Supporting Information for

REVIEW

Enhancing cancer immunotherapy: Nanotechnology-mediated immunotherapy overcoming immunosuppression

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Table S1 Summary of nanomedicine overcoming tumor immunosuppression.

Target	Nanomedicine	Classification	Advantage and unique characteristic	Mechanism	Cancer	Ref.
TAMs	HA-PeiPLGA-MTX NPs	Polymer nanoparticle	Targeted malignant breast cells	NF-κB signaling was inhibited and M2 TAMs shifted to M1 phenotype	4T1 mouse model	1
	PHNPs@DPA-S-S-BSA-MA@3-MA	Inorganic nanoparticle	GSH-responsive, targeted TAMs	Nanoparticles activate NF-κB p65 and promote the polarization of TAMs into M1 type macrophages	MDA-MB-231 mouse model	2
	P/ML-NNG	Nanogel	MMP2-responsive, targeted T cells, and targeted TAMs	P/ML-NNG can release drugs to different targets and simultaneously inhibit PD-1/PD-L1 and NF-κB pathway, thereby repolarizing M2 TAMs to M1 TAMs	B16 mouse model	3
	LDH@155 nanoparticles	Layered double hydroxide nanoparticle	Endosomal escape, regulate the expression of pro-inflammatory factors, and costimulatory molecules	LDH@155 nanoparticles effectively activated NF-κB expression in TAMs, and induced polarization of TAMs towards M1 phenotype	TC-1 mouse model	4

		in MDSCs.			
IL-12/α-TOS loaded TRN	Inorganic nanoparticle	Good solubility, biocompatibility, degradability, and pH sensitivity	Microenvironment responsive nanocarriers release IL12 and promote the repolarization of TAMs into M1 phenotype.	4T1 mouse model	5
TNPs	Polymer nanoparticle	No toxicity and responsive release	The released IL-12 promoted the polarization of TAMs into M1 phenotype.	HepG2 mouse model	6
BLZ945/Sel NPs	Lipid nanoparticle	Stability, higher internalization in M2 macrophages, and sustained release	Supramolecular nanoparticles continuously inhibit both CSF1R and MAPK signaling pathways, promoting the repolarization of M2 macrophages to the M1 phenotype.	4T1 mouse model	7
α-PDL1-CSF-LNPs	Lipid nanoparticle	Biocompatibility, antibody tethering, and efficient drug loading capacity	α-PDL1-CSF-LNPs can simultaneously target and inhibit the PDL1 and CSF1R pathways, thereby promoting the transformation of M2 phenotype into M1	B16/F10 mouse model	8

			phenotype.		
P/T@MM NPs	Polymer nanoparticle	Actively targeting the tumor site and immune escape	Biomimetic nanoparticles repolarises M2 macrophages into M1 macrophages by altering their epigenetic properties	breast cancer	9
R848@LNPs	Polymer nanoparticle	Targeted M2 macrophages, biocompatibility and biodegradability	R848@LNPs can target CD206 positive M2 like TAMs and convert them into anti-tumor M1 macrophages.	4T1 mouse model	10
Iron oxide nanoparticles	Inorganic nanoparticle	Hemolysis	Iron oxide nanoparticles differentiate M2 like TAMs into M1 phenotypes	LLC mouse model	11
MIX-NPs	Polymer nanoparticle	pH-responsive, core-shell separation, selective targeting of TAMs and cancer cells	Twin-like charge-switchable nanoparticles selectively silence MFN1, thereby inhibiting mitochondrial fusion in TAMs and promoting repolarization of TAMs from M2 to M1 phenotype.	4T1 mouse model	12
DMSN-PEI@125a	Inorganic nanoparticle	Large pore size, volume, high surface areas, and	DMSN-PEI@125a bind to the 3'-untranslated region of targeted mRNA and	TC-1 mouse	13

			protecting gene stability	repolarize TAMs.	model	
	CuPP	Nanoenzyme	High physiological stability, tunable enzyme-like activities, and low cost	CuPP promotes the transition of M2 macrophages to M1 macrophages by increasing the O_2 level in TME.	4T1 mouse model	14
	OX40L M1-exos	Exosomes	Immune evasion, participate in intercellular communication	OX40L M1-exos promoted the reprogramming of TAMs into M1 macrophages by activating the OX40/OX40L pathway	4T1 mouse model	15
	PTEN mRNA NPs	Polymer nanoparticle	Protecting gene stability	PTEN mRNA nanoparticles promote the permeation of $CD8^+$ T cells in tumor tissues and reverse TIME.	B16-F10 mouse model	16
T cells	Biomimetic nanoparticles	Inorganic nanoparticle	Homologous adhesion, crossing the blood-brain barrier	The combination of biomimetic nanoparticles and PX reduced PD-1 and TIM-3 on T cells by downregulating TET2 expression, and inhibited GRK2 for stabilizing S1PR1 expression on T cells surface.	GL261 mouse model	17

	FeS-GOx@PTX	Self-assembly nanoparticle	High tumor permeability and low toxicity	FeS-GOx@PTX can promote T cell infiltration and completely eliminate primary tumors by inducing ICD.	4T1 mouse model	18
	PLGA-ICG	Polymer nanoparticle	Biocompatible, biodegradable, low toxicity and sustained release	PLGA-ICG disrupts ECM by generating heat, thereby increasing the infiltration of CAR T cells.	WM115 mouse model	19
	VNP_{siLdha}	Lipid nanoparticle	Protecting gene stability and preventing premature gene release	VNP_{siLdha} neutralize tumor acidity by reducing lactate production, thereby restoring T cells function.	B16-F10 and 4T1 mouse model	20
	CD-MnOx@CM	Inorganic nanoparticle	Biocompatibility, catalytic ability, and targeted tumor cells	CD-MnOx@CM not only effectively activated $CD8^+$ T cells, but also regulated ROS levels in TME by catalyzing the decomposition of H_2O_2 into O_2 within the tumor to promote T cell survival.	B16-F10 mouse model	21
Tregs	Fluorine-assembled nanoparticles	Inorganic nanoparticle	Redox and photodynamic effect	Fluorine-assembled nanoparticles reversed Tregs mediated immunosuppression by	4T1 mouse model	22

			alleviating hypoxia and reducing GSH content.		
tLyp1-CH NPs	Polymer nanoparticle	Stability and targeted Tregs	tLyp1 peptide coupled hybrid nanoparticles inhibited the phosphorylation of STAT3 and STAT5, reducing Tregs within the tumors.	B16 mouse model	23
Supramolecular photodynamic nanoparticles	Cyclodextrin inclusion complex	Reduce phototoxicity and responsive release	Supramolecular photodynamic nanoparticles can reduce Tregs levels and increase infiltration of $CD8^+$ T cells in TME, thereby reversing TIME.	4T1 mouse model	24
LBL-hNPs	Polymer nanoparticle	Photothermal effect, photodynamic effect, and pH-sensitive	LBL-hNPs reduced the inhibitory function of Tregs and improved the anti-tumor efficiency of PDT	B16/BL6 mouse model	25
Cur NPs	Polymer nanoparticle	High bioavailability and safety	Curcumin nanoparticles inhibited MEK/ERK signaling and effectively reduced the increase of Tregs in tumors.	4T1 mouse model	26
UA liposomes	Liposome	Improve solubility, extend	UA liposomes can reduce tumor site Tregs	4T1 mouse	27

			half-life, and non-toxic	by inhibiting STAT5 phosphorylation and IL-10 secretion.	model	
	Iron oxide nanoparticles	Inorganic nanoparticle	Biodegradation and photothermal effect	Iron oxide nanoparticles-mediated PTT can preferentially eliminate Tregs at the tumor sites.	4T1 mouse model	28
MDSCs	HDL NPs	Inorganic nanoparticle	Targeted MDSCs	HDL NPs significantly inhibited the activity of MDSCs and inhibited tumor growth.	B16F10 and LLC mouse model	29
	FIT NPs	Inorganic nanoparticle	Efficient drug loading, TME responsive, and Targeted MDSCs	FIT NPs can enhance the efficacy of PTT by inducing ICD and reducing the function of MDSCs.	CT26 mouse model	30

	IR780/Met NPs	Inorganic nanoparticle	Control release effect, large pore size, and produce O_2	The nanoplatform overcomed tumor hypoxia by inhibiting mitochondrial respiration, thereby inhibiting the immunosuppressive function induced by MDSCs.	B16F10 mouse model	31
	R-mPDV/PDV/DOX/ siL	Polymer nanoparticle	Redox reaction, Lysosome escape, and targetability	R-mPDV/PDV/DOX/siL efficiently silence LDHA expression and induce ICD.	4T1 mouse model	32
	LPPR	Polymer nanoparticle	Extend half-life, reduce toxicity, and improve stability	LPPR can increase cytotoxic T cells infiltration and reduce immunosuppressive cells recruitment by inhibiting TAFs activation *in vivo*.	4T1 mouse model	33
TAFs	DMSN@MIPs	Inorganic nanoparticle	Large pore size, volume, and high surface areas	DMSN@MIPs inhibited the activation of TAFs and increased the levels of immune cells (DCs, $CD8^+$ T cells, and NK cells) .	4T1 mouse model	34
	PMs-Ba	Polymer	Long cycle characteristics,	PMs-Ba increased cytotoxic T cells	4T1 mouse	35

	nanoparticle	low toxicity, and biocompatibility	infiltration and stimulated the tumor immune microenvironment by inhibiting TAFs activation.	model	
PEG-SAB-Lip	Liposome	Long cycle characteristics, low toxicity, and biocompatibility	PEG-SAB-Lip can remodel the tumor fibrotic microenvironment and increase the infiltration of $CD4^+$, $CD8^+$ T cells, and M1 macrophage.	4T1 mouse model	36
Self-adaptive nanoregulator	Micella	Adjustable form and ROS-responsive release	The self-adaptive nanoregulator interfered with tumor fibrosis and IDO1-kyurenine axis induced T cells failure by delivering TAFs inhibitor and indoleamine 2,3-dioxygenase 1 inhibitor.	Panc02 and KPC mouse model	37
Biomimetic nanoparticles	Solid lipid nanoparticle	Simultaneously targeting cancer cells and TAFs, immune evasion, long-term circulation and tumor-homing capability	Biomimetic nanoparticles simultaneously blocked the glycolysis of cancer cells and TAFs, reduced lactate production in TME, and activated immune responses.	4T1 mouse model	38

NK cells	Gal/IL-15@CaLN	Inorganic nanoparticle	Biocompatibility and acid-responsive release	Gal/IL-15@CaLN enhance T cells immunity by activating NK cells.	CT26 mouse model	39
	SCND-SIS3	Self-assembly nanoparticle	Bioavailability and biocompatibility	SCND-SIS3 enhance NK cell-mediated immune response by inhibiting Smad3-mediated Ndrg1 transcription.	LLC mouse model	40
	STING-LNPs	Lipid nanoparticle	Long-term circulation and biocompatibility	STING-LNPs kill metastatic cancer cells in the circulation by activating NK cells.	Renca mouse model	41
	SHP-1/Cbl siRNA LNPs	Lipid nanoparticle	Multi-targeting, high specificity, and stability	Nanoparticles enhance the ability of NK cells to kill cancer cells by silencing the expression of SHP-1, Cb1-b, and c-Cb1 in NK cells.	221.Cw4-HLA mouse model	42
	SeNPs	Inorganic nanoparticle	Biocompatibility, enzymes and ROS-responsive	The oxidative metabolites produced by SeNPs enhance tumor chemotherapy immunotherapy by activating NK cells.	MDA-MB-231 mouse model	43

DCs	Pem/Se	Inorganic nanoparticle	Safety and ROS-responsive	The selenite produced by Pem/Se can activate NK cells *via* inhibiting HLA-E.	A549 mouse model	44
	CC-6td NP	Self-assembly nanoparticle	Carrier-free, no adverse immune reactions, and	CC-6td NP can simultaneously regulate the anti-tumor cascade immune response initiated by DCs.	MC38 mouse model	45
	mHMnO-Dox	Inorganic nanoparticle	Homologous targeting and biocompatibility	The release of $Mn2^{+}$ from mHMnO-Dox promotes DCs maturation and induces anti-tumor immune response by activating cGAS-STING.	4T1 mouse model	46
	aDCM@PLGA/RAPA	Polymer nanoparticle	Homologous adhesion, crossing the blood-brain barrier.	aDCM@PLGA/RAPA stimulate the maturation of DCs and activate the infiltration of T cells, thereby inducing anti-tumor immunity.	C6-LUC mouse model	47
	PAG/BTZ	Polymer nanoparticle	pH-responsive, high loading content, and prolonging the blood circulation time	The BTZ released by PAG/BTZ is responsible for inducing ICD, while AG is responsible for promoting the maturation of	4T1 mouse model	48

				DCs, thereby better inducing anti-tumor immune responses.		
	RNA-NPs	Composite nanoparticle	Condense RNA and penetrate the negatively charged cell membrane	RNA-NPs promote the maturation of DCs to initiate anti-tumor immune responses.	CT26 mouse model	49
	Ru@ICG BLZ NPs	Inorganic nanoparticle	Responsive release and low toxicity	Ru@ICG-BLZ NPs can repolarize TAMs into M1 phenotype and eliminate tumor cells through phototherapy.	CT26 mouse model	50
Non-specific targeted	Cur-CSNPs	Inorganic nanoparticle	ROS-responsive and NIR-responsive	Cur-CSNPs downregulate the expression of HIF-1 and promote polarization of M2 macrophages towards M1 macrophages.	4T1 and MDA-MB-231 mouse model	51
	Lipo Zol/IR NPs	Lipid nanoparticle	Targeting the tumor site，large pore size, volume, and high surface areas	Lipo Zol/IR NPs release Zol in TEM and were selectively engulfed by TAMs, causing them to repolarize from the immunosuppressed M2 phenotype to the	4T1 mouse model	52

			immunostimulated M1 phenotype.		
IL@H-PP	Inorganic nanoparticle	Stability and high photothermal conversion efficiency	IL@H-PP can induce an increase in ROS in TAMs by releasing copper ions, thereby repolarizing them to an M1 phenotype.	4T1 mouse model	53
LT-NPs	Self-assembly nanoparticle	Low toxicity, high drug loading rate, and specifically cleaved in tumor cells	LT-NPs can effectively stimulate the maturation of DCs and initiate anti-tumor immune responses.	CT26 mouse model	54
iPS-MnO_2@Ce6	Inorganic nanoparticle	Biocompatibility and high photo/thermal stability	iPS-MnO_2@Ce6 promote the maturation of DCs, thereby activating T cells and NK cells, and inducing immune responses	Lewis mouse model	55
$^{LY}iCluster_{siRNA}$	Polymer nanoparticle	pH-responsive and avoiding gene degradation	$^{LY}iCluster_{siRNA}$ significantly increased the permeation of $CD8^+$ T cells and inhibited tumor growth	Panc02 mouse model	56

PHNPs@DPA-S-S-BSA-MA@3-MA, 3-MA loaded porous hollow iron oxide nanoparticles modified with mannose; IL-12/α-TOS loaded TRN, TME-responsive nanocarriers loaded with IL-12 or α-TOS; TNPs, tumor-responsive therapeutic nanoparticles for co-delivery of IL-12 and doxorubicin; BLZ945/Sel NPs, BLZ945 and selumetinib loaded supramolecular nanoparticles; P/T@MM NPs, TMP195 loaded macrophage membrane-coated biomimetic nanoparticles; R848@LNPs, R848@LNPs labeled with 5(6)-carboxyfluorescein; MIX-NPs, twin-like

charge-switchable nanoparticles; tLyp1-CH NPs, tLyp1 peptide coupled hybrid nanoparticles; Cur NPs, curcumin nanoparticles; IR780/Met NPs, IR780 and metformin loaded nanoplatform; SHP-1/Cbl siRNA LNPs, lipid-based nanoparticles for SHP-1 and Cbl siRNA delivery

References

1. Cavalcante RMS, Ishikawa U, Silva ES, Silva AA, Araújo AA, Cruz LJ, et al. STAT3/NF-*κ*B signalling disruption in M2 tumour-associated macrophages is a major target of PLGA nanocarriers/PD-L1 antibody immunomodulatory therapy in breast cancer. *Brit J Pharmacol* 2021;**178**:2284-304.
2. Li K, Lu L, Xue CC, Liu J, He Y, Zhou J, et al. Polarization of tumor-associated macrophage phenotype porous hollow iron nanoparticles for tumor immunotherapy *in vivo*. *Nanoscale* 2020;**12**:130-44.
3. Liu Y, Liang S, Jiang DD, Gao T, Fang YX, Fu SL, et al. Manipulation of TAMs functions to facilitate the immune therapy effects of immune checkpoint antibodies. *J Control Release* 2021;**336**:621-34.
4. Yang LN, Sun J, Liu Q, Zhu RR, Yang QN, Hua JH, et al. Synergetic functional nanocomposites enhance immunotherapy in solid tumors by remodeling the immunoenvironment. *Adv Sci* 2019;**6**:1802012.
5. Wan YF, Yu WJ, Li JM, Peng N, Ding X, Wang YL, et al. Multi-functional carboxymethyl chitin-based nanoparticles for modulation of tumor-associated macrophage polarity. *Carbohyd Polym* 2021;**267**:118245.
6. Li TS, Liu ZH, Fu X, Chen YQ, Zhu SL, Zhang J. Co-delivery of interleukin-12 and doxorubicin loaded nano-delivery system for enhanced immunotherapy with polarization toward M1-type macrophages. *Eur J Pharm Biopharm* 2022;**177**:175-83.
7. Ramesh A, Brouillard A, Kumar S, Nandi D, Kulkarni A. Dual inhibition of CSF1R and MAPK pathways using supramolecular nanoparticles enhances macrophage immunotherapy. *Biomaterials* 2020;**227**:119559.

8. Ramesh A, Malik V, Ranjani HA, Smith H, Kulkarni AA. Rational combination of an immune checkpoint inhibitor with CSF1R inhibitor-loaded nanoparticle enhances anticancer efficacy. *Drug Deliv Transl Re* 2021;**11**:2317-27.
9. Yue YL, Li FF, Li Y, Wang YZ, Guo XJ, Cheng ZX, et al. Biomimetic nanoparticles carrying a repolarization agent of tumor-associated macrophages for remodeling of the inflammatory microenvironment following photothermal therapy. *Acs Nano* 2021;**15**:15166-79.
10. Figueiredo P, Lepland A, Scodeller P, Fontana F, Torrieri G, Tiboni M, et al. Peptide-guided resiquimod-loaded lignin nanoparticles convert tumor-associated macrophages from M2 to M1 phenotype for enhanced chemotherapy. *Acta Biomater* 2021;**133**:231-43.
11. Costa da Silva M, Breckwoldt MO, Vinchi F, Correia MP, Stojanovic A, Thielmann CM, et al. Iron induces anti-tumor activity in tumor-associcated macrophages. *Front Immunol* 2017;**8**:1479.
12. Zhao M, Li J, Liu JW, Xu MX, Ji HR, Wu SW, et al. Charge-switchable nanoparticles enhance cancer immunotherapy based on mitochondrial dynamic regulation and immunogenic cell death induction. *J Control Release* 2021;**335**:320-32.
13. Yang LN, Li F, Cao YS, Liu Q, Jing GX, Niu JT, et al. Multifunctional silica nanocomposites prime tumoricidal immunity for efficient cancer immunotherapy. *J Nanobiotechnol* 2021;**19**:328.
14. Zeng WW, Yu M, Chen T, Liu YQ, Yi YF, Huang CY, et al. Polypyrrole nanoenzymes as tumor microenvironment modulators to reprogram macrophage and potentiate immunotherapy. *Adv Sci (Weinh)* 2022;**9**:2201703.
15. Yu YK, Li TX, Ou MT, Luo R, Chen HZ, Ren H, et al. OX40L-expressing M1-like macrophage exosomes for cancer immunotherapy. *J Control Release* 2024;**365**:469-79.
16. Lin YX, Wang Y, Ding JX, Jiang AP, Wang J, Yu MA, et al. Reactivation of the tumor suppressor PTEN by mRNA nanoparticles

enhances antitumor immunity in preclinical models. *Sci Transl Med* 2021;**13**:eaba9772.

17. Wang TT, Zhang H, Han YB, Zheng Q, Liu HH, Han MX, et al. Reversing T cell dysfunction to boost glioblastoma immunotherapy by paroxetine-mediated GRK2 inhibition and blockade of multiple checkpoints through biomimetic nanoparticles. *Adv Sci* 2023;**10**:e2204961.
18. Ren H, Yong JH, Yang QQ, Yang Z, Liu ZY, Xu Y, et al. Self-assembled FeS-based cascade bioreactor with enhanced tumor penetration and synergistic treatments to trigger robust cancer immunotherapy. *Acta Pharm Sin B* 2021;**11**:3244-61.
19. Chen Q, Hu QY, Dukhovlinova E, Chen GJ, Ahn S, Wang C, et al. Photothermal therapy promotes tumor infiltration and antitumor activity of CAR T cells. *Adv Mater* 2019;**31**:e1900192.
20. Zhang YX, Zhao YY, Shen JZ, Sun X, Liu Y, Liu H, et al. Nanoenabled modulation of acidic tumor microenvironment reverses anergy of infiltrating T cells and potentiates anti-PD-1 therapy. *Nano Lett* 2019;**19**:2774-83.
21. Lu Y, Li LH, Du JW, Chen JL, Xu XY, Yang XF, et al. Immunotherapy for tumor metastasis by artificial antigen-presenting cells *via* targeted microenvironment regulation and T-cell activation. *Acs Appl Mater Inter* 2021;**13**:55890-901.
22. Li ZT, Deng YY, Sun HH, Tan CX, Li HM, Mo FY, et al. Redox modulation with a perfluorocarbon nanoparticle to reverse Treg-mediated immunosuppression and enhance anti-tumor immunity. *J Control Release* 2023;**358**:579-90.
23. Ou W, Thapa RK, Jiang LY, Soe ZC, Gautam M, Chang JH, et al. Regulatory T cell-targeted hybrid nanoparticles combined with immuno-checkpoint blockage for cancer immunotherapy. *J Control Release* 2018;**281**:84-96.
24. He SQ, Wang LL, Wu DX, Tong F, Zhao H, Li HM, et al. Dual-responsive supramolecular photodynamic nanomedicine with activatable

immunomodulation for enhanced antitumor therapy. *Acta Pharm Sin B* 2024;**14**:765-80.

25. Ou W, Jiang L, Thapa RK, Soe ZC, Poudel K, Chang JH, et al. Combination of NIR therapy and regulatory T cell modulation using layer-by-layer hybrid nanoparticles for effective cancer photoimmunotherapy. *Theranostics* 2018;**8**:4574-90.
26. Hossain DMS, Panda AK, Chakrabarty S, Bhattacharjee P, Kajal K, Mohanty S, et al. MEK inhibition prevents tumour-shed transforming growth factor-*β*-induced T-regulatory cell augmentation in tumour milieu. *Immunology* 2015;**144**:561-73.
27. Zhang N, Liu SN, Shi SY, Chen YT, Xu FW, Wei XH, et al. Solubilization and delivery of Ursolic-acid for modulating tumor microenvironment and regulatory T cell activities in cancer immunotherapy. *J Control Release* 2020;**320**:168-78.
28. Chen HW, Luan X, Paholak HJ, Burnett JP, Stevers NO, Sansanaphongpricha K, et al. Depleting tumor-associated Tregs *via* nanoparticle-mediated hyperthermia to enhance anti-CTLA-4 immunotherapy. *Nanomedicine-Uk* 2020;**15**:77-92.
29. Plebanek MP, Bhaumik D, Bryce PJ, Thaxton CS. Scavenger receptor type B1 and lipoprotein nanoparticle inhibit myeloid-derived suppressor cells. *Mol Cancer Ther* 2018;**17**:686-97.
30. Zhang T, Xiong HG, Ma XB, Gao Y, Xue P, Kang YJ, et al. Supramolecular tadalafil nanovaccine for cancer immunotherapy by alleviating myeloid-derived suppressor cells and heightening immunogenicity. *Small Methods* 2021;**5**:e2100115.
31. Zuo HQ, Hou YC, Yu YJ, Li ZQ, Liu HX, Liu C, et al. Circumventing myeloid-derived suppressor cell-mediated immunosuppression using an oxygen-generated and -economized nanoplatform. *Acs Appl Mater Inter* 2020;**12**:55723-36.
32. Xia CY, Li M, Ran GY, Wang XH, Lu ZZ, Li T, et al. Redox-responsive nanoassembly restrained myeloid-derived suppressor cells recruitment through autophagy-involved lactate dehydrogenase A silencing for enhanced cancer immunochemotherapy. *J Control Release*

2021;**335**:557-74.

33. Zhang HY, Chen LY, Zhao Y, Luo NC, Shi JB, Xu SJ, et al. Relaxin-encapsulated polymeric metformin nanoparticles remodel tumor immune microenvironment by reducing CAFs for efficient triple-negative breast cancer immunotherapy. *Asian J Pharm Sci* 2023;**18**:100796.
34. He Y, Wu SY, Yuan YB, Sun YC, Ai QJ, Zhou RQ, et al. Remodeling tumor immunosuppression with molecularly imprinted nanoparticles to enhance immunogenic cell death for cancer immunotherapy. *J Control Release* 2023;**362**:44-57.
35. Zheng F, Luo YJ, Liu YQ, Gao YY, Chen WY, Wei K. Nano-baicalein facilitates chemotherapy in breast cancer by targeting tumor microenvironment. *Int J Pharmaceut* 2023;**635**:122778.
36. Chen YN, Hu MR, Wang SW, Wang Q, Lu HY, Wang F, et al. Nano-delivery of salvianolic acid B induces the quiescence of tumor-associated fibroblasts *via* interfering with TGF-β1/Smad signaling to facilitate chemo- and immunotherapy in desmoplastic tumor. *Int J Pharm* 2022;**623**:121953.
37. Pan JX, Lai Y, Zhang SA, Zhang HJ, Shan YM, Huang LJ, et al. Self-adaptive nanoregulator to mitigate dynamic immune evasion of pancreatic cancer. *Adv Mater* 2023;**35**:e2305798.
38. Zang SY, Huang KX, Li JX, Ren KB, Li T, He X, et al. Metabolic reprogramming by dual-targeting biomimetic nanoparticles for enhanced tumor chemo-immunotherapy. *Acta Biomater* 2022;**148**:181-93.
39. Sun XS, Xu XX, Wang J, Zhang XY, Zhao ZT, Liu XC, et al. Acid-switchable nanoparticles induce self-adaptive aggregation for enhancing antitumor immunity of natural killer cells. *Acta Pharm Sin B* 2023;**13**:3093-105.

40. Lian GY, Wan Y, Mak TS, Wang QM, Zhang J, Chen J, et al. Self-carried nanodrug (SCND-SIS3): a targeted therapy for lung cancer with superior biocompatibility and immune boosting effects. *Biomaterials* 2022;**288**:121730.
41. Nakamura T, Sasaki S, Sato Y, Harashima H. Cancer immunotherapy with lipid nanoparticles loaded with a stimulator of interferon genes agonist against renal tumor lung metastasis. *Pharmaceutics* 2023;**16**:31.
42. Biber G, Sabag B, Raiff A, Ben-Shmuel A, Puthenveetil A, Benichou JIC, et al. Modulation of intrinsic inhibitory checkpoints using nano-carriers to unleash NK cell activity. *EMBO Mol Med* 2022;**14**:e14073.
43. Wei ZY, Yi Y, Luo Z, Gong XY, Jiang YX, Hou DY, et al. Selenopeptide nanomedicine activates natural killer cells for enhanced tumor chemoimmunotherapy. *Adv Mater* 2022;**34**:e2108167.
44. Pan SJ, Li TY, Tan YZ, Xu HP. Selenium-containing nanoparticles synergistically enhance Pemetrexed&NK cell-based chemoimmunotherapy. *Biomaterials* 2022;**280**:121321.
45. Qin XH, Zhang MZ, Zhao ZP, Du Q, Li Q, Jiang Y, et al. A carrier-free photodynamic nanodrug to enable regulation of dendritic cells for boosting cancer immunotherapy. *Acta Biomater* 2022;**147**:366-76.
46. Wang P, Wang YF, Li HM, Wang MM, Wang Y, Wang XF, et al. A homologous-targeting cGAS-STING agonist multimodally activates dendritic cells for enhanced cancer immunotherapy. *Acta Biomater* 2024;**177**:400-13.
47. Ma XY, Kuang L, Yin Y, Tang L, Zhang Y, Fan Q, et al. Tumor-antigen activated dendritic cell membrane-coated biomimetic nanoparticles with orchestrating immune responses promote therapeutic efficacy against glioma. *ACS Nano* 2023;**17**:2341-55.
48. Xu XD, Wang R, Li DD, Xiang JJ, Zhang W, Shi XY, et al. Guanidine-modified nanoparticles as robust BTZ delivery carriers and

activators of immune responses. *J Control Release* 2023;**357**:310-8.

49. Su LH, Pan W, Li XX, Zhou XY, Ma XP, Min YZ. Utilizing chemotherapy-induced tumor RNA nanoparticles to improve cancer chemoimmunotherapy. *Acta Biomater* 2023;**158**:698-707.
50. Liu YN, Wen YY, Chen X, Zhu XF, Yu QQ, Gong YC, et al. Inflammation-responsive functional Ru nanoparticles combining a tumor-associated macrophage repolarization strategy with phototherapy for colorectal cancer therapy. *J Mater Chem B* 2019;**7**:6210-23.
51. Zhang LJ, Huang R, Shen YW, Liu J, Wu Y, Jin JM, et al. Enhanced anti-tumor efficacy by inhibiting HIF-1α to reprogram TAMs core-satellite upconverting nanoparticles with curcumin mediated photodynamic therapy. *Biomater Sci-Uk* 2021;**9**:6403-15.
52. Jian H, Wang XB, Song PP, Wu XQ, Zheng RX, Wang YJ, et al. Tumor microcalcification-me diate d relay drug delivery for photodynamic immunotherapy of breast cancer. *Acta Biomater* 2022;**140**:518-29.
53. Tong F, Hu HL, Xu YY, Zhou Y, Xie R, Lei T, et al. Hollow copper sulfide nanoparticles carrying ISRIB for the sensitized photothermal therapy of breast cancer and brain metastases through inhibiting stress granule formation and reprogramming tumor-associated macrophages. *Acta Pharm Sin B* 2023;**13**:3471-88.
54. Choi J, Shim MK, Yang S, Hwang HS, Cho H, Kim J, et al. Visible-light-triggered prodrug nanoparticles combine chemotherapy and photodynamic therapy to potentiate checkpoint blockade cancer immunotherapy. *ACS Nano* 2021;**15**:12086-98.
55. Liu YL, Yang JX, Liu B, Cao W, Zhang JP, Yang YM, et al. Human iPS cells loaded with MnO2-based nanoprobes for photodynamic and simultaneous enhanced immunotherapy against cancer. *Nanomicro Lett* 2020;**12**:127.
56. Wang Y, Gao ZX, Du XJ, Chen SB, Zhang WC, Wang JL, et al. Co-inhibition of the TGF-β pathway and the PD-L1 checkpoint by

pH-responsive clustered nanoparticles for pancreatic cancer microenvironment regulation and anti-tumor immunotherapy. *Biomater Sci-Uk* 2020;**8**:5121-32.