_2, and the effects of ultrasound. These structures possess excellent electron transfer capabilities, enabling rapid catalysis of H_2O_2 to O_2, alleviating hypoxia. They can also activate NK cells, reverse the immunosuppressive TME, and significantly enhance therapeutic efficacy.
Zhengwei Xu, 2025[195]	A live biotherapeutic agent combined with cyanobacteria	Cyano@DicTBS-ZnNCs	BC	PDT	Utilize cyanobacteria to perform photosynthesis to produce O_2, thereby alleviating tumor hypoxia. Under 660 nm laser irradiation, it generates $•^1O_2$. It can dually inhibit quinone oxidoreductase 1 and pyruvate dehydrogenase kinase 1, enhancing antitumor efficacy and inducing ICD through PDT
Anatoly Peshkov, 2025[196]	Fluorinated oxalate nanodrugs	FOC NM	Various tumors	Modulate immune responses	React with hydrogen peroxide to produce chemiluminescence and enhanced ^{19}F NMR signals. Under ROS conditions, the nanodrugs degrade, releasing the model fluorophore rubrene and enhancing the cytotoxicity of doxorubicin
Haitao Yuan, 2025[197]	Photosensitizing lipid nanoparticles co-loaded with poly[(9,9-dioctylfluorene-2,7-diyl)-alt-(benzo [2,1,3] thiadiazole-4,7-diyl)] and roxadustat	PFBT@Rox Lip	CRC	PDT	Increase erythropoietin levels, improve oxygenation status, and promote tumor vascular normalization. Under white light irradiation, they generate Type I and Type II ROS, inducing endoplasmic reticulum stress and ICD
Kai Zhong, 2025[198]	Manganese peroxide/ergothioneine liposomes	MnPO2/MC3	Various tumors	Modulate immune responses	Achieve charge reversal through protonation, enhancing transcellular transport capacity, and deeply deliver oxygen and manganese ions into tumor tissues. They catalyze the generation of •OH from H_2O_2 and increase the infiltration of $CD8^+$ T cells

Xiang He, 2024[199]	IR780@O_2 nanobubbles	IR780@O2 NBs	TNBC	SPDT, pyroptosis	Possessing the SPDT effect, it simultaneously releases oxygen to alleviate tumor hypoxia and generates a large amount of ROS to induce pyroptosis. In this process, CSF and CXCL may serve as potential targets for pyroptosis in TNBC cells
ChiHung Hsiao, 2025[200]	Chlorella glycol chitosan iron oxide nanoparticles	CHL-GCS-IO NPs	Bladder cancer	PDT, PTT, ferroptosis	Under light conditions, oxygen is produced through photosynthesis. The drug is magnetically responsive, enabling magnetic targeting therapy to enhance drug accumulation at the tumor site. It combines PTT and ferroptosis. Upon NIR irradiation, local hyperthermia is generated to induce tumor cell death and promote the activation of DCs, NK cells, and CD8+ T cells
Da Zhang, 2025[201]	Lipid-coated hafnium silicate nanoparticles	Lipid@mHfSiO2 sipc	Various tumors	Modulate immune responses	Directly transfer high-energy electrons to the low-energy triplet state of a photosensitizer under X-ray irradiation, thereby generating $\bullet^1O_2$. This process induces the infiltration of immune cells, produces an abscopal effect, and stimulates the generation of memory T cells
Yuqi Tang, 2025[202]	Magnetic silica doped polymeric nanoparticles	MSDP NPs	HCC	PDT, PTT	Utilizing NIR-II technology to enhance tumor targeting through J-aggregation, generating Type I ROS, inducing pyroptosis, inhibiting tumor cell proliferation, and enhancing drug accumulation
Xinran Qu, 2025[203]	Manganese - doped hydroxyapatite nanorods loaded with the exosome inhibitor GW4869 and ROS - cleavable lipid DSPE - TK - mPEG	GMHL	CRC, Melanoma	Piezoelectric effect, Modulate immune responses	Reduce band-gap energy to enhance piezocatalytic activity, increasing ROS generation under ultrasound stimulation. Meanwhile, they inhibit exosome secretion, reduce PD-L1 expression, trigger the cleavage of the lipid layer, promote DC maturation, and enhance T-cell activity

YuHsiang Lee, 2025[204]	Indocyanine green and camptothecin-loaded perfluorochemical cancer-derived exosomes	ICFESs	Melanoma	PDT, PTT	Under NIR irradiation, it generates PTT and $•^1O_2$ to induce tumor cell death, while the released drug provides a chemotherapeutic effect
Yashi Li, 2025[205]	A microneedle patch based on catalase	PS@CAT NPs	BC	PDT	Restores the catalytic activity of CAT to catalyze the generation of oxygen from endogenous H_2O_2, and achieves minimally invasive, spatially targeted transdermal drug delivery through the microneedle patch
Qiantong Liu, 2025[206]	Carbon/manganese nanoparticles targeting nucleolin	AMMCN@DOX	BC	CDT	Catalyze the generation of oxygen from H_2O_2 under acidic conditions to alleviate tumor hypoxia, and enhance therapeutic efficacy by generating •OH through the Fenton reaction
Yawen Guo, 2025[207]	Ferroptosis-inducing, catalase-loaded M1 macrophage exosomes modified with RS17	FeSR780@CAT@Mex-RS17	Lung cancer	Ferroptosis	Release Fe^{3+} and CAT, generate •OH through the Fenton reaction to induce ferroptosis. The produced ROS and ferroptosis jointly induce ICD, release DAMPs, and activate immune responses
Yue Liu, 2025[208]	Catalase and JQ1-loaded liposomes modified with RGD	C/J-LipoRGD	Melanoma	Modulate immune responses	CAT catalyzes the decomposition of excess H_2O_2 in tumors to improve hypoxia, while simultaneously downregulating PD-L1 expression, reversing T cell exhaustion, and enhancing the efficacy of RT and immunotherapy.
YuLin Zhong, 2024[209]	Zinc-rich Co_3O_4/nitrogen-doped porous carbon-glucose oxidase	Zn-Co3O4/NC-GOx	BC	Ferroptosis	The glucose oxidase reaction generates H_2O_2 and gluconic acid to achieve starvation therapy, can release Zn^{2+} to induce cell apoptosis, consume GSH, reduce the consumption of ROS, and promote ferroptosis

Kun Qiao, 2025[210]	Cancer cell membrane-coated platinum-palladium bimetallic nanozymes	MPPC@CM	BC	Ferroptosis	Catalyze the generation of O_2 from H_2O_2, alleviating the hypoxic state of the tumor microenvironment, consuming GSH, and producing a large amount of ROS. These actions disrupt the antioxidant defense mechanisms within tumor cells, induce ferroptosis, and promote the maturation of DCs and infiltration of $CD8^+$ T cells
Yang Zhu, 2025[211]	Ruthenium single-atom nanozyme-driven titanium dioxide-based sonosensitizer	Ru/TiO_2-x SAE	GBM	Ferroptosis	Enhances the separation efficiency of electron-hole pairs, increases oxygen adsorption, and improves ROS generation. By mimicking the activities of catalase and glutathione peroxidase 4, it alleviates hypoxia and reductivity, and triggers ferroptosis mediated by lipid peroxidation
Wanying Sun, 2025[212]	Cobalt sulfide-lactate oxidase/hyaluronic acid	Co3S4@LOx/HA	HCC	Modulate immune responses	Generating H_2O_2 and •OH through self-circulating cascade catalytic reactions, consuming GSH, lactic acid, and inhibiting the activity of thioredoxin reductase, enhancing ROS accumulation, inducing DNA damage, activating STING-related immune responses, and promoting the maturation of DCs and the activation of T cells
Yuanyuan Zhang, 2025[213]	Quantum dots/PluriSIn 1@nanoparticles@membrane	QD/POM1@NP@M	CRC	SDT	Under ultrasound irradiation, ROS are generated and ICD is induced, with the release of ATP. This process also inhibits the activity of CD39, reducing the degradation of ATP to adenosine.
Gahyun Lee, 2025[214]	Folic acid-functionalized liposome nanoparticles containing perfluorohexane, co-loaded with oxygen and doxorubicin	HON_FA@DOX	BC	Induce cell apoptosis	These nanoparticles achieve tumor-specific binding via the folate receptor α, while enhancing oxygen-carrying capacity and reducing the expression of HIF-1α. The co-loaded DOX induces tumor cell apoptosis through mechanisms such as the inhibition of topoisomerase II

Zhenzhen Luo, 2025[215]	Apoptin-loaded zeolitic imidazolate framework-8 with platinum nanoparticles	AP@ZIF-8Pt	HCC	Apoptosis	By loading the apoptotic protein apoptin to induce apoptosis in hepatocellular carcinoma cells, catalyzing the production of O_2 from endogenous H_2O_2. Transcriptomic analysis indicates that it functions through pathways related to heat generation, stem cell pluripotency regulation, ribosomes, prion diseases, and the PI3K-Akt signaling pathway
Yang Liu, 2025[216]	Polymer micelles containing docetaxel and triptolide	PVGLIG-MTX-D/T-NMs	Ovarian cancer	Modulate immune responses	Enhancing nanoparticle uptake through folate receptor-mediated endocytosis, and inhibiting EMT and tumor cell angiogenesis by regulating the expression levels of E-Cadherin, N-Cadherin, matrix metalloproteinases, HIF-1α, and vascular endothelial growth factor
Shiye Du, 2025[217]	The Fe (III)-metal Pt (II)-porphyrin framework	FPTM-LP	TNBC	Regulate oxidative stress	By inhibiting oxidative phosphorylation, releasing lonidamine, promoting the generation of Fe^{2+}, •OH and $•^1O_2$, stabilizing DNA damage, and downregulating the expression of HIF-1α
Xi Zhang, 2025[218]	A multifunctional polyester nano-platform	BFN2-DR/HIF-1α siRNA@O_2	BC	PDT，siRNA technology	Through photochemical internalization technology, promotes the escape of siRNA from lysosomes, enhances gene silencing efficiency, alleviates tumor hypoxia, and enhances PDT efficacy, while simultaneously silencing HIF-1α via siRNA
Lei Lei, 2025[219]	Tumor vasculature-targeted nanosized covalent–organic polymer	TVM	HCC	PDT	By inhibiting the glycolysis pathway to reduce oxygen consumption, alleviating tumor hypoxia, while simultaneously suppressing PD-L1 expression and inducing ICD
Mingli Wei, 2025[220]	Aminolevulinic acid and verteporfin-loaded low-density lipoprotein nanoparticles with	AV@LDL&CaO2 MNs	Melanoma	Regulate oxidative stress	Capable of decomposing to produce O_2 and calcium ions, while simultaneously exacerbating mitochondrial damage through a ROS storm. This action synergistically enhances immunogenicity, downregulates the infiltration of M2-type TAMs within the tumor, and reshapes the

	calcium peroxide				immunosuppressive TME
Yunji Sun, 2025[221]	A multifunctional nanocarrier system	H-MnO2@IR825-VC	Prostate cancer	PDT, PTT, CDT	Decompose H_2O_2 to produce oxygen, thereby alleviating tumor hypoxia. Generate heat and ROS through PTT and PDT to induce tumor cell apoptosis. CDT is achieved by catalyzing H_2O_2 to produce •OH using MnO_2
Heejin Ha, 2025[222]	Oxygen-loaded- sensitive liposomes co-loaded with oxygen and razuprotafib	OD_PSL@AKB	Various tumors	Modulate immune responses	Rapidly release oxygen and razuprotafib. Razuprotafib activates the Tie-2 signaling pathway by inhibiting vascular endothelial protein tyrosine phosphatase, restores the expression of VE-cadherin, enhances the connections between vascular endothelial cells, and reduces the abnormality of tumor blood vessels
Xingyu Luo, 2025[223]	Zinc-doped copper-based metal-organic framework nanoparticles modified with 5-aminolevulinic acid, with platelet membrane surface modification	5-ALA@Zn-CuTz@PM NPs	BC	PDT, CDT	Inhibit the activity of heme oxygenase-1, reduce the conversion of protoporphyrin IX to non-photosensitive heme, increase the intracellular concentration of effective photosensitizers, and enhance PDT efficacy. Meanwhile, they catalyze the decomposition of H_2O_2 to generate •OH, consume GSH, alleviate tumor hypoxia, and enhance CDT effects
Neha Mehrotra, 2025[224]	Tumor-targeting gold-doped copper sulfide dual-plasmonic nanodots	Au-doped Cu1.92S（ACSH NDs）	BC	PTT, CDT	Convert light energy into thermal energy under NIR irradiation for tumor thermoablation, while generating $•^1O_2$ and •OH, consuming GSH, and enhancing CDT efficacy. These nanodots target breast cancer cells overexpressing CD44, improving tumor selectivity and drug accumulation

Chen Su, 2025[225]	Liquid metal nanodroplets-biologically reducible guanidinated hyperbranched polyamide amine	LMND@HSG	BC	Cell apoptosis	These materials degrade to produce ROS, trigger the release of NO under acidic conditions, consume GSH, cause DNA damage and mitochondrial dysfunction, and ultimately induce apoptosis in tumor cells
Javier Bonet Aleta, 2025[226]	Copper hexacyanoferrate nanocubes	CuHCF	GBM	Regulate oxidative stress	Capable of accelerating the oxidation of GSH while simultaneously generating ROS, and exhibiting higher catalytic activity in tumor cells with high GSH concentrations
Huan Zhao, 2025[227]	Iron-tetrahydroxy-1,4-benzoquinone/STING agonist SR-717	Fe-THBQ/SR	BC, Melanoma	PDT, ferroptosis	Generate ROS under 1064 nm laser irradiation. It induces ferroptosis by consuming GSH and inhibiting glutathione peroxidase 4, while simultaneously causing DNA damage to activate the STING pathway. This process promotes vascular normalization and induces ICD
Zixuan Chen, 2025[228]	DNA tetrahedron-triphenylphosphonium-gold nanoclusters-black phosphorus quantum dots	tDNA-TPP-AuNCs-BPQDs	HCC	PTT	Enhance antitumor and antimetastatic effects by enzyme-activated fluorescence imaging and amplified mitochondrial oxidative stress via DNA tetrahedrons, convert intracellular H_2O_2 to O_2 to alleviate hypoxia, adsorb intracellular GSH, and further amplify mitochondrial oxidative stress with PTT, successfully inducing ICD
Tianyue Xu, 2025[229]	A cisplatin prodrug nanosystem loaded with ozone	O3_PFD@PtF	TNBC	RT	The ROS generated from ozone disrupts the intracellular redox balance, promotes the reductive-responsive release of cisplatin, alleviates the hypoxic state, enhances the efficacy of RT, and triggers ICD

Zhipeng Han, 2024[230]	Nanoparticles	FePt/MnO2@PEG	Osteosarcoma	Ferroptosis	Enhance radiation capture through high atomic number elements, which are capable of decomposing H_2O_2 to produce oxygen, consuming GSH to induce ferroptosis, and enhancing the sensitivity of tumor cells to radiotherapy
Chen Xiao, 2025[231]	Copper ionophore CuET nanocrystals stabilized by polydopamine and hydroxyethyl starch form a nanomedicine	CuET@PHF	TNBC	PTT, cuproptosis	Overcomes tumor hypoxia through the photothermal effect. This approach alleviates the downregulation of FDX1, a protein related to cuproptosis, while simultaneously modulating tumor mechanics (including tumor stiffness and vascular normalization). It also disrupts TCA proteins to induce cell death, thereby enhancing the efficacy of cuproptosis
Jun Ma, 2025[232]	Cancer cell membrane-coated poly lactic-co-glycolic acid encapsulated Ca-Fe peroxide clusters and polyarginine nanocatalysts	CCM-PLGA-CaFe-R NPs	GBM	CDT	Capable of releasing CaFe clusters to generate Fe^{3+}/Fe^{2+} and H_2O_2, sustaining the Fenton reaction, while simultaneously releasing NO to promote the reduction of Fe^{3+} to Fe^{2+}, and amplify the generation of •OH
Zhijin Fan, 2024[233]	Iron-tetrakis (4-carboxyphenyl) porphyrin-R848-polyethyl ene glycol	FeMOF-RP	Melanoma	PDT, ferroptosis	Generating ROS, depleting GSH, and releasing iron ions to induce ferroptosis and ICD, stimulating the transformation of M2 macrophages into M1 macrophages, releasing tumor-associated antigens, and enhancing the immune response.
Jiajia Luo, 2025[234]	Auranofin/PluriSIn 1@Hypoxia-responsive micelles	Aur/Plu@HM	Ovarian cancer	Ferroptosis	Trigger drug release and consume antioxidant molecules in the hypoxic TME, and enhance ferroptosis and inhibit the growth of ovarian cancer cells through the co-delivery targeting stearoyl-CoA desaturase 1 and ferroptosis inducers

Dong Wang, 2025[235]	Fe@Ag-doped ZnSe quantum dots	FAQD	Various tumors	SDT, CDT	Trigger the Fenton reaction to produce •OH under ultrasound stimulation. These quantum dots inhibit the non-radiative recombination of excitons, thereby enhancing the production efficiency of $•^1O_2$ and improving the efficacy of SDT. They also promote the accumulation of nanoparticles at the tumor site
Rongjun Zhang, 2025[236]	AID nanomedicine	Atovaquone, IR820, Doxorubicin (AID)	BC	PTT	Inhibits the activity of mitochondrial electron transport chain complex I/II/III/IV/V, disrupts the mitochondrial oxidative respiratory chain, reduces oxygen consumption, and generates a mild thermal effect under NIR irradiation, thereby improving blood flow within the tumor
Jian Sun, 2024[237]	The MnO_2/BSA/PDA composite nano-platform	MBD&C	BC	Modulate immune responses	By activating the TRPV1 channel, inducing Ca^{2+} overload, reducing the secretion of CGRP and SP, alleviating tumor hypoxia, and enhancing the infiltration and activity of immune cells.
Nikhil Rai, 2025[238]	Redox-responsive sodium alginate nanogels	MMC-GalG/g/PMMA@BIS	BC	Modulate immune responses	Utilize the high levels of GSH to trigger drug release, exhibit good biocompatibility and stability, reduce systemic toxicity, and enhance drug accumulation and therapeutic efficacy
Zhijie Zhang, 2025[239]	Copper-diethyldithiocarbamate/indocyanine green nanoparticles	CuET/ICG NPs	TNBC	PDT	By interfering with mitochondria and activating the AMPK pathway, the AMPK-mediated proteasomal pathway reduces the membrane expression of PD-L1, decreases oxygen consumption, and alleviates tumor hypoxia. These actions enhance the efficacy of PDT, induce ICD, release DAMPs, and promote the maturation of DCs and the activation of T cells

Yue Wu, 2025[240]	Gambogic acid/boron nitride liposomes	GA/BN LIP	CRC	PDT, PTT	The drug directly kills tumor cells and enhances the efficacy of PTT, while also targeting mitochondria to achieve the combination of PTT and PDT
Yinfei Zheng, 2025[241]	Hollow mesoporous nanorods	HmBMH@MSA-2	BC	Modulate immune responses	Generate •OH through the Fenton reaction, which disrupts mitochondria and DNA, activate the cGAS-STING pathway, and in combination with anti-IL-35 blockade, reduce Breg cell-mediated suppression of NK cells
Zeyu Duan, 2025[242]	Mitochondria-targeted I type PDT drugs	Rh-PTZ	BC	PDT	generate $•O_2^-$ and •OH under LED white light irradiation. These drugs accumulate in the cellular mitochondria, producing a large amount of Type I ROS to induce mitochondrial dysfunction. Mitochondria-targeted PDT induces ICD, releases DAMPs, and promotes the maturation of DCs and the infiltration of CD8+ T cells
ChengAo Li, 2025[243]	Nanoplatform for targeting mitochondria with near-infrared photodynamic therapy	NZ@TG	HCC	PDT	By targeting mitochondria, the generation of ROS is localized near the oxygen-rich mitochondria, inducing oxidative damage, triggering ICD, releasing DAMPs, and promoting the maturation of DCs and the activation of T cells
QiuYing Deng, 2025[244]	Supramolecular nanomedicine based on protein immobilization	FPA/DOX	Cervical cancer	Modulate immune responses	Responsive release of benzaldehyde groups under hypoxic and acidic microenvironments, which undergo covalent cross-linking reactions with lysosomal proteins, leading to increased lysosomal membrane permeability. This subsequently triggers lysosome-dependent cell death and promotes the rapid entry of the drug DOX into the cell nucleus.

PDT, photodynamic therapy; PTT, photothermal therapy; SDT, sonodynamic therapy; SPDT, sono-photodynamic therapy; CT, chemotherapy; RT, radiotherapy; BC, breast cancer; TNBC, triple-negative breast cancer; HCC, hepatocellular carcinoma; PDAC, pancreatic ductal adenocarcinoma; CRC, colorectal cancer; GBM, glioblastoma multiforme; AMPK, AMP-activated protein kinase pathway; STAT3, signal transducer and activator of transcription 3; HIF-1α, hypoxia-inducible factor 1 alpha; NIR, near-infrared light; ROS, reactive oxygen species; CAT, catalase; $•{}^1O_2$, singlet oxygen; •OH, hydroxyl radical; $•O_2^-$, superoxide anion; H_2O_2, hydrogen peroxide; O_2, oxygen; NO, nitric oxide; CDT, chemodynamic therapy; ICD, immunogenic cell death; DAMPs, damage-associated molecular patterns; DCs, dendritic cells; Breg, regulatory B cells; NK,

natural killer cells; CAFs/TAFs, cancer-associated fibroblasts; TAMs, tumor-associated macrophages; GSH, glutathione; DOX, doxorubicin; CGRP, calcitonin gene-related peptide; SP, substance P; TCA, tricarboxylic acid cycle; CSF, colony-stimulating factor; CXCL, C-X-C motif chemokine ligand; BODIPY, boron - dipyrromethene; TRPV1, transient receptor potential vanilloid 1; FDX1, ferredoxin 1; ATP, adenosine triphosphate; EMT, epithelial - mesenchymal transition; LED, light - emitting diode; PD-L1, programmed death - ligand 1; NMR, nuclear magnetic resonance.

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Additional Table 5. Nanomaterials related to other tumor microenvironments

Author, year	tumor microenvironment	Material type	Material name	Cancer	Treatments	Impact
Fotios Mpekris, 2021[247]	Stromal	Nanomedicine	Doxil	Breast cancer lung metastasis	Altering vasculature	Relieving vascular compression and improving tumor vasculature normalization through the use of antihistamine and antifibrotic drug tranilast
Shaoqing Chen, 2024[248]	Stromal	Telmisartan nanoparticles encapsulated with red blood cell membranes	ECM/Tel	BC	RT, modulates immune responses	By blocking the AT1R receptor, it inhibits the TGF-β signaling pathway, suppresses the activation of TAFs, reduces the formation of the tumor stroma, alleviates tumor hypoxia, and enhances the radiosensitivity of tumor cells
Myrofora Panagi, 2022[249]	Stromal	Tranilast-loaded polymer micelles	Tranilast/m	TNBC	Modulate immune responses	By targeting the TGF-β signaling pathway in TAFs, reduce the levels of collagen and hyaluronic acid in the tumor stroma, decrease tumor stiffness, and enhance drug accumulation and distribution. Combined with ICB, they can increase the infiltration of immune cells. Shear wave elastography is used to monitor changes in tumor stiffness and predict the efficacy of nano-immunotherapy
Songtao Dong, 2022[250]	Stromal	Larotrectinib-disulfide-cetyl alcohol nanoparticles	LTX-SS-CA	TNBC	Modulate immune responses	Employing GSH pulse therapy promotes drug accumulation and release, inhibits the activity of CAFs, and enhances the efficacy of PD-1 blockade therapy
Yu Chen, 2020[251]	Stromal	Hyaluronic acid-Fe3+-phenyl-2,4-dinitrobenz	HFePQS	PDAC	Regulating oxidative stress	By triggering the Fenton reaction under GSH conditions to generate highly toxic •OH radicals, inducing oxidative damage, releasing Fe^{3+} in TAMs to induce polarization towards the M1 phenotype, reducing

		enesulfonate-quinone self-assembly nanocomplex				the activation of TAFs, decreasing stromal deposition, and enhancing drug permeability
Antonia Charalambous, 2024[252]	Stromal	PEGylated liposomal doxorubicin, PEGylated liposomes co-encapsulating alendronate and doxorubicin	PLD, PLAD	Fibrosarcoma and osteosarcoma	Modulate immune responses	By modulating the TME through ketotifen, reduce tumor stiffness, enhance the accumulation of nanomedicines in the tumor, promote the polarization of M1-type TAMs, and increase the infiltration and activity of cytotoxic $CD8^+$ T cells
Kamalpreet Kaur Sandha, 2025[253]	Stromal	Liposomal doxorubicin incorporated alginate hydrogel	L-dox@alg hydrogel	BC	Modulate immune responses	Relieving fibrosis in the tumor microenvironment by inhibiting autophagy, reducing the levels of ECM components, and simultaneously decreasing the activation of TAFs by inhibiting the TGF-β signaling pathway
Patricia González-Callejo, 2025[254]	Stromal	Extracellular vesicles (EVs) secreted by cancer stem cells (CSCs) and differentiated cancer cells (DCCs)	EVsCSC, EVsDCC	TNBC	Modulate immune responses	EVsCSC can activate an α-SMA-positive myofibroblast subpopulation known as myCAFs, increasing endothelial cell remodeling and enhancing angiogenesis to promote the remodeling of the pre-metastatic niche in the lung. In contrast, EVsDCC activates secretory CAFs, triggering the IL-6/IL-8 signaling pathway to maintain the phenotype

Yuxin Zhang, 2025[255]	Stromal	Chondroitin sulfate-glutathione-sensitive linker-dasatinib	CS-GFLG-DAS	TNBC	Modulate immune responses	Utilizing chondroitin sulfate to target tumor cells and CAFs, releases the drug to inhibit CAFs activity, reduces ECM deposition, and improves the efficacy of ICB therapy
Simona Camorani, 2024[256]	Stromal	Bispecific nucleic acid aptamer-modified nanoparticles	Iren-AuSiO2_Aptamer	TNBC	PDT, PTT	By targeting tumor cells and stromal cells through aptamers specific to the EGFR and the PDGFRβ, achieve dual targeting of tumor and stromal cells, and utilize PDT and PTT to kill both tumor and stromal cells
Mengli Liu, 2025[257]	Stromal	Janus bimesoporous silica nanomotors, loaded with AIEgen NDA-FT, DSPE-PEG-RGD, and DOX	M&P-NFT/R/DOX	CRC	Nanomotors, PTT	Generate a photothermal effect under 808 nm laser irradiation, driving the self-propelled motion of the nanomotors. They release drugs in a pH-responsive manner, disrupt tumor stromal cells and the ECM, reduce the resistance of tumor tissue, and utilize NIR-II fluorescence emission for high-resolution imaging to monitor the distribution of nanomotors in the tumor in real time
George Sharbeen, 2021[258]	Stromal	Nanomedicine targeting SLC7A11	Star 3+SLC7A11-siRNA	PDAC	siRNA technology	By using gene-silencing nanomedicine to specifically inhibit SLC7A11, it reduces the proliferation and antioxidant capacity of CAFs, inhibits their collagen-remodeling ability, decreases tumor fibrosis, and enhances drug penetration
Youshuai Meng, 2024[259]	Stromal	Triphenylphosphonium-functionalized gold nanoparticles	Dox@TPAu	PDAC	PTT	Achieve mitochondrial targeting. Combined with PTT, this drug can enhance drug accumulation and efficacy in tumor cells while reducing systemic toxicity

Yasmeen Ezzeldeen, 2021[260]	Stromal	Honokiol transosomes	HKTs	Melanoma	Modulate immune responses	By downregulating the TGF-β signaling pathway to alleviate immune suppression, reducing the expression of CD47 to enhance immune cell phagocytosis, and decreasing the expression of the stem cell marker CD133 to reduce the stemness properties of the tumor
Eric Voltà Durán, 2023[261]	Stromal	Fluorescent nanoparticles targeting PDGFR-β, nanotoxins targeting PDGFR-β, containing the catalytic domain PE24 of Pseudomonas aeruginosa exotoxin A	PDGFD-GFP-H6, PDGFD-NT-H6	CRC	Modulate immune responses	By targeting PDGFR-β^+ CAFs through PDGFD, induce tumor tissue necrosis, significantly reduce tumor volume growth, and have no significant toxic side effects
Qian Wang, 2025[262]	Stromal	Bismuth vanadate nanorods loaded with platinum nanodots	BiVO4Pt（BVP）	BC	PDT, PTT	Under dual activation by ultrasound and NIR light, generate heat and ROS, disrupt the ECM, enhance ICD, and simultaneously catalyze the conversion of H_2O_2 to O_2, thereby alleviating tumor hypoxia
Alice Perucca, 2025[263]	Stromal	Micro immune response on-chip	MIRO	HER2+ BC	Modulate immune responses	Through IL2-driven immune modulation and combined treatment with trastuzumab, the migration speed and diffusion of immune cells are increased, overcoming stromal immune suppression

Xiaohu Yang, 2024[264]	Stromal	Nano-remodelers containing hyaluronidase, stromal cell-derived factor-1α, and DOX	DAS@P/H/pp	Pancreatic cancer	Modulate immune responses	Release drugs through an acid-responsive release mechanism, degrade the ECM, enhance the chemotaxis of NK cells by releasing SDF-1α, and simultaneously monitor the infiltration and distribution of NK cells in the tumor using NIR-II fluorescence imaging technology
Lingdong Jiang, 2024[265]	Stromal	Acid-degradable nanomicelles	SOR-NO@BLN	HCC	Modulate immune responses	Release NO to degrade the ECM, while simultaneously utilizing NO-mediated increased expression of matrix metalloproteinases to enhance tumor penetration
Yali Wu, 2024[266]	Stromal	CAF-derived extracellular vesicles loaded with the GLUT1 inhibitor BAY-876	cEV-B6	Lung cancer	Modulate immune responses	Inhibit glucose transporter 1 to reduce glucose uptake in lung cancer cells and CAFs, decrease lactate accumulation, and simultaneously reverse the activated phenotype of CAFs, reduce ECM stiffness, and enhance the infiltration of $CD3^+$and $CD8^+$ T cells in the tumor core
Hongjuan Zhao, 2025[267]	Stromal	Collagen/elastin-based hydrogels loaded with fatty acid transporter inhibitor lipofermata and TGF-β inhibitor SB-505124	Lipo/SB@Scaffold	Melanoma	Pyroptosis	Block fatty acid uptake by melanoma cells and protumor neutrophils through fatty acid transporter inhibition. The TGF-β inhibitor in the drug synergizes with lipid starvation to polarize locally enriched neutrophils post-surgery towards the cytotoxic N1 phenotype. N1 neutrophils induce pyroptosis via a ROS-dependent pathway, activate macrophages, produce pro-inflammatory cytokines, recruit a second wave of neutrophils, and form a positive feedback loop
Bowen Wu, 2024[268]	Stromal	pH/GSH-sensitive cationic	T-AsiG-CPL	PDAC	Modulate immune responses	Restore the energy metabolic homeostasis of PDAC cells and pancreatic stellate cells, and reduce ECM deposition

		liposomes				
Ha Kyeong Lee, 2025[269]	Stromal	DEVD motif antibody-drug conjugates	DEVD ADC	HER2+ BC	Apoptosis	Target HER2-positive cells, utilize cathepsin B in lysosomes to release drugs. During the process of inducing apoptosis, caspase-3 is activated and released, further cleaving the DEVD chain to amplify the bystander effect
Chao Hong, 2024[270]	Stromal	Ginsenoside Rh2-based multifunctional liposomes	Rh2-lipo	BC	Modulate immune responses	By replacing cholesterol and PEG in the liposomes with ginsenoside Rh2, enhance the uptake of liposomes in TAFs and tumor cells, improve targeting and penetration capabilities, reshape the tumor vasculature network, and reduce the expression of stromal collagen
Yue Yan, 2021[271]	Stromal	Loaded with acid-activated photosensitizers targeted to the EGFR	Erb-AAPS	Ovarian cancer	PDT	By regulating tumor vasculature through thalidomide and combining PDT to eliminate tumor stromal cells and modulate the TME, significantly enhancing the tumor accumulation and cell accessibility of antibody-modified nano-photosensitizers
Lijia Luo, 2024[273]	Stromal	Lipid bilayer-coated mesoporous silica nanoparticles, used for loading nintedanib	Silicasome-Nintedanib	PDAC	Modulate immune responses	This drug targets VEGFR, PDGFR, and FGFR, reducing vascular density and collagen content, enhancing the ratio of $CD8^+$/$FoxP3^+$ T cells, and simultaneously synergizing with anti-PD-L1 immunotherapy through the extracellular signal-regulated kinase pathway
Giovanni Marco Saladino, 2025[274]	Stromal	Magnetic nanoparticles, surface-modified with FITC and	Ferumoxytol-FITC, Ferumoxytol-FITC-VDA	GBM	Altering vasculature	Target tumor vasculature to disrupt vascular integrity and enhance nanoparticle penetration in tumor tissue

		the vascular disrupting agent				
Junning Ma, 2023[275]	Stromal	FS cell membrane-coated PLGA nanoparticles, as well as mitotane-loaded FSNPs	FSNPs, M-FSNPs	Invasive pituitary adenomas	Apoptosis	FSNPs enhance the enhanced permeability and retention effect, improving nanoparticle accumulation. M-FSNPs can more effectively induce apoptosis and have improved the therapeutic efficacy of mitotane in both ectopic and orthotopic pituitary adenoma models
Ying Chen, 2025[276]	Stromal	Nanomedicine	PTX-SS-3′HPT @RGD-HA NPs	BC	Modulate immune responses	By targeting CD44 and αvβ integrin receptors, it enhances tumor-specific drug deposition and utilizes a GSH-activated payload release mechanism to downregulate MMP-9/N-cadherin and restore E-cadherin expression, thereby inhibiting paclitaxel-induced EMT and neutralizing pro-metastatic effects
Mengmeng Yang, 2023[277]	Stromal	Nanomedicine	HA-LSL/siTGF-β	TNBC	Modulate immune responses	By targeting tumor cells and stromal cells, and utilizing a release mechanism triggered by hyaluronic acid and GSH, the delivery of TGF-β siRNA is efficiently achieved, leading to the silencing of the TGF-β signaling pathway
Zeliang Wu, 2025[278]	Stromal	SiTwist/fucoxanthin@hydroxyethyl starch-cholesterol	siTwist/FX@HES-CH	TNBC	siRNA technology	By co-delivering fucoxanthin and twist siRNA, it inhibits tumor cell proliferation and metastasis, reduces the activation of CAFs, and decreases ECM deposition
Yuxin Zhang, 2023[279]	Stromal	Dasatinib@chondroitin sulfate-DTM-ca	DAS@CDC	TNBC	Modulate immune responses	By entering CAFs through CD44 receptor-mediated internalization, it can revert CAFs to normal fibroblasts, block their interaction with tumor cells, reduce the synthesis of ECM proteins, and simultaneously

		bazitaxel				inhibit tumor cell proliferation and metastasis, thereby shrinking tumor volume and suppressing pulmonary metastasis
Wenqiang Chen, 2025[282]	Mechanical	The multifunctional nanoplatform CAD/DMS@PEG/PEI-PBA	CD@PB NPs	BC	Modulate immune responses	Facilitate drug escape, downregulate the thick stroma, weaken mechanical barriers, mediate nuclear pore expansion, promote the entry of DOX into the nucleus, induce ICD, and reshape the immunosuppressive TME
Jitang Chen, 2021[283]	Mechanical	Hydroxyethyl starch-dihydrophorphyrin e6 conjugate self-assembled nanoparticles	HES–Ce6 NPs	TNBC	PDT	Generate more ROS under 660 nm laser irradiation, reduce collagen deposition, relieve solid stress, release tumor vascular compression, and promote drug accumulation and penetration
Ziying Li, 2021[284]	Mechanical	Elastically tunable self-assembled oleanolic acid nanostructures	Rigid OA-NPs and flexible OA-NGs	BC	Apoptosis	OA-NGs have less endocytosis, enhance lysosomal escape through deformation, actively penetrate the tumor interior, and simultaneously reduce collagen production. They also mediate cytotoxic effects by inducing apoptosis, cell cycle arrest, and ROS generation, and inhibit CAFs through the TGF-β1/Smad signaling pathway
Sheng Lin, 2025[285]	Mechanical	Dual prodrug nanoparticles	cRGD-pro (S&T) NPs	TNBC	Modulate immune responses	Active targeting through the overexpressed integrins on tumor cells induces vascular occlusion, normalizes the elevated interstitial fluid pressure, promotes the accumulation of chemotherapeutic drugs, and enhances drug retention and cytotoxicity
Ze Zheng, 2023[286]	Mechanical	Lignin-based embolic nanogels	DOX-pN-KL	HCC	Modulate immune responses	Utilizing the mechanical support of branched lignin and the π-π stacking interaction between lignin aromatic rings and DOX, achieve high drug loading and good sustained-release effects. They are temperature-sensitive, presenting a flowable sol state at low

						temperatures and transitioning to a gel state at body temperature. These nanogels can block blood vessels at various levels for an extended period and continuously release DOX, effectively inhibiting tumor growth and metastasis
Rui Wang, 2023[287]	Mechanical	CD133-targeted hybrid nanovesicles	CD133-grafted Cy5.5/PFOB@P-HVs	Pancreatic Cancer	SDT	Target cancer stem cells in pancreatic cancer cells, generate thermal and mechanical effects under high-intensity focused ultrasound irradiation, enhance the delivery efficiency of nanovesicles, and inhibit tumor growth
Mingxiao Fang, 2025[288]	Mechanical	Ultrasound-activated oncolytic nanosystem	cRGD-Lip@PFP	CRC	SDT	Undergoes a phase transition under ultrasound irradiation. The nanomedicine expands from the nanoscale to the microscale and ruptures to produce a cavitation effect, inducing necroptosis-like oncolytic cell death. It simultaneously releases DAMPs and DNA fragments, activating the cGAS-STING pathway, relieving tumor hypoxia, and reversing immune suppression. When combined with αPD-L1, it can enhance antitumor effects
Yi Tang, 2025[289]	Mechanical	Anti-PD-L1-modified docetaxel and perfluoropentane-loaded liquid-gas phase-transition lipid nanoparticles	aPDL1-DTX/PFP@Lipid	PDAC	Low-intensity pulsed ultrasound	Low-intensity pulsed ultrasound triggers the phase transition of nanoparticles from liquid to gas, forming microbubbles, releasing oxygen, and simultaneously promoting the polarization of M1-type macrophages, reducing fibrosis, decreasing tumor interstitial pressure, and enhancing drug penetration
Zheng Li, 2024[290]	Mechanical	ICG-loaded soft nanogels and	ICG@2% NGs, DOX@15%	BC	PTT, modulates immune responses	The soft nanogels possess excellent deformability, enabling efficient penetration and uniform distribution in tumors. Combined with

		doxorubicin-loaded hard nanogels	NGs			mild-PTT, they can inhibit CAFs, degrade the ECM, and modulate the tumor mechanical microenvironment. The hard nanogels, under the effect of mild photothermal therapy mediated by soft nanogels, show more significant tumor penetration and antitumor efficiency compared to soft nanogels.
Antoine Uzel, 2023[291]	Mechanical	Hybrid lipid nanoparticles containing 5 nm gold nanoparticles	DOX-Au-LNPs	BC	Nanosecond pulse laser	Utilizing the resonant interaction between a nanosecond pulse laser (527 nm) and the plasmonic mode of the hybrid nano-carrier, a single-pulse irradiation triggers the release of DOX. The release mechanism may involve the explosive vaporization of the thin water layer near the gold nanoparticle clusters or the thermomechanical decomposition of the overheated lipid layer. This increases the amount of DOX in target cells, leading to cancer cell death
Fotios Mpekris, 2024[292]	Mechanical	PEGylated liposomal doxorubicin	Doxil	Fibrosarcoma and osteosarcoma	Modulate immune responses	Combined with ketotifen and sonopermeation, it can reduce collagen and hyaluronic acid levels by 50%, double the pericyte coverage, normalize tumor vasculature, improve tumor perfusion (increased sixfold), and enhance drug delivery
Haomiao Bai, 2025[293]	Mechanical	Cobalt single-atom-doped molybdenum disulfide nanoflowers	SA-Co@MoS_2	BC, HCC	Piezoelectric effect	Cobalt single atoms induce lattice distortion and out-of-plane polarization, forming a large number of sulfur vacancies, narrowing the intrinsic bandgap of the material, promoting the effective separation and migration of charge carriers, efficiently generating ROS under ultrasound stimulation, while depleting GSH, leading to cell cycle arrest and apoptosis, inducing ferroptosis, and decomposing H_2O_2 to O_2 to relieve tumor hypoxia
Hong Deng, 2024[294]	Mechanical	Three different surface-charge types of dextran	DEAE-Ce6, SSD-Ce6, CMD-Ce6	BC	Modulate immune responses	The positively charged DEAE-Ce6 nanogels, compared to the negatively charged nanogels, exhibit superior targeting to TAMs and can monitor their targeting effects through the fluorescence imaging of

		nanogels				Ce6
Lejia Zhang, 2023[295]	Mechanical	Graphyne oxide	GDYO	OSCC	PDT	GDYO-mediated PDT can increase the mechanical stiffness of OSCC, alter the cholesterol levels in the cell membrane and the organization of F-actin cytoskeleton, enhance cell stiffness, making cancer cells more recognizable and susceptible to killing by CTLs, promote T cell cytotoxicity and the secretion of inflammatory cytokines, and trigger antitumor immune responses
Shan Lu, 2024[298]	Microbial	MnO_2 nanoparticles	MnO_2 NPs	BC	Modulate immune responses	Utilizing engineered salmonella to colonize within the tumor, activate the STING signaling pathway, promote the secretion of type I interferon, recruit a large number of neutrophils and polarize them to the N1 phenotype, express PD-L1, and enhance the infiltration and activation of $CD8^+$ T cells
Fenggang Qi, 2021[299]	Microbial	Photosynthetic cyanobacteria-hybridized black phosphorus nanosheets	Cyan@BPNSs	BC	PDT	Utilizing the photosynthetic cyanobacteria to perform photosynthesis under 660 nm laser irradiation, generating oxygen and converting it into $^1O_2$ to enhance the efficacy of photodynamic therapy
Xiaoxi Wang, 2025[300]	Microbial	The engineered bacteria-nanoparticle hybrid platform	M-CHNP/D	Melanoma	Modulate immune responses	Penetrate deep into tumor tissues, neutralize the acidic TME, induce tumor cells to produce Chemokine C-C motif ligand 3, recruit DCs, enhance the antigen-presenting capacity of DCs and the number of innate immune cells, and shift them towards an antitumor functional state
Chenyang Yin, 2022[301]	Microbial	Bio-nanosonosensitizers based on gold	Bac@ARS	Multiple types of tumors	SDT	By being activated by low-intensity ultrasound, generate ROS, decompose H_2O_2 into O_2, induce ICD, relieve tumor hypoxia, enhance SDT efficacy, and simultaneously utilize the natural tropism of

		nanoparticles, ruthenium dioxide nanoparticles, and selenium nanoparticles				Listeria innocua for specific drug delivery
Tian Hu, 2025[302]	Microbial	A bioactive biotic motor system based on anaerobic bacteria	MDPP@Bif	BC	CT, modulates immune responses	Utilizes the self-propulsion characteristics of anaerobic bacteria to simultaneously deliver DOX and immune checkpoint inhibitors to tumor tissues, reducing immune evasion and activating T cells
Haiting Xu, 2025[303]	Microbial	Nanomedicine-engineered bacteria	LR-S-CD/CpG @LNP	CRC	PDT, PTT	Generate photothermal and photodynamic effects under NIR laser irradiation, induce ICD, release tumor antigens and CpG oligonucleotides, activate DC maturation, produce indole-3-aldehyde through tryptophan metabolism to enhance antitumor immune responses, and simultaneously modulate the gut microbiota to increase the abundance of beneficial bacteria, inhibiting colorectal tumors and their liver metastasis
Chunxiao Gao, 2023[304]	Microbial	Metronidazole-fluorouracil nanoparticles	MTI-FDU	CRC	Modulate immune responses	Release drugs under the high concentration of GSH in the TME, can target the microbiota within the tumor, eliminate protumor bacteria, directly kill tumor cells, increase the infiltration of $CD8^+$ T cells, and inhibit the activity of immunosuppressive cells
Qingxia Shi, 2024[305]	Microbial	Cryo-microneedle-delivered nanogold-decorated	CryoMNs-R.r-Au	Melanoma	PTT	Under laser irradiation, the photoelectron conversion efficiency of Rhodospirillum promotes the transfer of electrons to the photosynthetic system of Rhodospirillum, increases lactate consumption and hydrogen production, improves tumor immune

		Rhodospirillum				activation, and reshapes the TME
QianRu Li, 2025[306]	Microbial	Bio-mineralized engineered bacterial outer membrane vesicles	OMVs@MnCaP-FA	BC, melanoma	Modulate oxidative stress	By releasing Ca^{2+} and Mn^{2+}, it induces mitochondrial damage, releases mitochondrial DNA, enhances the recognition of mitochondrial DNA by cyclic GMP-AMP synthase, promotes the generation of cyclic GMP-AMP, activates the STING signaling pathway, and simultaneously depletes lactate
Sejin Son, 2023[307]	Microbial	Yeast mannan-based nanocapsules	Mann-NC	Multiple types of tumors	Modulate immune responses	Activating Dectin-2 and Toll-like receptor 4 on DCs promotes the differentiation of $CD4^+$ T cells into the TH17 phenotype, thereby secreting cytokines such as IL-17 to recruit and activate $CD8^+$ T cells and natural killer cells
Lijun Hu, 2025[308]	Microbial	Light-sensitive bacterial system	E@L-P/ICG	CRC	PTT	Generates a mild photothermal effect under laser irradiation, triggering bacterial self-rupture and death of surrounding tumor cells, and stimulating the generation of high endothelial venules to promote the recruitment and retention of lymphocytes, forming TLS, and further enhancing the infiltration of T cells and B cells
Ze Mi, 2025[309]	Microbial	Engineered Salmonella typhimurium strains	SLCVNP20009	CRC	Modulate immune responses	Colonize tumors and release tumor necrosis factor superfamily member 14, forming a ligand-receptor pair with herpesvirus entry mediator, inducing a robust cellular immune response. They can also modulate the proportion of innate lymphoid cells in the gut, induce the formation of mature TLS, and activate T cell-mediated antitumor immune responses
QiChao Yang, 2025[310]	Microbial	Bacterial membrane-coated covalent organic	COF-306@FM	BC	Modulate immune responses	Possessing good cancer cell uptake ability, it induces the formation of TLS within tumors by enhancing the infiltration of $CD8^+$ T cells and B cells

		frameworks				
Zitong Zhao, 2025[312]	Inflamed	A tumor cell corpse-based nanoplatform, carrying anti-PD-1 antibodies and drug-loaded liposomes	Cell-αPD-1/Liposome	TNBC	Modulate immune responses	Utilizes the tumor cell corpses as carriers, leveraging their natural antigenicity and targeting ability, to enhance drug accumulation through the anti-PD-1 antibodies and drug-loaded liposomes
Dan Liu, 2023[313]	Inflamed	pH-responsive nanoparticles	PMM NPs	BC, CRC	Modulate the inflammatory response	Capable of activating the STING signaling pathway, enhancing the secretion of type I interferons and pro-inflammatory cytokines, promoting the maturation and activation of DCs, reducing the proportion of regulatory T cells, and polarizing M2-type macrophages
Jiayi Lin, 2025[314]	Inflamed	Lentinan microneedle platform	PPS/RS17-M6P3@MN	BC, melanoma	Modulate immune responses	Preventing the degradation of CD47 on red blood cells, promoting the polarization of macrophages towards the M2 phenotype, and restoring and enhancing macrophage phagocytosis
Min Liu, 2025[315]	Inflamed	Bio-mineralized copper sulfide nanoparticles	BCS NPs	BC	PTT	Possessing good photothermal ablation effects, it can neutralize ROS through an electron-donating mechanism, reduce the production of inflammatory factors, inhibit the recruitment of MDSCs, and produce an abscopal effect
Xiaoyu Liu, 2023[316]	Inflamed	PD-L1 trap gene nanocarriers	nano-PD-L1 trap	HCC	Modulate immune responses	Block the PD-1/PD-L1 signaling pathway, reduce the proportion of M2-type macrophages, and promote the infiltration of cytotoxic $CD8^+$ T cells
Luis Miguel Carrasco Díaz,	Inflamed	Nanotoxins based on T22	T22-DITOX-H6	CRC	Pyroptosis	Targeting $CXCR4^+$ cells, carrying the catalytic domain of diphtheria toxin, activates pyroptosis and releases DAMPs by targeting $CXCR4^+$

2025[317]		peptide				cancer cells, attracting eosinophil infiltration, and releasing cytotoxic granules
Yi Cao, 2024[318]	Inflamed	Multifunctional nano-liposomes,	ICG-SB@Lip-ZA	BC	PTT	By generating heat under NIR irradiation, it has a good tumor ablation effect, simultaneously blocks the mevalonate pathway, induces apoptosis of TAMs, inhibits the TGF-β signaling pathway, reduces the proliferation of CAFs, eliminates physical barriers, and promotes T cell infiltration
YuYi Ling, 2025[319]	Inflamed	Phosphorescent rhenium(I) complexes	Re5	TNBC	Cuproptosis	Enrich copper ions in mitochondria, disrupt redox balance, interfere with the tricarboxylic acid cycle and energy metabolism pathways, induce cuproptosis, and also activate the AMPK signaling pathway while inhibiting the PI3K/AKT/mTOR signaling pathway
Flavia Castro, 2025[320]	Inflamed	Chitosan/γ-polyglutamic acid (Ch/γ-PGA) nanoparticles	Ch/γ-PGA	TNBC	Modulate the inflammatory response	Activating Toll-like receptors, particularly the TLR4 and MyD88 signaling pathways, enhances antitumor T cell responses, inhibits the function of regulatory T cells, increases the expression of major histocompatibility complex, and stimulates pro-inflammatory macrophage activity. They also increase the infiltration of $CD8^+$ T cells and inflammatory macrophages while reducing the number of immunosuppressive cells
Hongbo Gao, 2025[321]	Inflamed	$MnTe_2$ nanosheets	MnTe2 NSs	CRC	Modulate immune responses	Induce endoplasmic reticulum stress in cells, atypically activate the cGAS-STING pathway, enhance the maturation of DCs, and promote the infiltration of $CD8^+$ T cells
Zhenfu Wen, 2023[322]	Inflamed	Nanovaccines	pECM nanovaccine	Nasopharyngeal carcinoma	Modulate the inflammatory response	By activating the LT-α and LT-β pathways, enhance the expression of chemokines such as CCL19/CCL21, CXCL10, and CXCL13, promote the normalization of blood and lymphatic vessels in the TME, and form TLS

YuHan Lin, 2025[323]	Inflamed	Mesoporous silica nanoparticles encapsulated with bacterial outer membrane vesicles	CpG@MSN-PEG/PEI@OMVs	BC, CRC	Modulate immune responses	Promoting the polarization of M1-type macrophages, maturation of DCs, and activation of IFN-γ-producing $CD4^+$ and $CD8^+$ T cells, while reducing the proportion of regulatory T cells and MDSCs
Gengjia Chen, 2025[324]	Inflamed	Nanovaccines	MLP-aTIM-3	HCC, PDAC, CRC	Modulate immune responses	By targeting T cell immunoglobulin and mucin domain-containing protein 3, it reverses T cell exhaustion and promotes the formation and maturation of TLS
Daniel Mendanha, 2024[325]	Inflamed	Liposomes containing docosahexaenoic acid (DHA) prepared by microfluidic technology	DHA liposomes	GBM	Modulate the inflammatory response	Rapidly taken up by macrophages, modulate the expression of inflammation-related genes and reduce the secretion of pro-inflammatory cytokines
Yitian Xu, 2025[326]	Inflamed	CMTM4-targeted siRNA liposomes	CMTM4-targeted siRNA liposomes	BC, melanoma, lung cancer	Modulate immune responses	Inhibiting tumor growth and extending the survival time of mouse models
Honglin Huang, 2025[327]	Inflamed	A photothermal mesoporous polydopamine core, loaded with lactate dehydrogenase	PsiL@M1M	BC	PTT	It has good photothermal ablation effects, can actively accumulate at inflammatory sites (primary tumors and pre-metastatic niches), and can reduce inflammatory responses by neutralizing inflammatory factors. It also interferes with lactate production through gene silencing, blocking the interaction between inflammation and LA

Haixuan Wu, 2025[329]	Neural	AsiRNA and enveloped by M1-type macrophage membranes Acid-responsive nanoparticles encapsulating bupivacaine	NP-BUP	TNBC	Modulate the nervous system	Targeting the noradrenergic nerves in the TME, it inhibits the release of the neurotransmitter norepinephrine, thereby reducing the infiltration of TAMs
Yifeng Lei, 2016[330]	Neural	Ferritin nanoparticles encapsulating carbachol and atropine	Nano-Cab NPs, Nano-Ato NPs	Pancreatic cancer	Modulate the nervous system	By targeting the neural microenvironment, Nano-Cab NPs promote tumor progression, while Nano-Ato NPs inhibit tumor progression

PDT, photodynamic therapy; PTT, photothermal therapy; SDT, sonodynamic therapy; BC, breast cancer; TNBC, triple-negative breast cancer; HCC, hepatocellular carcinoma; PDAC, pancreatic ductal adenocarcinoma; CRC, colorectal cancer; GBM, glioblastoma multiforme; OSCC, oral squamous cell carcinoma; DOX, doxorubicin; ECM, extracellular matrix; CAFs/TAFs, cancer-associated fibroblasts; TGF-β, transforming growth factor-β; AT1R, angiotensin II Type 1 receptor; TAMs, tumor-associated macrophages; ICD, immunogenic cell death; NIR, near-infrared light; ROS, reactive oxygen species; EMT, epithelial-mesenchymal transition; PEG, polyethylene glycol; HER2, human epidermal growth factor receptor 2; DEVD, Asp-Glu-Val-Asp; ICB, immune checkpoint inhibitors; GSH, glutathione; NO, nitric oxide; EGFR, epidermal growth factor receptor; VEGFR, vascular endothelial growth factor receptor; PDGFR, platelet-derived growth factor receptor; FGFR, fibroblast growth factor receptor; PDGFD, platelet-derived growth factor D; PD-L1, programmed death-ligand 1; SMA, smooth muscle actin; SLC7A11, solute carrier family 7 member 11; SDF-1α, stromal cell-derived factor 1α; DAMPs, damage-associated molecular patterns; cGAS-STING, cyclic GMP-AMP synthase-stimulator of interferon genes; CTLs, cytotoxic T lymphocytes; DCs, dendritic cells; TLS, tertiary lymphoid structures; CpG, cytosine-phosphate-guanine; GMP-AMP, guanosine monophosphate-adenosine monophosphate; MDSC, myeloid-derived suppressor cells; LA, lactic acid; AMPK, AMP-activated protein kinase pathway; PI3K, phosphatidylinositol 3-kinase; AKT, protein kinase B; mTOR, mammalian target of rapamycin; TLR4, toll-like receptor 4; MyD88, myeloid differentiation primary response protein 88; CXCR, C-X-C motif chemokine receptor; LT-α, lymphotoxin-α; LT-β, lymphotoxin-β; CCL, chemokine (C-C motif) ligand; CXCL, chemokine (C-X-C motif) ligand; IFN, interferon.

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