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TI A nanotherapeutic approach for fighting the odds against the malignant disorders
SO JOURNAL OF NANOPARTICLE RESEARCH
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DT Review
DE Inorganic nanomaterials; Immunotherapy; Nanoparticles; Nano-carriers; T-cell expansion; Nanomedicine; Comparative study
ID NANOSTRUCTURED LIPID CARRIERS; IRON-OXIDE NANOPARTICLES; DRUG-DELIVERY SYSTEM; T-CELL IMMUNOTHERAPY; MAGNETIC NANOPARTICLES; CANCER-IMMUNOTHERAPY; SURFACE MODIFICATION; GOLD NANOPARTICLES; BASEMENT-MEMBRANE; QUANTUM DOTS
AB Cancer, a combination of haematological and neoplastic malignancies, is a dreadful disease accounting for major fatalities worldwide. The domain of innovative nanoparticle-based technology has revolutionized the field of cancer therapeutics and imaging. With an emphasis on various nano-immunotherapeutic approaches, this study highlights the most recent developments in nano-immune engineering for metastatic tumours. Nanotechnology-based cancer immunotherapy has powered the (i) activation of T-cells in the tumour microenvironment (TME), (ii) preparation of efficient nanovaccines via nano-carriers and (iii) generation of smart nanomaterials which change their size/shape (size range of 1 to 1000 nm) and functionality upon activation in TME. The tumour microenvironment has an important, albeit contentious, role in controlling nanoparticle (NP) dispersion and subsequent biological consequences. The current study promotes the harnessing of potential peripheral immune cells by avoiding the creation of a pre-metastatic niche and, thus, suppressing tumour recurrence. This review descriptively accounts for a wide array of nanomaterials based on their polymeric constituents. Moreover, the current article explores the obstacles of integrating nanoscale immunomodulators and presents a forward-looking view of the novel nanotechnology-based approaches that may eventually prove helpful in eliminating metastatic illnesses.
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TI Prospective Subunit Nanovaccine against Mycobacterium tuberculosis Infection-Cubosome Lipid Nanocarriers of Cord Factor, Trehalose 6,6 ' Dimycolate
SO ACS APPLIED MATERIALS & INTERFACES
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DT Article
DE Mycobacterium tuberculosis (H37Rv); cord factor trehalose 6,6 ' dimycolate (TDM); cubosomes; nanovaccine; immune response
ID INNATE IMMUNITY; CUBIC PHASES; 6,6'-DIMYCOLATE; BCG; PHARMACOKINETICS; FORMULATIONS; PATHOGENESIS; VACCINATION; GENERATION; GRANULOMAS
AB An improved vaccine is urgently needed to replace the now more than 100-year-old Bacillus Calmette-Guerin (BCG) vaccine against tuberculosis (TB) disease, which represents a significant burden on global public health. Mycolic acid, or cord factor trehalose 6,6 ' dimycolate (TDM), a lipid component abundant in the cell wall of the pathogen Mycobacterium tuberculosis (MTB), has been shown to have strong immunostimulatory activity but remains underexplored due to its high toxicity and poor solubility. Herein, we employed a novel strategy to encapsulate TDM within a cubosome lipid nanocarrier as a potential subunit nanovaccine candidate against TB. This strategy not only increased the solubility and reduced the toxicity of TDM but also elicited a protective immune response to control MTB growth in macrophages. Both pre-treatment and concurrent treatment of the TDM encapsulated in lipid monoolein (MO) cubosomes (MO-TDM) (1 mol %) induced a strong proinflammatory cytokine response in MTB-infected macrophages, due to epigenetic changes at the promoters of tumor necrosis factor alpha (TNF-a) and interleukin 6 (IL-6) in comparison to the untreated control. Furthermore, treatment with MO-TDM (1 mol %) cubosomes significantly improved antigen processing and presentation capabilities of MTB-infected macrophages to CD4 T cells. The ability of MO-TDM (1 mol %) cubosomes to induce a robust innate and adaptive response in vitro was further supported by a mathematical modeling study predicting the vaccine efficacy in vivo. Overall, these results indicate a strong immunostimulatory effect of TDM when delivered through the lipid nanocarrier, suggesting its potential as a novel TB vaccine.
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FX The authors acknowledge the RMIT Micro Nano Research Facility (MNRF) for providing access to equipment and resources as well as the use other facilities within the RMIT. We would like to acknowledge the CSIRO Manufacturing Morphology and Structure Group within the Materials Characterisation and Modelling Program for the TEM contribution to this project. Part of this research was undertaken on the SAXS/WAXS beamline at the Australian Synchrotron, part of ANSTO. The mathematical modeling was partially supported by internal funding from the Cockrell Foundation (Dogra, Cristini). Thanks to the Rebecca L Cooper Medical Research Foundation (S. Soni); C.E.C. acknowledges support from an ARC DECRA Fellowship (DE160101281) and RMIT for a Vice Chancellor's Senior Research Fellowship.
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TI Prospective Subunit Nanovaccine against Mycobacterium tuberculosis
Infection-Cubosome Lipid Nanocarriers of Cord Factor, Trehalose 6,6'
Dimycolate
SO ACS APPLIED MATERIALS & INTERFACES
LA English
DT Article; Early Access
DE Mycobacterium tuberculosis (H37Rv); cord factor trehalose 6,6'
dimycolate (TDM); cubosomes; nanovaccine; imm un e response
ID INNATE IMMUNITY; CUBIC PHASES; 6,6'-DIMYCOLATE; BCG; PHARMACOKINETICS;
FORMULATIONS; PATHOGENESIS; VACCINATION; GENERATION; GRANULOMAS
AB An improved vaccine is urgently needed to replace the now more than 100-year-old Bacillus Calmette-Gue ' rin (BCG) vaccine against tuberculosis (TB) disease, which represents a significant burden on global

public health. Mycolic acid, or cord factor trehalose 6,6' dimycolate (TDM), a lipid component abundant in the cell wall of the pathogen Mycobacterium tuberculosis (MTB), has been shown to have strong immunostimulatory activity but remains underexplored due to its high toxicity and poor solubility. Herein, we employed a novel strategy to encapsulate TDM within a cubosome lipid nanocarrier as a potential subunit nanovaccine candidate against TB. This strategy not only increased the solubility and reduced the toxicity of TDM but also elicited a protective immune response to control MTB growth in macrophages. Both pre-treatment and concurrent treatment of the TDM encapsulated in lipid monoolein (MO) cubosomes (MO-TDM) (1 mol %) induced a strong proinflammatory cytokine response in MTB-infected macrophages, due to epigenetic changes at the promoters of tumor necrosis factor alpha (TNF-alpha) and interleukin 6 (IL-6) in comparison to the untreated control. Furthermore, treatment with MO-TDM (1 mol %) cubosomes significantly improved antigen processing and presentation capabilities of MTB-infected macrophages to CD4 T cells. The ability of MO-TDM (1 mol %) cubosomes to induce a robust innate and adaptive response in vitro was further supported by a mathematical modeling study predicting the vaccine efficacy in vivo. Overall, these results indicate a strong immunostimulatory effect of TDM when delivered through the lipid nanocarrier, suggesting its potential as a novel TB vaccine.
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WC Nanoscience & Nanotechnology; Materials Science, Multidisciplinary
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Deng, Xin-Chen
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Zhang, Xian-Zheng
TI Fused Cytomembrane-Camouflaged Nanoparticles for Tumor-Specific Immunotherapy
SO ADVANCED HEALTHCARE MATERIALS
LA English
DT Article; Early Access
DE adjuvants; fused cytomembranes; nanovaccines; tumor immunotherapy; whole antigens
ID DENDRITIC CELLS; ANTITUMOR IMMUNITY; CANCER; NANOVACCINES; CD80; NANOMATERIALS; MACROPHAGES; ACTIVATION; BLOCKADE; DELIVERY

AB Tumor immunotherapy is commonly hindered by inefficient delivery and presentation of tumor antigens as well as immunosuppressive tumor microenvironment. To overcome these barriers, a tumor-specific nanovaccine capable of delivering tumor antigens and adjuvants to antigen-presenting cells and modulating the immune microenvironment to elicit strong antitumor immunity is reported. This nanovaccine, named FCM@4RM, is designed by coating the nanocore (FCM) with a bioreconstituted cytomembrane (4RM). The 4RM, which is derived from fused cells of tumorous 4T1 cells and RAW264.7 macrophages, enables effective antigen presentation and stimulation of effector T cells. FCM is self-assembled from Fe(II), unmethylated cytosine-phosphate-guanine oligodeoxynucleotide (CpG), and metformin (MET). CpG, as the stimulator of toll-like receptor 9, induces the production of pro-inflammatory cytokine and the maturation of cytotoxic T lymphocytes (CTLs), thereby enhancing antitumor immunity. Meanwhile, MET functions as the programmed cell death ligand 1 inhibitor and can restore the immune responses of T cells against tumor cells. Therefore, FCM@4RM exhibits high targeting capabilities toward homologous tumors that develop from 4T1 cells. This work offers a paradigm for developing a nanovaccine that systematically regulates multiple immune-related processes to achieve optimal antitumor immunotherapy.
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TI In Situ Sprayed Nanovaccine Suppressing Exosomal PD-L1 by Golgi Apparatus Disorganization for Postsurgical Melanoma Immunotherapy
SO ACS NANO
LA English
DT Article
DE biomimetic; immunotherapy; Golgiapparatusdisorganization; exosomal PD-L1; in situ sprayed hydrogel vaccine
ID ACQUIRED-RESISTANCE; CANCER; BLOCKADE; METASTASIS; SURVIVAL; THERAPY; DRIVEN; ROLES
AB Theanti-PD-L1 immunotherapy has shown promise in treatingcancer.However, certain patients with metastatic cancer have low responseand high relapse rates. A main reason is systemic immunosuppressioncaused by exosomal PD-L1, which can circulate in the body and inhibitT cell functions. Here, we show that Golgi apparatus-Pd-l1 (-/-) exosome hybrid membrane coated nanoparticles(GENPs) can significantly reduce the secretion of PD-L1. The GENPscan accumulate in tumors through homotypic targeting and effectivelydeliver retinoic acid, inducing disorganization of the Golgi apparatusand a sequence of intracellular events including alteration of endoplasmicreticulum (ER)-to-Golgi trafficking and subsequent ER stress, whichfinally disrupts the PD-L1 production and the release of exosomes.Furthermore, GENPs could mimic exosomes to access draining lymph nodes.The membrane antigen of PD-l1 (-/-) exosome on GENPs can activate T cells through a vaccine-like effect,strongly promoting systemic immune responses. By combining GENPs withanti-PD-L1 treatment in the sprayable in situ hydrogel,we have successfully realized a low recurrence rate and substantiallyextended survival periods in mice models with incomplete metastaticmelanoma resection.
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DT Review
DE stimuli-responsive; polymer nanoparticle; nanovaccine; immunotherapy; cancer; antigen-presenting cells; adjuvants; antigens
ID DELIVERY-SYSTEM; CANCER-IMMUNOTHERAPY; ANTIGEN-DELIVERY; IN-VITRO; DENDRITIC CELLS; CO-DELIVERY; IMMUNE-RESPONSE; NANOPARTICLES; VACCINE; PH
AB The development of nanovaccines that employ polymericdeliverycarriers has garnered substantial interest in therapeutic treatmentof cancer and a variety of infectious diseases due to their superiorbiocompatibility, lower toxicity and reduced immunogenicity. Particularly,stimuli-responsive polymeric nanocarriers show great promise for deliveringantigens and adjuvants to targeted immune cells, preventing antigendegradation and clearance, and increasing the uptake of specific antigen-presentingcells, thereby sustaining adaptive immune responses and improvingimmunotherapy for certain diseases. In this review, the most recentadvances in the utilization of stimulus-responsive polymer-based nanovaccinesfor immunotherapeutic applications are presented. These sophisticatedpolymeric nanovaccines with diverse functions, aimed at therapeuticadministration for disease prevention and immunotherapy, are furtherclassified into several active domains, including pH, temperature,redox, light and ultrasound-sensitive intelligent nanodelivery systems.Finally, the potential strategies for the future design of multifunctionalnext-generation polymeric nanovaccines by integrating materials sciencewith biological interface are proposed.
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ID STROMAL CELLS; CANCER; DEPLETION; IMMUNITY
AB Cancer-associated fibroblasts (CAFs), which are dominantcell typesin the tumor microenvironment (TME), support tumor growth by secretingcytokines and forming an extracellular matrix (ECM) that hampers thepenetration of chemical and biological therapeutics within the tumorand thereby limits their therapeutic efficacy. Here, we report a cancernanovaccine targeting fibroblast activation protein alpha (FAP)-expressingCAFs as a potential pan-tumor vaccine. We predicted immunodominantFAP-specific epitope peptides in silico and selectedtwo candidate peptides after in vitro and in vivo screening for immunogenicity and antitumor efficacy.Next, we developed a nanoparticle-based vaccine that displays

thetwo selected epitope peptides on the surface of lipid nanoparticlesencapsulating CpG adjuvant (FAP(PEP)-SLNPs). Immunizationwith one of two FAP(PEP)-SLNP nanovaccines led to considerablegrowth inhibition of various tumors, including desmoplastic tumors,by depleting FAP(+) CAFs and thereby reducing ECM productionin the TME while causing little appreciable adverse effects. Furthermore,when combined with a chemotherapeutic drug, the FAP(PEP)-SLNPnanovaccine increased drug accumulation and resulted in a synergisticantitumor efficacy far better than that of each corresponding monotherapy.These findings suggest that our FAP(PEP)-SLNP nanovaccinehas potential for use as an "off-the-shelf" pan-tumorvaccine applicable to a variety of tumors and may be a suitable platformfor use in various combination therapies.
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TI Pharmacological impact of microRNAs in head and neck squamous cell carcinoma: Prevailing insights on molecular pathways, diagnosis, and nanomedicine treatment
SO FRONTIERS IN PHARMACOLOGY
LA English
DT Review
DE head and neck squamous cell carcinoma; microRNA; molecular signaling; nanomedicine; nanovaccines
ID GOLD NANOPARTICLES; IN-VITRO; MAGNETIC NANOPARTICLES; CIRCULATING MICRORNAS; EXPRESSION PROFILES; RADIATION-THERAPY; DOWN-REGULATION; DRUG-DELIVERY; STEM-CELLS; CANCER
AB Head and neck squamous cell carcinoma is a disease that most commonly produce tumours from the lining of the epithelial cells of the lips, larynx, nasopharynx, mouth, or oro-pharynx. It is one of the most deadly forms of cancer. About one to two percent of all neo-plasm-related deaths are attributed to head and neck squamous cell carcinoma, which is responsible for about six percent of all cancers. MicroRNAs play a critical role in cell proliferation, differentiation, tumorigenesis, stress response, triggering apoptosis, and other physiological process. MicroRNAs regulate gene expression and provide new diagnostic, prognostic, and therapeutic options for head and neck squamous cell carcinoma. In this work, the role of molecular signaling pathways related to head and neck squamous cell carcinoma is emphasized. We also provide an overview of MicroRNA downregulation and overexpression and its role as a diagnostic and prognostic marker in head and neck squamous cell carcinoma. In recent years, MicroRNA nano-based therapies for head and neck squamous cell carcinoma have been explored. In addition, nanotechnology-based alternatives have been discussed as a promising strategy in exploring therapeutic paradigms aimed at improving the efficacy of conventional cytotoxic chemotherapeutic agents against head and neck squamous cell carcinoma and attenuating their cytotoxicity. This article also provides information on ongoing and recently completed clinical trials for therapies based on nanotechnology.
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SO CHEMMEDCHEM
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DT Review
DE cancer nanovaccines; immune microenvironment; immune response; nanocarriers; tumor antigens
ID METASTATIC MELANOMA; CROSS-PRESENTATION; CTLA-4 BLOCKADE; VACCINE; IMMUNOTHERAPY; COMBINATION; DELIVERY; CELLS; INTERLEUKIN-2; STRATEGIES
AB Many advances have been made recently in the field of cancer immunotherapy, particularly with the

development of treatments such as immune checkpoint inhibitors and adoptive cellular immunotherapy. The efficacy of immunotherapy is limited, however, owing to high levels of tumor heterogeneity and the immunosuppressive environments of advanced malignant tumors. Therefore, therapeutic anticancer vaccines have gradually become powerful tools for inducing valid antitumor immune responses and regulating the immune microenvironment. Tumor vaccines loaded in nanocarriers have become an indispensable delivery platform for tumor treatment because of their enhanced stability, targeting capability, and high level of safety. Through a unique design, cancer nanovaccines activate innate immunity and tumor-specific immunity simultaneously. For example, the design of cancer vaccines can incorporate strategies such as enhancing the stability and targeting of tumor antigens, combining effective adjuvants, cytokines, and immune microenvironment regulators, and promoting the maturation and cross-presentation of antigen-presenting cells (APCs). In this review, we discuss the design and preparation of nanovaccines for remodeling tumor antigen immunogenicity and regulating the immunosuppressive microenvironment.
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TI In Situ STING-Activating Nanovaccination with TIGIT Blockade for Enhanced Immunotherapy of Anti-PD-1-Resistant Tumors
SO ADVANCED MATERIALS
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DE anti-PD-1-resistant tumors; biomimetic materials; immunotherapy; nanovaccination; STING
ID ANTITUMOR; RESISTANCE; PATHWAY
AB Immunotherapies comprising programmed cell death protein 1/PD ligand 1 (PD-1/PD-L1) immune checkpoint inhibitors are effective cancer treatments. However, the low response rate and immunoresistance resulting from alternative immune checkpoint upregulation and inefficient immune stimulation by T cells are problematic. The present report describes a biomimetic nanoplatform that simultaneously blocks the alternative T-cell immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domain (TIGIT) checkpoint and activates the stimulator of interferon genes (STING) signaling pathway in situ for enhanced antitumor immunity. The nanoplatform is engineered by fusing a red blood cell membrane with glutathione-responsive liposome-encapsulated cascade-activating chemoagents (beta-lapachone and tirapazamine), and anchoring them with a detachable TIGIT block peptide (named as RTLT). In the tumor environment, the peptide is spatiotemporally released to reverse T-cell exhaustion and restore antitumor immunity. The cascade activation of chemotherapeutic agents causes DNA damage and inhibits the repair of double-stranded DNA, which induces robust in situ STING activation for an efficient immune response. The RTLT inhibits anti-PD-1-resistant tumor growth, and prevents tumor metastasis and recurrence in vivo by inducing antigen-specific immune memory. This biomimetic nanoplatform thus provides a promising strategy for in situ cancer vaccination.
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NR 36
TC 0
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U1 43
U2 43
PU WILEY-V C H VERLAG GMBH
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J9 ADV MATER
JI Adv. Mater.
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AF Sun, Wenqi
Ji, Panpan
Zhou, Tian
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Zhang, Liang
Wei, Mengying
Yang, Guodong
Yuan, Lijun
TI Ultrasound Responsive Nanovaccine Armed with Engineered Cancer Cell Membrane and RNA to Prevent Foreseeable Metastasis
SO ADVANCED SCIENCE
LA English
DT Article
DE alternative splicing; antigen presentation; cancer vaccine; sonosensitizer
ID ANTIGEN PRESENTATION; DENDRITIC CELLS; VACCINES; BREAST; NANOPARTICLES; GENERATION
AB Cancer vaccine has been considered as a promising immunotherapy by inducing specific anti-tumor immune response. Rational vaccination at suitable time to efficiently present tumor associated antigen will boost tumor immunity and is badly needed. Here, a poly (lactic-co-glycolic acid) (PLGA)-based cancer vaccine of nanoscale is designed, in which engineered tumor cell membrane proteins, mRNAs, and sonosensitizer chlorin e6 (Ce6) are encapsulated at high efficiency. The nanosized vaccine can be efficiently delivered into antigen presentation cells (APCs) in lymph nodes after subcutaneous injection. In the APCs, the encapsulated cell membrane and RNA from engineered cells, which have disturbed splicing resembling the metastatic cells, provide neoantigens of metastatic cancer in advance. Moreover, the sonosensitizer Ce6 together with ultrasound irradiation promotes mRNA escape from endosome, and augments antigen presentation. Through 4T1 syngeneic mouse model, it has been proved that the proposed nanovaccine is efficient to elicit antitumor immunity and thus prevent cancer metastasis.
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FX Acknowledgements W.S. and P.J. contributed equally to this work. The authors gratefully acknowledge Jing Zhang and Zhenzhen Hao for technical assistance. This work was supported by the National Natural Science Foundation of China (NSFC) (82272010, 32271199, 82202195).
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NR 55
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Liang, Yujie
TI CCR7 Mediated Mimetic Dendritic Cell Vaccine Homing in Lymph Node for Head and Neck Squamous Cell Carcinoma Therapy
SO ADVANCED SCIENCE

LA English
DT Article
DE CCR7; head and neck squamous cell carcinoma; lymph node targeting; nanovaccines; tumor-derived exosomes
ID TUMOR-DERIVED EXOSOMES; NANOPARTICLES; ACTIVATION; TRANSPORT; ANTIGENS
AB Immunotherapy has been recognized as one of the most promising treatment strategies for head and neck squamous cell carcinoma (HNSCC). As a pioneering trend of immunotherapy, dendritic cell (DC) vaccines have displayed the ability to prime an immune response, while the insufficient immunogenicity and low lymph node (LN) targeting efficiency, resulted in an unsubstantiated therapeutic efficacy in clinical trials. Herein, a hybrid nanovaccine (Hy-M-Exo) is developed via fusing tumor-derived exosome (TEX) and dendritic cell membrane vesicle (DCMV). The hybrid nanovaccine inherited the key protein for lymphatic homing, CCR7, from DCMV and demonstrated an enhanced efficiency of LN targeting. Meanwhile, the reserved tumor antigens and endogenous danger signals in the hybrid nanovaccine activated antigen presenting cells (APCs) elicited a robust T-cell response. Moreover, the nanovaccine Hy-M-Exo displayed good therapeutic efficacy in a mouse model of HNSCC. These results indicated that Hy-M-Exo is of high clinical value to serve as a feasible strategy for antitumor immunotherapy.
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C3 Sun Yat Sen University; Sun Yat Sen University; Sun Yat Sen University; Xuzhou Medical University; Xuzhou Medical University
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FU National Natural Science Foundation of China [81972544, 82072995]; Program of Xuzhou Science and Technology [KC22040]; Scientific Research Start-up Fund for Talent in Xuzhou Medical University [D2022023]
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NR 45
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Yang, Wenqin
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Lei, Lei
Lin, Ruyi
Li, Jiamei
Li, Yuan
Gao, Huile
TI In Situ Tumor Vaccine for Lymph Nodes Delivery and Cancer Therapy Based on Small Size Nanoadjuvant
SO SMALL
LA English
DT Article; Early Access
DE antigen delivery; CTLA4; in situ vaccines; losartan; lymph node targets; tumor vaccines
ID CHECKPOINT BLOCKADE; BREAST-CANCER; NANOPARTICLES; MICROENVIRONMENT; HYDROGEL; IMMUNOTHERAPY; COMBINATION; NANOVACCINE; EFFICACY; RECEPTOR
AB Tumor vaccine is a promising cancer treatment modality, however, the convenient antigens loading in vivo and efficient delivery of vaccines to lymph nodes (LNs) still remain a formidable challenge. Herein, an in situ nanovaccine strategy targeting LNs to induce powerful antitumor immune responses by converting the primary tumor into whole-cell antigens and then delivering these antigens and nanoadjuvants simultaneously to LNs is proposed. The in situ nanovaccine is based on a hydrogel system, which loaded with doxorubicin (DOX) and nanoadjuvant CpG-P-ss-M. The gel system exhibits ROS-responsive release of DOX and CpG-P-ss-M, generating abundant in situ storage of whole-cell tumor antigens. CpG-P-ss-M adsorbs tumor antigens through the positive surface charge and achieves charge reversal, forming small-sized and negatively charged tumor vaccines in situ, which are then primed to LNs. Eventually, the tumor vaccine promotes antigens uptake by dendritic cells (DCs), maturation of DCs, and proliferation of T cells. Moreover, the vaccine combined with anti-CTLA4 antibody and losartan inhibits tumor growth by 50%, significantly increasing the percentage of splenic cytotoxic T cells (CTLs), and generating tumor-specific immune responses. Overall, the treatment effectively inhibits primary tumor growth and induces tumor-specific immune response. This study provides a scalable strategy for in situ tumor vaccination.
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NR 77
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SN 1613-6810
EI 1613-6829
J9 SMALL
JI Small
PD 2023 APR 20
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WC Chemistry, Multidisciplinary; Chemistry, Physical; Nanoscience & Nanotechnology; Materials Science, Multidisciplinary; Physics, Applied; Physics, Condensed Matter
WE Science Citation Index Expanded (SCI-EXPANDED)
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PT J
AU Wen, ZF
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AF Wen, Zhenfu

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Zeng, Zhipeng
Chen, Yongming
Liu, Lixin
TI Nanovaccines Fostering Tertiary Lymphoid Structure to Attack Mimicry Nasopharyngeal Carcinoma
SO ACS NANO
LA English
DT Article
DE Nanovaccine; Nasopharyngeal carcinoma; STING; Tertiary lymphoid structures; TLR9 agonist
ID IMMUNE-RESPONSES; DENDRITIC CELLS; IMMUNOTHERAPY; INDUCTION; SECONDARY; CANCER; TUMORS
AB Tertiary lymphoid structures (TLSs) are formed in inflamed tissues, and recent studies demonstrated that the appearance of TLSs in tumor sites is associated with a good prognosis for tumor patients. However, the process of natural TLSs' formation was slow and uncontrollable. Herein, we developed a nanovaccine consisting of Epstein-Barr virus nuclear antigen 1 (EBNA1) and a bi-adjuvant of Mn2+ and cytosine-phosphate-guanine (CpG) formulated with tannic acid that significantly inhibited the development of mimicry nasopharyngeal carcinoma by fostering TLS formation. The nanovaccine activated LT-alpha and LT-beta pathways, subsequently enhancing the expression of downstream chemokines, CCL19/ CCL21, CXCL10 and CXCL13, in the tumor microenvironment. In turn, normalized blood and lymph vessels were detected in the tumor tissues of the nanovaccine group, correlated with increased infiltration of lymphocytes. Especially, the proportion of the B220+ CD8+ T, which was produced via trogocytosis between T and B cells during activation of T cells, was increased in tumors of the nanovaccine group. Furthermore, the intratumoral effector memory T cells (Tem), CD45+, CD3+, CD8+, CD44+, and CD62L-, did not decrease after blocking the egress of T cells from tumor-draining lymph nodes by FTY-720. These results demonstrated that the nanovaccine can foster TLS formation, which thus enhances local immune responses significantly, delays tumor outgrowth, and prolongs the median survival time of murine models of mimicry nasopharyngeal carcinoma, demonstrating a promising strategy for nanovaccine development.
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U2 16
PU AMER CHEMICAL SOC
PI WASHINGTON
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WC Chemistry, Multidisciplinary; Chemistry, Physical; Nanoscience & Nanotechnology; Materials Science, Multidisciplinary
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SC Chemistry; Science & Technology - Other Topics; Materials Science
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PT J
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TI Immunization with nanovaccines containing mutated K-Ras peptides and imiquimod aggravates heterotopic pancreatic cancer induced in mice
SO FRONTIERS IN IMMUNOLOGY
LA English
DT Article
DE KRAS; nanovaccine; pancreatic cancer; imiquimod (IMQ); chitosan; polyarginine
ID LOADED CHITOSAN NANOPARTICLES; TLR7 AGONIST; VACCINE; CELLS; IMMUNOSUPPRESSION; NANOCAPSULES; MECHANISM; CARCINOMA; PROTEINS; DELIVERY
AB PurposeThe growing incidence and lethality of pancreatic cancer urges the development of new therapeutic approaches. Anti-tumoral vaccines can potentiate the immune response against the tumor, targeting specific antigens expressed only on tumor cells. In this work, we designed new vaccines for pancreatic cancer, composed by chitosan nanocapsules (CS NCs) containing imiquimod (IMQ) as adjuvant, and targeting the K-Ras mutation G12V. Experimental designWe tested the immunogenicity of our vaccines in mice, carrying different combinations of K-Ras mutated peptides. Then, we analyzed their prophylactic and therapeutic efficacy in mice bearing heterotopic pancreatic cancer. ResultsUnexpectedly, although good results were observed at short time points, the different combinations of our CS NCs vaccines seemed to potentiate tumor growth and reduce survival rate. We propose that this effect could be due to an inadequate immune response, partially because of the induction of a regulatory tolerogenic response. ConclusionOur results call for caution in the use of some NCs containing IMQ in the immunotherapy against pancreatic cancer.
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NR 50
TC 0

Z9 0
U1 1
U2 1
PU FRONTIERS MEDIA SA
PI LAUSANNE
PA AVENUE DU TRIBUNAL FEDERAL 34, LAUSANNE, CH-1015, SWITZERLAND
SN 1664-3224
J9 FRONT IMMUNOL
JI Front. Immunol.
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WC Immunology
WE Science Citation Index Expanded (SCI-EXPANDED)
SC Immunology
GA E2RM1
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PT J
AU Su, RP
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Yin, Weimin
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Li, Yan
Li, Yongyong
TI CaCO3 powder-mediated biomineralization of antigen nanosponges synergize with PD-1 blockade to potentiate anti-tumor immunity
SO JOURNAL OF NANOBIOTECHNOLOGY

LA English
DT Article
DE Nanovaccine; CaCO3 powder; Biomineralization; Antigen-presenting cells; Antigen-specific CD8(+) T cell responses
ID CALCIUM-CARBONATE; STABILIZATION; INFECTION; OVALBUMIN; CATALYST; VATERITE
AB Antigen self-assembly nanovaccines advance the minimalist design of therapeutic cancer vaccines, but the issue of inefficient cross-presentation has not yet been fully addressed. Herein, we report a unique approach by combining the concepts of "antigen multi-copy display" and "calcium carbonate (CaCO3) biomineralization" to increase cross-presentation. Based on this strategy, we successfully construct sub-100 nm biomineralized antigen nanosponges (BANSs) with high CaCO3 loading (38.13 wt%) and antigen density (61.87%). BANSs can be effectively uptaken by immature antigen-presenting cells (APCs) in the lymph node upon subcutaneous injection. Achieving efficient spatiotemporal coordination of antigen cross-presentation and immune effects, BANSs induce the production of CD4(+) T helper cells and cytotoxic T lymphocytes, resulting in effective tumor growth inhibition. BANSs combined with anti-PD-1 antibodies synergistically enhance anti-tumor immunity and reverse the tumor immunosuppressive microenvironment. Overall, this CaCO3 powder-mediated biomineralization of antigen nanosponges offer a robust and safe strategy for cancer immunotherapy.
C1 [Su, Runping; Gu, Jingjing; Sun, Juanjuan; Zang, Jie; Zhao, Yuge; Zhang, Tingting; Chong, Gaowei; Yin, Weimin; Zheng, Xiao; Liu, Bingbing; Huang, Li; Ruan, Shuangrong; Dong, Haiqing; Li, Yan; Li, Yongyong] Tongji Univ, Shanghai Skin Dis Hosp, Inst Biomed Engn & Nano Sci, Sch Med, Shanghai 200092, Peoples R China.
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FU National Natural Science Foundation of China [32271387]; Talent Program of Shanghai Municipal Health Commission [2022XD052]; Shanghai Natural Science Foundation [23ZR1465200]; Sci-Tech Innovation 2030 - Major Project of Brain science and brain-inspired intelligence technology [2021ZD0202003]; Fundamental Research Funds for the Central Universities [2022-4-YB-09]
FX This work was financially supported through grants from the National Natural Science Foundation of China (32271387), Talent Program of Shanghai Municipal Health Commission(2022XD052), Shanghai Natural Science Foundation(23ZR1465200), Sci-Tech Innovation 2030 - Major Project of Brain science and brain-inspired intelligence technology (2021ZD0202003), Fundamental Research Funds for the Central Universities (2022-4-YB-09).
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NR 34
TC 0
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U1 11
U2 11
PU BMC
PI LONDON
PA CAMPUS, 4 CRINAN ST, LONDON N1 9XW, ENGLAND
EI 1477-3155
J9 J NANOBIOTECHNOL
JI J. Nanobiotechnol.
PD APR 7
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IS 1
AR 120
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WC Biotechnology & Applied Microbiology; Nanoscience & Nanotechnology
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Peng, Xueyu
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Qiu, Liping
Qu, Fengli
Tan, Weihong
TI Aptamer-Functionalized Nanovaccines: Targeting In Vivo DC Subsets for Enhanced Antitumor Immunity
SO ACS APPLIED MATERIALS & INTERFACES
LA English
DT Article
DE aptamer; nanovaccine; DC subset-targeting; T cell activation; cancer immunoprevention
ID EPIGALLOCATECHIN GALLATE EGCG; PLASMACYTOID DENDRITIC CELLS; ADJUVANTS; POLYPHENOL; SELECTION; ANTIGENS; SELEX
AB Cancer vaccines, which directly pulsed in vivo dendritic cells (DCs) with specific antigens and immunostimulatory adjuvants, showed great potential for cancer immunoprevention. However, most of them were limited by suboptimal outcomes, mainly owing to overlooking the complex biology of DC phenotypes. Herein, based on adjuvant-induced antigen assembly, we developed aptamer-functionalized nanovaccines for in vivo DC subset-targeted codelivery of tumor-related antigens and immunostimulatory adjuvants. We chose two aptamers, iDC and CD209, and tested their performance on DC targeting. Our results verified that these aptamer-functionalized nanovaccines could specifically recognize circulating classical DCs (cDCs), a subset of DCs capable of priming nai''ve T cells, noting that iDC outperformed CD209 in this regard. With excellent cDC-targeting capability, the iDC-functionalized nanovaccine induced potent antitumor immunity, leading to effective inhibition of tumor occurrence and metastasis, thus providing a promising platform for cancer immunoprevention.
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FU National Key Research Program [2021YFA0910100, 2019YFA0905800]; National Natural Science Foundation of China [NSFC 21922404, 22174039, 21827811]; Science and Technology Project of Hunan Province [2021RC4022, 2019SK2201, 2017XK2103]
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NR 31
TC 0
Z9 0
U1 20
U2 20
PU AMER CHEMICAL SOC
PI WASHINGTON
PA 1155 16TH ST, NW, WASHINGTON, DC 20036 USA
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EI 1944-8252
J9 ACS APPL MATER INTER
JI ACS Appl. Mater. Interfaces
PD APR 19
PY 2023
VL 15
IS 15
BP 18590
EP 18597
DI 10.1021/acsami.2c20846
EA APR 2023
PG 8
WC Nanoscience & Nanotechnology; Materials Science, Multidisciplinary
WE Science Citation Index Expanded (SCI-EXPANDED)
SC Science & Technology - Other Topics; Materials Science
GA D8NE4
UT WOS:000967552100001
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PT J
AU Yan, H
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Liu, ZY
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Zhang, Y
AF Yan, Huan

Lin, Guibin
Liu, Zhanyan
Gu, Fei
Zhang, Yuan
TI Nano-adjuvants and immune agonists promote antitumor immunity of peptide amphiphiles
SO ACTA BIOMATERIALIA
LA English
DT Article
DE PolyIC; Anti-CD40 antibody; Nanovaccine; Peptide amphiphile; Antitumor immunity; Anti-4-1BB antibody
ID NF-KAPPA-B; TUMOR-ANTIGEN; INNATE; RESPONSES; ACTIVATION; INDUCTION; CELLS; EXPRESSION; RESISTANCE; RECEPTORS
AB Immunostimulatory cues play an important role in priming antitumor immunity and promoting the efficacy of subunit cancer vaccines. However, the clinical use of many immunostimulatory agents is often hampered by their inefficient in vivo delivery which may decrease immune response to the vaccination. To promote vaccine efficacy, we develop vaccine formulations which integrate three key elements: (1) a nano-adjuvant formulated by conjugating an agonistic anti-CD40 monoclonal antibody (alpha CD40) to the surface of a polyIC-loaded lipid nanoparticle, (2) a peptide amphiphile containing an optimized CD8 + T-cell epitope that derived from a melanoma antigen gp100, (3) an agonistic anti-4-1BB monoclonal antibody (alpha 4-1BB) that boosts the efficacy of vaccinations. In a syngeneic mouse model of melanoma, the vaccine formulations enhanced innate immunity and activated multiple innate immune signaling pathways within draining lymph nodes, as well as promoted antigen-specific immune responses and reduced immunosuppression in the tumor microenvironment, leading to profound tumor growth inhibition and prolonged survival. Thus, our vaccine formulations represent an attractive strategy to stimulate antitumor immunity and control tumor progression.
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FU National Natural Science Foundation of China [82172080]; Basic and Applied Basic Research Foundation of Guangdong Province [2020A1515111204]; Fundamental Research Funds for the Central Universities [2020ZYGXZR099]; Recruitment Program of Global Experts
FX This work was supported by National Natural Science Founda- tion of China (82172080) , Basic and Applied Basic Research Foun- dation of Guangdong Province (2020A1515111204) , the Fundamen- tal Research Funds for the Central Universities (2020ZYGXZR099) and the Recruitment Program of Global Experts. We would like to thank the Research Core Facilities at the South China University of Technology.
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NR 54
TC 0
Z9 0
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U2 5
PU ELSEVIER SCI LTD
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WC Engineering, Biomedical; Materials Science, Biomaterials
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SC Engineering; Materials Science
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PT J
AU Liu, HX
Xie, ZG
Zheng, M
AF Liu, Hongxin
Xie, Zhigang
Zheng, Min
TI Carbon Dots and Tumor Antigen Conjugates as Nanovaccines for Elevated Cancer Immunotherapy
SO SMALL
LA English
DT Article
DE cancer immunotherapy; carbon dots; nanovaccines; tumor antigens
ID BLOCKADE
AB Cancer immunotherapy has become one of the current research hotspots. However, the deficiencies including restricted immunogenicity, insufficient antigen presentation, and low responsive rate limited their therapeutic applications. Own to the small size and excellent biocompatibility, carbon dots (CDs) can serve as nanovectors to improve the efficacy of cancer immunotherapy. Herein, a tumor antigen-based nanovaccines (GMal+B16F10-Ag and GMal+CT26-Ag) by the conjugation of CDs with the tumor cell-derived antigens (B16F10-Ag and CT26-Ag) is constructed. These nanovaccines can be effectively taken up by dendritic cells (DC2.4), promote DC cell maturation, cross-present the antigen to T cells, specifically target B16F10 melanoma or CT26 colon cancers, and inhibit tumor growth distinctly. This work illustrates the promise of CDs acting as versatile carriers for antigen delivery to achieve the optimal immunotherapeutic outcomes.
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FU National Natural Science Foundation of China [51873023]; Science and Technology Development Plan of Changchun City [21ZY38]
FX Acknowledgements The financial support from the National Natural Science Foundation of China (No. 51873023), and the Science and Technology Development Plan of Changchun City (No. 21ZY38).
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NR 40
TC 0
Z9 0
U1 38
U2 38
PU WILEY-V C H VERLAG GMBH
PI WEINHEIM
PA POSTFACH 101161, 69451 WEINHEIM, GERMANY
SN 1613-6810
EI 1613-6829
J9 SMALL
JI Small
PD AUG
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WE Science Citation Index Expanded (SCI-EXPANDED)
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PT J
AU Lv, XJ
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Min, J
Wang, HR
Xu, YY
Zhang, ZM
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AF Lv, Xinjing
Huang, Jie
Min, Jie
Wang, Hairong
Xu, Yunyun
Zhang, Zimu
Zhou, Xiuxia
Wang, Jian
Liu, Zhuang
Zhao, He
TI Multi-signaling pathway activation by pH responsive manganese particles for enhanced vaccination
SO JOURNAL OF CONTROLLED RELEASE
LA English
DT Article
DE cancer nanovaccine; Immunotherapy; Checkpoint blockade; Metalloimmunotherapy
ID DNA VACCINES
AB As metal ions play important roles in the process of immunomodulation, immunotherapy based on metal ions has attracted tremendous interests in recent years. Here, we screened common metal ions and found that Mn2+ could enhance the immune function in vitro. A new type of nanovaccine is thus fabricated by a biomimetic approach using nanoscale coordination polymer formed by Mn2+ and 2-methylimidazole (2-MI) to encapsulate ovalbumin (OVA) protein, a model antigen, obtaining OVA@MM nanoparticles. Compared to free OVA, OVA@MM nano -particles could more effectively induce the maturation of bone marrow-derived dendritic cells (BMDCs) and their subsequent antigen cross-presentation. The particles made of Mn2+ and 2-MI could activate immune-regulated signal pathways to enhance the immune functions of BMDCs. Such OVA@MM nanovaccine could not only provide prophylactic effect to inhibit the growth of B16-OVA tumor on immunized mice, but also significantly inhibit tumor growth in the mice with B16-OVA tumor combined with anti-programmed cell death protein 1 (anti-PD-1) antibody. Therefore, this nanovaccine platform based on Mn2+, 2-MI and antigen may provide a simple, effective and broadly applicable strategy to enhance adaptive immunity against cancer and other diseases.
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RI Wang, Jian/ITW-0790-2023

FU National Key Research and Development Program of China [2021YFF0701800]; National Natural Science Foundation of China [52032008, 21927803]; Jiangsu Social Development Project [BE2019658, BE2020659]; Suzhou science and technology project [SKJY2021107]; Jiangsu health commission project [M2022120, Szlcyxzx202104]; Natural Science Foundation of the Jiangsu Higher Education Institutions of China [21KJB320010]; Collaborative Innovation Center of Suzhou Nano Science and Technology; Ministry of Education of China
FX This work was supported by the National Key Research and Development Program of China (2021YFF0701800), the National Natural Science Foundation of China (52032008, 21927803), the Jiangsu Social Development Project (BE2019658, BE2020659), Suzhou science and technology project (SKJY2021107), the Jiangsu health commission project (M2022120, Szlcyxzx202104), the Natural Science Foundation of the Jiangsu Higher Education Institutions of China (21KJB320010), the Collaborative Innovation Center of Suzhou Nano Science and Technology and the '111' program from the Ministry of Education of China. The scheme was created by BioRender.
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NR 55
TC 0
Z9 0
U1 13
U2 13
PU ELSEVIER
PI AMSTERDAM
PA RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS
SN 0168-3659
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J9 J CONTROL RELEASE
JI J. Control. Release
PD MAY
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VL 357
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EP 119
DI 10.1016/j.jconrel.2023.01.078
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WC Chemistry, Multidisciplinary; Pharmacology & Pharmacy
WE Science Citation Index Expanded (SCI-EXPANDED)
SC Chemistry; Pharmacology & Pharmacy
GA D2JB2
UT WOS:000967025200001
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PT J
AU Shin, H
Kang, S
Chae, SY
Won, C
Min, DH
AF Shin, Hojeong
Kang, Seounghun
Chae, Se-Youl
Won, Cheolhee
Min, Dal-Hee
TI Development of a Cancer Nanovaccine to Induce Antigen-specific Immune Responses Based on Large-Sized Porous Silica Nanoparticles
SO ACS APPLIED MATERIALS & INTERFACES
LA English
DT Article
DE anticancer immunity; antigen depot; cancer immunotherapy; nanovaccine; silica nanoparticles
ID VACCINE; IMMUNOTHERAPY; ACTIVATION; CELLS

AB Cancer vaccine is one of the immunotherapeutic strategies aiming to effectively deliver cancer antigens to professional antigen-presenting cells such as dendritic cells (DCs), macrophages, and B cells to elicit a cancer-specific immune response. Despite the advantages of the cancer vaccine that can be applied to various cancer types, the clinical approach is limited due to the non-specific or adverse immune responses, stability, and safety issues. In this study, we report an injectable nanovaccine platform based on large-sized (similar to 350 nm) porous silica nanoparticles (PSNs). We found that large-sized PSNs, called PS3, facilitated the formation of an antigen supply depot at the site of injection so that a single injection of PSN-based nanovaccine elicited sufficient tumor-specific cell-mediated and humoral immune response. As a result, antigen-loaded PS3 induced successful tumor regression in prophylactic and therapeutic vaccination.
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FU Lemonex Inc. [LEMONEX-SN201709-3-12, LEMONEX-SN201901-3-30, LEMON-EX-SN202003-3-60]
FX Funding This work was supported by Lemonex Inc. (LEMONEX-SN201709-3-12, LEMONEX-SN201901-3-30, and LEMON-EX-SN202003-3-60) .
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NR 40
TC 0
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U1 6
U2 6
PU AMER CHEMICAL SOC
PI WASHINGTON
PA 1155 16TH ST, NW, WASHINGTON, DC 20036 USA
SN 1944-8244
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J9 ACS APPL MATER INTER
JI ACS Appl. Mater. Interfaces
PD MAR 22
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IS 11
BP 13860
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WC Nanoscience & Nanotechnology; Materials Science, Multidisciplinary
WE Science Citation Index Expanded (SCI-EXPANDED)
SC Science & Technology - Other Topics; Materials Science
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ER

PT J
AU Zhao, XY
Zhang, JT
Chen, BB
Ding, XK
Zhao, NN
Xu, FJ
AF Zhao, Xiaoyi
Zhang, Jiatong
Chen, Beibei
Ding, Xiaokang
Zhao, Nana
Xu, Fu-Jian
TI Rough Nanovaccines Boost Antitumor Immunity Through the Enhancement of Vaccination Cascade and Immunogenic Cell Death Induction
SO SMALL METHODS
LA English
DT Article; Early Access
DE cascade; immunogenic cell death; intrinsic properties; MnOx nanoparticles; nanovaccines
ID SILICA NANOPARTICLES; CANCER VACCINES; DELIVERY; IMMUNOTHERAPY
AB Nanovaccines have attracted intense interests for efficient antigen delivery and tumor-specific immunity. It is challenging to develop a more efficient and personalized nanovaccine to maximize all steps of the vaccination cascade by exploiting the intrinsic properties of nanoparticles. Here, biodegradable nanohybrids (MP) composed of manganese oxide nanoparticles and cationic polymers are synthesized to load a model antigen ovalbumin to form MPO nanovaccines. More interestingly, MPO could serve as autologous nanovaccines for personalized tumor treatment taking advantage of in situ released

tumor-associated antigens induced by immunogenic cell death (ICD). The intrinsic properties of MP nanohybrids including morphology, size, surface charge, chemical, and immunoregulatory functions are fully exploited to enhance of all steps of the cascade and induce ICD. MP nanohybrids are designed to efficiently encapsulate antigens by cationic polymers, drain to lymph nodes by appropriate size, be internalized by dendritic cells (DCs) by rough morphology, induce DC maturation through cGAS-STING pathway, and enhance lysosomal escape and antigen cross-presentation through the "proton sponge effect". The MPO nanovaccines are found to efficiently accumulate in lymph nodes and elicit robust specific T-cell immune responses to inhibit the occurrence of ovalbumin-expressing B16-OVA melanoma. Furthermore, MPO demonstrate great potential to serve as personalized cancer vaccines through the generation of autologous antigen depot through ICD induction, activation of potent antitumor immunity, and reversal of immunosuppression. This work provides a facile strategy for the construction of personalized nanovaccines by exploiting the intrinsic properties of nanohybrids.
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Kim, Byung-Soo
TI Senescent cancer cell-derived nanovesicle as a personalized therapeutic cancer vaccine
SO EXPERIMENTAL AND MOLECULAR MEDICINE
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DT Article
ID IMMUNOTHERAPY; EXOSOMES; 1ST
AB Cancer: Turning tumors into vaccinesTherapeutic vaccines derived from tumor cells could provide a personalized strategy for training the immune system to find and destroy cancer. Past efforts to develop such vaccines have been hampered by the challenge of identifying tumor-specific proteins that elicit a strong immune response. To overcome this, Byung-Soo Kim and colleagues at Seoul National University pursued a strategy in which they subjected tumor cells to chemical treatments that halted proliferation and stimulated production of immunity-activating signaling molecules. The cells were then broken up into membrane-encased fragments filled with tumor-derived biomolecules. Mice dosed with such vaccines, which carry a diverse mix of antigens, showed a potent anti-cancer response, resulting in tumor cell death and significantly improved survival. By treating cells from patient biopsies in this fashion, clinicians could potentially derive potent, individually tailored tumor vaccines.

The development of therapeutic cancer vaccines (TCVs) that provide clinical benefits is challenging mainly due to difficulties in identifying immunogenic tumor antigens and effectively inducing antitumor immunity. Furthermore, there is an urgent need for personalized TCVs because only a limited number of tumor antigens are shared among cancer patients. Several autologous nanovaccines that do not require the identification of immunogenic tumor antigens have been proposed as personalized TCVs. However, these nanovaccines generally require exogenous adjuvants (e.g., Toll-like receptor agonists) to improve vaccine immunogenicity, which raises safety concerns. Here, we present senescent cancer cell-derived nanovesicle (SCCNV) as a personalized TCV that provides patient-specific tumor antigens and improved vaccine immunogenicity without the use of exogenous adjuvants. SCCNVs are prepared by inducing senescence in cancer cells ex vivo and subsequently extruding the senescent cancer cells through nanoporous membranes. In the clinical setting, SCCNVs can be prepared from autologous cancer cells from the blood of liquid tumor patients or from tumors surgically removed from solid cancer patients. SCCNVs also contain interferon-gamma and tumor necrosis factor-alpha, which are expressed during senescence. These endogenous cytokines act as adjuvants and enhance vaccine immunogenicity, avoiding the need for exogenous adjuvants. Intradermally injected SCCNVs effectively activate dendritic cells and tumor-specific T cells and inhibit primary and metastatic tumor growth and tumor recurrence. SCCNV therapy showed an efficacy similar to that of immune checkpoint blockade (ICB) therapy and synergized with ICB. SCCNVs, which can be prepared using a simple and facile procedure, show potential as personalized TCVs.
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TI Nanotechnology for next-generation cancer immunotherapy: State of the art and future perspectives
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DE Immunotherapy; Nanotechnology; Cancer vaccine; Cancer therapy; Immunosuppressive tumor microenvironment
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AB Over the past decade, immunotherapy aiming to activate an effective antitumor immune response has ushered in a new era of cancer treatment. However, the efficacy of cancer immunotherapy is limited by low response rates and high systemic toxicity. Nanotechnology is an encouraging platform for the development of next-generation cancer immunotherapy to effectively treat advanced cancer. Nanotechnology-enabled immunotherapy has remarkable advantages, ranging from the increased bioavailability and stability of immunotherapeutic agents to the enhanced activation of immune cells and favorable safety profiles. Nanotechnology-enabled immunotherapy can target solid tumors through reprogramming or stimulating immune cells (i.e., nanovaccines); modulating the immunosuppressive tumor microenvironment; or targeting tumor cells and altering their responses to immune cells to generate effective antitumor immunity. In this Oration, I introduce the advanced strategies currently being pursued by our laboratory and other groups to improve the therapeutic efficacy of cancer immunotherapy and discuss the potential challenges and future directions.
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U2 11
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SC Chemistry; Pharmacology & Pharmacy
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PT J
AU Manna, S
Maiti, S
Shen, JJ
Weiss, A
Mulder, E
Du, WJ
Esser-Kahn, AP
AF Manna, Saikat
Maiti, Sampa
Shen, Jingjing
Weiss, Adam
Mulder, Elizabeth
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Esser-Kahn, Aaron P.
TI Nanovaccine that activates the NLRP3 inflammasome enhances tumor specific activation of anti-cancer immunity
SO BIOMATERIALS
LA English
DT Article
DE Nanovaccine; Biomaterials; Adjuvant; Inflammasome; Neoantigen therapy
ID DENDRITIC CELLS; VACCINE
AB Neoantigen cancer vaccines that target tumor specific mutations are emerging as a promising modality for cancer immunotherapy. To date, various approaches have been adopted to enhance efficacy of these therapies, but the low immunogenicity of neoantigens has hindered clinical application. To address this challenge, we developed a polymeric nanovaccine platform that activates the NLRP3 inflammasome, a key immunological signaling pathway in pathogen recognition and clearance. The nanovaccine is comprised of a poly (orthoester) scaffold engrafted with a small-molecule TLR7/8 agonist and an endosomal escape peptide that facilitates lysosomal rupture and NLRP3 inflammasome activation. Upon solvent transfer, the polymer self-assembles with neo-antigens to form similar to 50 nm nanoparticles that facilitate co-delivery to antigen-presenting cells. This polymeric activator of the inflammasome (PAI) was found to induce potent antigen-specific CD8(+) T cell responses char-acterized by IFN-gamma and GranzymeB secretion. Moreover, in combination with immune checkpoint blockade therapy, the nanovaccine stimulated robust anti-tumor immune responses against established tumors in EG.7-OVA, B16.F10, and CT-26 models. Results from our studies indicate that NLRP3 inflammasome activating nanovaccines demonstrate promise for development as a robust platform to enhance immunogenicity of neo-antigen therapies.
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PI OXFORD
PA THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND
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SC Engineering; Materials Science
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AU Zhuang, XD
Li, B
Liu, XY
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Wang, XY
Yu, M
AF Zhuang, Xiaoduan
Li, Bang
Liu, Xiaoyan
Fan, Tingting
Lan, Xinyue
Wang, Xinying
Yu, Meng
TI The colorectal cancer-specific microbiome regulation and immune response activation via an artificial biomimetic nanovaccine
SO CHEMICAL ENGINEERING JOURNAL
LA English
DT Article
DE Microbiome regulation; Biomimetic drug carrier; Drug -resistance; Tumor microenvironment; Orthotopic colorectal cancer
ID FUSOBACTERIUM-NUCLEATUM; TUMOR; PROLIFERATION; CELLS; ROS
AB The tumor microbiome has been reported to be composed of tumor-type-specific intracellular bacteria and is closely related to tumor progression and the response to anticancer therapies. Although antitumor treatments focusing on the abnormal tumor microenvironment (TME), such as anti-bacterial or TME regulatory approaches, have been shown to significantly improve antitumor efficacy, strategies that can interfere with the microbial environment to inhibit tumor growth and activate immune response are rare. Here, we have constructed an artificially modified biomimetic nanovaccine PMO for the first time using an inactivated anaerobic bacterium P. anaerobius, a colorectal cancer (CRC)-specific bacterium carrying therapeutical agents to regulate the microbial environment. The PMO could sneak into tumors due to its natural affinity to CRC, which has a particularly rich and diverse microbiome that results in therapy resistance. The PMO could not only achieve significant tumor growth suppression by precisely delivering therapeutical MnO2 and OXA to CRC tissues but also effectively prevent tumor recurrence by the cascade reaction of activating the tumor immune responses after reshaping the microbial environment. This nanovaccine has provided the tremendous clinical potential for designing new treatment strategies for drug-resistant tumors from the perspective of microbial environmental regulation and improving the prognosis of patients.
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PT J
AU Goradel, NH
Nemati, M
Bakhshandeh, A
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AF Goradel, Nasser Hashemi
Nemati, Mahnaz
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Negahdari, Babak
TI Nanovaccines for cancer immunotherapy: Focusing on complex formation between adjuvant and antigen
SO INTERNATIONAL IMMUNOPHARMACOLOGY
LA English
DT Review
DE Immunotherapy; Cancer vaccine; Nanovaccine; Nanocomplex; Immune response
ID CO-DELIVERY; ONCOLYTIC ADENOVIRUS; CELLULAR-IMMUNITY; DENDRITIC CELLS; NANOPARTICLES; VACCINE; ANTITUMOR; RECEPTOR; DNA; PROTEIN
AB As an interesting cancer immunotherapy approach, cancer vaccines have been developed to deliver tumor antigens and adjuvants to antigen-presenting cells (APCs). Although the safety and easy production shifted the vaccine designing platforms toward the subunit vaccines, their efficacy is limited due to inefficient vaccine delivery. Nanotechnology-based vaccines, called nanovaccines, address the delivery limitations through codelivery of antigens and adjuvants into lymphoid organs and APCs and their intracellular release, leading to cross-presentation of antigens and induction of potent anti-tumor immune responses. Although the nanovaccines, either as encapsulating agents or biomimetic nanoparticles, exert the desired anti-tumor activities, there is evidence that the mixing formulation to form nanocomplexes between antigens and adjuvants based on the electrostatic interactions provokes high levels of immune responses owing to Ags' availability and faster release. Here, we summarized the various platforms for developing cancer vaccines and the advantages of using delivery systems. The cancer nanovaccines, including nanoparticle-based and biomimetic-based nanovaccines, are discussed in detail. Finally, we focused on the nanocomplexes formation between antigens and adjuvants as promising cancer nanovaccine platforms.
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TC 0
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U2 12
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AF Chen, Haolin
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TI Carrier-free subunit nanovaccine amplifies immune responses against tumors and viral infections
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DT Article
DE Adjuvant; Diprovocim; Immune therapy; Nanovaccine; Subunit antigens
ID DELIVERY SYSTEMS; NANOPARTICLES; CANCER; ADJUVANTS; VACCINE
AB Codelivering subunit antigens and Toll-like receptor (TLR) molecular adjuvants via nanocarriers can stim-ulate potent innate and specific immune responses. Simple and effective nanovaccines fabrication is cru-cial for application. However, most nanovaccines were fabricated by introducing additional delivery mate-rials, increasing safety risk, cost and processing complexity. Herein, a carrier-free nanovaccine was facilely prepared using a TLR1/TLR2 adjuvant, Diprovocim, rich in benzene rings that could interact with aromatic residues in subunit antigens through pi-pi stacking without additional materials. The carrier-free

nanovac-cines with a narrow size distribution could target lymph nodes (LNs) after intravenous injection to mice. The carrier-free nanovaccines based on ovalbumin (OVA) can stimulate strong antibody titers and CD4+ and CD8+ T cell immune responses in mice, and it synergized with anti-PD1 showing a potent tumor suppression in B16F10-OVA tumor model of mice. Furthermore, the carrier-free nanovaccine with glyco-protein E (gE), a glycoprotein of the varicella-zoster virus (VZV), also showed potent humoral and cellular immune responses. Therefore, using subunit proteins to support Diprovocim by pi-pi stacking provides a new approach for the preparation and application of novel vaccines for tumor therapy and prevention of infectious diseases.Statement of significance Codelivering subunit antigens and adjuvants via nanocarriers stimulate potent innate and specific im-mune responses. However, existing delivery materials for fabricating nanovaccines will inevitably increase the cost of preparation, controllability, process complexity and safety assessment. Therefore, this study easily prepared carrier-free nanovaccines using the benzene ring-rich TLR1/TLR2 adjuvant Diprovocim, which can interact with aromatic residues in subunit antigens via pi-pi stacking without additional mate-rials. The carrier-free nanovaccines of OVA demonstrated a potent tumor inhibition in treating melanoma in combination with anti-PD1. And the nanovaccines of gE stimulated a strong antibody titer and cellular immune response for herpes zoster. Thus, the present study provides a new approach for the preparation of subunit vaccines to combat various cancers and virus infections.
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Chen, Longlong
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Shi, Xuequn
TI Facile preparation of a metal-phenolic network-based lymph node targeting nanovaccine for antitumor immunotherapy
SO ACTA BIOMATERIALIA
LA English
DT Article
DE Metal -phenolic networks; Cancer vaccine; Lymph node targeting; Cellular immune response; Chlorogenic acid; Regulatory T cells
ID CHECKPOINT; POLARIZATION; RESISTANCE; CELLS
AB Cancer vaccines are being explored for enhanced cancer immunotherapy and prophylaxis. Some of their prevailing weaknesses, however, such as complicated preparation, poor biocompatibility, and failure to elicit strong cellular immune responses, have limited their further clinical applications. Here, we reported a multifunctional nanovaccine that was prepared in a quick and simple way. During the self-assembly of metal-phenolic networks (MPNs), the antigen ovalbumin (OVA) and immunoreactive chlorogenic acid (CHA) were simultaneously loaded. Owing to its dual pH and reduction sensitivities, the nanovaccine could deliver antigens into the cytoplasm of dendritic cells (DCs) and facilitate the cross-presentation of antigens. Moreover, the results of in vivo immunization assays demonstrated that the nanovaccine signifi-cantly excited the antigen presentation of DCs and provoked a robust cellular immune response with the restrained activation of regulatory T cells (Tregs), by targeting lymph nodes and executing the function of CHA. In vivo antitumor assays indicated that the nanovaccine with good biocompatibility afforded con-spicuous cancer treatment and prevention effects. Overall, the nanovaccine presented in this study shows a promise for potentiating cancer immunotherapy by the lymph node-targeted delivery.Statement of significanceCancer nanovaccines can be used for cancer immunotherapy. However, some existing shortcomings, such as cumbersome preparation, poor biocompatibility, and failure to elicit strong immune responses, limit the clinical application of cancer nanovaccines. This study developed a multifunctional nanovaccine that was readily prepared through the self-assembly of metal-phenolic networks. The nanovaccine with dual pH and reduction sensitivities could efficiently promote the antigen lysosome escape and cross -presentation. In vivo , it efficiently delivered antigen into lymph nodes and provoked strong cellular im-mune responses, and thus it showed significant cancer immunotherapy and prevention effect.
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TI Hyaluronate decorated polyethylene glycol linked poly (lactide-co-glycolide) nanoparticles encapsulating MUC-1 peptide augmented mucosal immune response in Balb/c mice through inhalation route
SO BIOCHIMICA ET BIOPHYSICA ACTA-GENERAL SUBJECTS
LA English
DT Article
DE Non small cell lung cancer; MUC-1 peptide; Hyaluronic acid; Cellular uptake; Cytokine production; Poly (D; L-lactide-co-glycolide)
ID THERAPEUTIC CANCER VACCINES; CELL; PROTEINS; MICROPARTICLES; NANOCARRIERS; PEGYLATION; SURVIVAL; L-BLP25; GROWTH; FLUID
AB Background and objectives: NSCLC (Non-Small Cell Lung Cancer) clutches highest mortality rate in man and women globally. The present study was conducted to target MUC-1 peptide (M-1) into antigen presenting cells by cargo the peptide into hyaluronic acid decorated polyethylene glycol linked poly (D, L-lactide-co-glycolide) nanoparticles (M-1-PL-co-GA-PEG-sHA-NPs) for generating mucosal immunity through inhalation (i.h.) route. Methodology and results: The mean particle size and surface charge of M-1-PL-co-GA-PEG-sHA-NPs was measured to be 136.2 +/- 18.38-nm and -28.34 +/- 6.77-mV, respectively, prepared by non-aggregated emulsion-diffusion evaporation method. The 28.42% percentage release of M-1 peptide from M-1-PL-co-GA-PEG-NPs was observed to be at 2 h and 95.29% at 8 h while the percentage release of M-1 peptide from M-1-PL-co-GA-PEG-sHA-NPs was observed to be 26.02% at 4 h and 97.95% at 24 h that proved the prolonged release of antigen. M-1-PL-co-GA-PEG-sHA-NPs demonstrated higher ($P < 0.05$) cellular uptake of 86.2% in RAW 264.7 cells in comparison to 27.6% of M-1-PL-co-GA-PEG-NPs. In addition, M-1-PL-co-GA-PEG-sHA-NPs induced remarkably ($P < 0.05$) elevated release of 80.6-pg/ml of TNF-alpha in comparison to 5-pg/ml by culture medium and 57.9-pg/ml of TNF-alpha by M-1-PL-co-GA-PEG-NPs. Similarly, M-1-PL-co-GA-PEG-sHA-NPs persuade remarkably ($P < 0.05$) elevated release of 225-pg/ml of IL-1 beta in comparison to 47-pg/ml by culture medium and 161.9-pg/ml of IL-1 beta by M-1-PL-co-GA-PEG-NPs. M-1-PL-co-GA-PEG-sHA-NPs might have been endocytosed

through receptor mediated pathway owing to presence of sHA. Mice immunized through i.h. route with M-1-PL-co-GA-PEG-sHA-NPs induced strong ($P < 0.05$) IgA antibody titre as compared to M-1-PL-co-GA-PEG-NPs and M-1 peptide in dose-dosage regimen. Conclusion: M-1-PL-co-GA-PEG-sHA-NPs nanovaccine warrants further analysis in xenograft model of NSCLC to showcase its antitumor capability.

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TI Nasal Tumor Vaccination Protects against Lung Tumor Development by Induction of Resident Effector and Memory Anti-Tumor Immune Responses
SO PHARMACEUTICS
LA English
DT Article
DE breast cancer; lung metastasis; vaccination; immune response; nanoparticles
ID NEGATIVE BREAST-CANCER; T-CELL ANERGY; INFILTRATING LYMPHOCYTES; DENDRITIC CELLS; SURVIVAL; METASTASIS; HYPERTHERMIA; EXPRESSION; DELIVERY; DORMANCY
AB Lung metastasis is a leading cause of cancer-related deaths. Here, we show that intranasal delivery of our engineered CpG-coated tumor antigen (Tag)-encapsulated nanoparticles (NPs)-nasal nano-vaccine-significantly reduced lung colonization by intravenous challenge of an extra-pulmonary tumor. Protection against tumor-cell lung colonization was linked to the induction of localized mucosal-associated effector and resident memory T cells as well as increased bronchiolar alveolar lavage-fluid IgA and serum IgG antibody responses. The nasal nano-vaccine-induced T-cell-mediated antitumor mucosal immune response was shown to increase tumor-specific production of IFN-gamma and granzyme B by lung-derived CD8(+) T cells. These findings demonstrate that our engineered nasal nano-vaccine has the potential to be used as a prophylactic approach prior to the seeding of tumors in the lungs, and thereby prevent overt lung metastases from existing extra pulmonary tumors.
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NR 54
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TI Overcoming Suppressive Tumor Microenvironment by Vaccines in Solid Tumor
SO VACCINES
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DT Review
DE cancer vaccines; immunosuppressive TME; solid tumor; immunotherapy; nanovaccines
ID ANTITUMOR IMMUNE-RESPONSES; MESSENGER-RNA VACCINES; LAHERPAREPVEC T-VEC; HUMAN-PAPILLOMAVIRUS; DENDRITIC CELLS; CERVICAL-CANCER; GLOBAL BURDEN; DNA; IMMUNOGENICITY; IMMUNOTHERAPY
AB Conventional vaccines are widely used to boost human natural ability to defend against foreign invaders, such as bacteria and viruses. Recently, therapeutic cancer vaccines attracted the most attention for anti-cancer therapy. According to the main components, it can be divided into five types: cell, DNA, RNA, peptide, and virus-based vaccines. They mainly perform through two rationales: (1) it trains the host immune system to protect itself and effectively eradicate cancer cells; (2) these vaccines expose the immune system to molecules associated with cancer that enable the immune system to recognize and destroy cancer cells. In this review, we thoroughly summarized the potential strategies and technologies for developing cancer vaccines, which may provide critical achievements for overcoming the suppressive tumor microenvironment through vaccines in solid tumors.
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NR 95
TC 0
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TI Cancer Cell Membrane-Coated Gambogic Acid Nanoparticles for Effective Anticancer Vaccination by Activating Dendritic Cells
SO INTERNATIONAL JOURNAL OF NANOMEDICINE
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DT Article
DE cancer immunotherapy; gambogic acid; nano-vaccine; tumor immune microenvironment; colorectal cancer
AB Purpose: Recent studies have shown that traditional Chinese medicine (TCM), such as gambogic acid (GA), is involved in the regulation of tumor immune microenvironment and can be combined with other anti-tumor treatment strategies. Here, we used GA as an adjuvant to construct a nano-vaccine to improve the anti-tumor immune response of colorectal cancer (CRC). Materials and Methods: We used a previously reported two-step emulsification method to obtain poly (lactic-co-glycolic acid) /GA nanoparticles (PLGA/GA NPs), and then CT26 colon cancer cell membrane (CCM) was used to obtain CCM-PLGA/GA NPs. This novel nano-vaccine, CCM-PLGA/GA NPs, was co-synthesized with GA as an adjuvant and neoantigen provided by CT26 CCM. We further confirmed the stability, tumor targeting, and cytotoxicity of CCM-PLGA/GA NPs. The regulatory effect on the tumor immune microenvironment, the anti-tumor efficacy, and the combined anti-tumor efficacy with anti-PD-1 monoclonal Antibodies (mAbs) of this novel nano-vaccine was also detected in vivo. Results: We successfully constructed the CCM-PLGA/GA NPs. In vitro and in vivo tests showed low biological toxicity, as well as the high tumor-targeting ability of the CCM-PLGA/GA NPs. Besides, we revealed a remarkable effect of CCM-PLGA/GA NPs to activate the maturation of dendritic cells (DCs) and the formation of a positive anti-tumor immune microenvironment. Conclusion: This novel nano-vaccine constructed with GA as the adjuvant and CCM providing the tumor antigen can not only directly kill tumors by enhancing the ability of GA to target tumors, but also indirectly kill tumors by regulating tumor immune microenvironment, providing a new strategy for immunotherapy of CRC.
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Tajbakhsh, Amir
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TI Biomimetic Nanovaccines: A Novel Approach in Immunization
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DT Review
DE Biomimetic nanoparticles; nanovaccines; immunization; conventional vaccines; vaccine delivery; nano-based drug delivery system; adjuvants; cancer cell membranes
ID OUTER-MEMBRANE VESICLES; VIRUS-LIKE PARTICLES; POLYMERIC NANOPARTICLES; TARGETED THERAPY; DRUG-DELIVERY; MESSENGER-RNA; GOLD NANOPARTICLES; SUBUNIT VACCINES; IMMUNE-RESPONSE; CHOLERA-TOXIN
AB As the World Health Organization (WHO) declared, vaccines prevent an average of 2-3 million deaths yearly from diseases. However, effective prophylactic and therapeutic vaccines have yet to be developed for eradicating the deadliest diseases, viz., types of cancer, malaria, human immunodeficiency virus (HIV), and most serious microbial infections. Furthermore, scores of the existing vaccines have disadvantages, such as failure to completely stimulate the immune system, in vivo instability, high toxicity, need for the cold chain, and multiple administrations. Thus, good vaccine candidates need to be designed to elicit adaptive immune responses. In this line, the integration of sciences along with the use of various technologies has led to the emergence of a new field in vaccine production called biomimetic nanovaccines (BNVs). Given that, nanotechnology can significantly contribute to the design of such vaccines, providing them with enhanced specificity and potency. Nanoparticles (NPs) and biomimetic NPs (BNPs) are now exploited as the main carriers for drug delivery systems, especially BNPs, whose biological mimicry makes them escape the immune system and transport drugs to the desired target. The drug accordingly seeks to camouflage itself with the help of NPs and the membranes taken from cells in the human body, including red blood cells (RBCs), white blood cells (WBCs), platelets, and cancer cells, for more effective and ideal delivery. As BNPs have recently become the center of attention in vaccine design, this review deliberates on the advances in BNVs.
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ID C-TYPE LECTIN; T-CELL RESPONSES; MHC-CLASS-I; TOLL-LIKE RECEPTORS; PROLONGED ANTIGEN PRESENTATION; TARGETING DC-SIGN; DENDRITIC CELLS; STEADY-STATE; MANNOSE RECEPTOR; NANOPARTICLE VACCINES
AB In view of the severe downsides of conventional cancer therapies, the quest of developing alternative strategies still remains of critical importance. In this regard, antigen cross-presentation, usually employed by dendritic cells (DCs), has been recognized as a potential solution to overcome the present impasse in anti-cancer therapeutic strategies. It has been established that an elevated cytotoxic T lymphocyte (CTL) response against cancer cells can be achieved by targeting receptors expressed on DCs with specific ligands. Glycans are known to serve as ligands for C-type lectin receptors (CLRs) expressed on DCs, and are also known to act as a tumor-associated antigen (TAA), and, thus, can be harnessed as a potential immunotherapeutic target. In this scenario, integrating the knowledge of cross-presentation and glycan-conjugated nanovaccines can help us to develop so called 'glyco-nanovaccines' (GNVs) for targeting DCs. Here, we briefly review and analyze the potential of GNVs as the next-generation anti-tumor immunotherapy. We have compared different antigen-presenting cells (APCs) for their ability to cross-present antigens and described the potential nanocarriers for tumor antigen cross-presentation. Further, we discuss the role of glycans in targeting of DCs, the immune response due to pathogens, and imitative approaches, along with parameters, strategies, and challenges involved in cross-presentation-based GNVs for cancer immunotherapy. It is known that the effectiveness of GNVs in eradicating tumors by inducing strong CTL response in the tumor microenvironment (TME) has been largely hindered by tumor glycosylation and the expression of different lectin receptors (such as galectins) by cancer cells. Tumor glycan signatures can be sensed by a variety of lectins expressed on immune cells and mediate the immune suppression which, in turn, facilitates immune evasion. Therefore, a sound understanding of the glycan language of cancer cells, and glycan-lectin interaction between the cancer cells and immune cells, would help in strategically designing the next-generation GNVs for anti-tumor immunotherapy.
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TI Engineering Energy-Responsive Magnetic Nanomaterials to Improve the Efficacy of Dendritic Cell-Based Immunotherapy
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DT Review
DE antigen presentation; dendritic cell; immunogenic death; magnetic nanoparticles; tumor immunotherapy
ID SUPERPARAMAGNETIC IRON-OXIDE; CANCER-THERAPY; SIRNA DELIVERY; CHEMOTHERAPEUTIC-AGENTS; ANTIGEN PRESENTATION; IMMUNE-RESPONSE; BREAST-CANCER; NANOPARTICLES; HYPERTHERMIA; NANOVACCINE
AB Effective diagnosis and treatment of cancer is still a great challenge to modern medicine. The advent of immunotherapy is revolutionizing the field of cancer research while drug toxicity and low responsive rates have become the most serious concerns in current treatment regimes. Dendritic cells (DCs) are the strongest antigen-presenting immune cells and play an important role in the initiation and regulation of the immune response. They can engulf a variety of foreign substances, including cell lysates and nucleic acids, and present antigens to activate the immune system. Some nanomaterials in vitro activation systems for DCs provide new ideas for immune-related therapies for tumors. Among these, magnetic nanoparticles (MNPs) have gradually become a major focus of basic scientific research and clinical treatment due to their advantages of good biocompatibility, low toxic side effects, and high ability to respond to external stimulus. The emergence of MNPs provides a novel, safe, and effective way to enhance the anti-tumor immune response. In this review, the application of MNPs as platform materials combined with DC immunotherapy is discussed, with the intention of providing a reference for future disease immunotherapy.

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TI Bacterial outer membrane vesicle-based cancer nanovaccines
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DE Cancer; cancer vaccines; outer membrane vesicles; nanocarriers; tumor antigen
ID VIRULENCE FACTORS; VACCINE; PLATFORM; NANOPARTICLES; ASSOCIATION; MECHANISM; GROWTH
AB Tumor vaccines, a type of personalized tumor immunotherapy, have developed rapidly in recent decades. These vaccines evoke tumor antigen-specific T cells to achieve immune recognition and killing of tumor cells. Because the immunogenicity of tumor antigens alone is insufficient, immune adjuvants and nanocarriers are often required to enhance anti-tumor immune responses. At present, vaccine carrier development often integrates nanocarriers and immune adjuvants. Among them, outer membrane vesicles (OMVs) are receiving increasing attention as a delivery platform for tumor vaccines. OMVs are natural nanovesicles derived from Gram-negative bacteria, which have adjuvant function because they contain pathogen associated molecular patterns. Importantly, OMVs can be functionally modified by genetic engineering of bacteria, thus laying a foundation for applications as a delivery platform for tumor nanovaccines. This review summarizes 5 aspects of recent progress in, and future development of, OMV-based tumor nanovaccines: strain selection, heterogeneity, tumor antigen loading, immunogenicity and safety, and mass production of OMVs.
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TI PEG Spacer Length Substantially Affects Antibody-Based Nanocarrier Targeting of Dendritic Cell Subsets
SO PHARMACEUTICS
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DT Article
DE antibody functionalization; nanoparticles; nanovaccine; dendritic cell targeting; PEG
ID PROTEIN ADSORPTION; LINKER LENGTH; NANOPARTICLES; CORONA; PHARMACOKINETICS; OPSONIZATION; GENERATION; DENSITY; KEY
AB Successful cell targeting depends on the controlled positioning of cell-type-specific antibodies on the nanocarrier's (NC) surface. Uncontrolled antibody immobilization results in unintended cell uptake due to Fc-mediated cell interaction. Consequently, precise immobilization of the Fc region towards the nanocarrier surface is needed with the Fab regions staying freely accessible for antigen binding. Moreover, the antibody needs to be a certain distance from the nanocarrier surface, influencing the targeting performance after formation of the biomolecular corona. This can be achieved by using PEG linker molecules. Here we demonstrate cell type-specific targeting for dendritic cells (DC) as cellular key regulators of immune responses. However, to date, dendritic cell targeting experiments using different linker lengths still need to be conducted. Consequently, we focused on the surface modification of nanocarriers with different molecular weight PEG linkers (0.65, 2, and 5 kDa), and their ability to reduce undesired cell uptake, while achieving efficient DC targeting via covalently immobilized antibodies (stealth targeting). Our findings demonstrate that the PEG linker length significantly affects active dendritic cell targeting from cell lines (DC2.4) to primary cells (BMDCs, splenocytic conventional DCs type 1 (cDC1)). While antibody-functionalized nanocarriers with a shorter PEG length (0.65 kDa) showed the best targeting in DC2.4, a longer PEG length (5 kDa) was required to specifically accumulate in BMDCs and splenocytic cDC1. Our study highlights that these crucial aspects must be considered when targeting dendritic cell subsets, which are of great importance in the fields of cancer immunotherapy and vaccine development.
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TI Translating the Manufacture of Immunotherapeutic PLGA Nanoparticles from Lab to Industrial Scale: Process Transfer and In Vitro Testing
SO PHARMACEUTICS
LA English
DT Article
DE drug delivery; PLGA; nanoparticles; nanomedicine; scale-up manufacturing; clinical translation
AB Poly(lactic-co-glycolic acid) (PLGA) nanoparticle-based drug delivery systems are known to offer a plethora of potential therapeutic benefits. However, challenges related to large-scale manufacturing, such as the difficulty of reproducing complex formulations and high manufacturing costs, hinder their clinical and commercial development. In this context, a reliable manufacturing technique suitable for the scale-up production of nanoformulations without altering efficacy and safety profiles is highly needed. In this paper, we develop an inline sonication process and adapt it to the industrial scale production of immunomodulating PLGA nanovaccines developed using a batch sonication method at the laboratory scale. The investigated formulations contain three distinct synthetic peptides derived from the carcinogenic antigen New York Esophageal Squamous Cell Carcinoma-1 (NY-ESO-1) together with an invariant natural killer T-cell (iNKT) activator, threitolceramide-6 (IMM60). Process parameters were optimized to obtain polymeric nanovaccine formulations with a mean diameter of 150 +/- 50 nm and a polydispersity index <0.2. Formulation characteristics, including encapsulation efficiencies, release profiles and in vitro functional and toxicological profiles, are assessed and statistically compared for each formulation. Overall, scale-up formulations obtained by inline sonication method could replicate the colloidal and functional properties of the nanovaccines developed using batch sonication at the laboratory scale. Both types of formulations induced specific T-cell and iNKT cell responses in vitro without any toxicity, highlighting the suitability of the inline sonication method for the continuous scale-up of nanomedicine formulations in terms of efficacy and safety.
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Song, XiaoKai
Li, XiangRui
TI Hepatocellular carcinoma-associated antigen 59 and ADP-ribosylation factor 1 with poly (lactic-co-glycolic acid): A promising candidate as nanovaccine against haemonchosis
SO MICROBIAL PATHOGENESIS
LA English
DT Article
DE PLGA nanoparticles; Haemonchus contortus; Hc-HCA59; Hc-ARF1; Nanovaccines; Goats
ID HAEMONCHUS-CONTORTUS; EXCRETORY/SECRETORY PRODUCTS; IMMUNE-RESPONSE; ANTHELMINTIC RESISTANCE; INFECTION; NANOPARTICLES; GTPASES; DESIGN; ARF1
AB Haemonchus contortus (H. contortus) ADP-ribosylation factor 1 (Hc-ARF1) and Hepatocellular carcinomaassociated antigen 59 (Hc-HCA59) are recognized to largely regulate the immune responses of host cells. However, studies about the protective efficacy of the two molecules are poorly unknown. In this research, combinations of recombinant Hc-HCA59 (rHc-HCA59) and Hc-ARF1 (rHc-ARF1) proteins were amalgamated with poly (lactic-co-glycolic acid) (PLGA) nanoparticles adjuvant in order to investigate their protection potential against H. contortus in goats. The results demonstrated that the levels of IgG, IgA, IgE, and IL-4 were noticeably enhanced in the rHc-HCA59 and rHc-ARF1 (rHc-HCA59+rHc-ARF1) group before H. contortus thirdstage larvae (L3) challenge. After the L3 challenge, the levels of IL-17, IL-9, and TGF-beta were considerably upregulated in the rHc-HCA59+rHc-ARF1 group. In the meantime, the abomasal worm burdens and the fecal eggs were reduced by 63.2% and 69.4% respectively in the rHc-HCA59+rHc-ARF1 group. According to the studies, PLGA nanoparticles immobilized with rHc-HCA59 and

rHc-ARF1 proteins conferred partial protection and were expected to be a potential candidate for developing nano vaccines to combat goat haemonchosis.
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NR 64
TC 0
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Yang, Yan
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He, Zelai
TI Assessing the Efficacy of a Tumor Nanovaccine and Artificial Antigen Presenting Cell-Based System as a Combination Therapy in a Mouse Model of Melanoma
SO JOURNAL OF BIOMEDICAL NANOTECHNOLOGY
LA English
DT Article
DE Melanoma; Tumor Vaccine; aAPC; Immunotherapy
ID CD4(+) T-CELLS; LYSATE VACCINE; NANOPARTICLES; RESPONSES; POLYMERS
AB Tumor cell lysate (TCL)-based vaccines contain a large number of tumor-specific and related antigens, albeit at low levels, that require active transfer and presentation by antigen-presenting cells (APCs) in vivo, which stimulate a weak immune response. The artificial APC (aAPC) system presented herein is a cell-based therapeutic system that can significantly enhance the immune response compared to TCL-based vaccines. This study combines these two treatment strategies to assess their in vitro and in vivo effects. We successfully prepared TCL-poly(lactic-co-glycolic acid)-PEI (TPP) and demonstrated that it was phagocytosedIP:by203.8.109.20theAPCsO:andThu, enhanced22 Septhe2022maturation09:47:02ofDCsin vitro. The use of TPP in combination with the aAPCs resulted in better antitumor effects compared to tindividual therapies. The combination Copyright: American Sc entific Publishe rs therapy induced a higher proportion of CD4+ T, C8+ T, and TRP2180-188-specific CD8+ T cells in comparison with the Delive ed by Inge a individual therapies. Additionally, the combination therapy enhanced the in vitro proliferation activity; greater inhibited regulatory T cells; and promoted inflammatory cytokine secretion, while reduced the production of inhibitory cytokines. In conclusion, the combination therapy consisting of the TPP tumor nanovaccine and the aAPC system enabled a broader immune response and achieve better antitumor effects compared to treatment with the individual therapies.
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Lu, Changchang
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Du, Juan
Liu, Baorui
TI Advanced Pancreatic Cancer Patient Benefit From Personalized Neoantigen Nanovaccine Based Immunotherapy: A Case Report
SO FRONTIERS IN IMMUNOLOGY
LA English
DT Article
DE pancreatic cancer; neoantigen nanovaccine; immunotherapy; T-cell responses; benefit
ID SECRETING TUMOR VACCINE; TRIAL; NIVOLUMAB; SAFETY; ADENOCARCINOMA; ACTIVATION; SURVIVAL
AB Personal neoantigen vaccines are considered to be effective methods for inducing, amplifying and diversifying antitumor T cell responses. We recently conducted a clinical study that combined neoantigen nanovaccine with anti-PD-1 antibody. Here, we reported a case with a clear beneficial outcome from this treatment. We established a process that includes comprehensive identification of individual mutations, computational prediction of new epitopes, and design and manufacture of unique nanovaccines for this patient. Nanovaccine started after a relapse in third-line treatment. We assessed the patient's clinical outcome and circulating immune response. In this advanced pancreatic cancer patient, the OS associated with the vaccine treatment was 10.5 months. A peptide-specific T-cell response against 9 of the 12 vaccine peptides could be detected sequentially. Robust neoantigen-specific T cell responses were also detected by IFN-gamma ELISPOT and intracellular cytokine staining. In conclusion, sustained functional neoantigen-specific T cell therapy combined with immune checkpoint targeting may be well suited to help control progressive metastatic pancreatic cancer.
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TI Research Progress of Nanovaccine in Tumor Immunotherapy
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AB In recent years, tumor immunotherapy has become a hot spot in the field of cancer treatment. Among them, nanovaccines combining tumor vaccines and nanotechnology provide new ideas for tumor immunotherapy. Nanovaccine can realize the co-loading of vaccine and adjuvant. The intelligent nanocarriers further realize the effective targeted delivery of antigen, promote the uptake and presentation of antigen, specifically activate antigen-specific immune response and effectively kill tumor cells. This article reviews the principles, advantages, types of nano materials, and clinical efficacy of nanovaccine to provide a more reliable reference for the design of nano-vaccine in the later stage.
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AB During the last 20+ years, research into the biomedical application of nanotechnology has helped in reshaping cancer treatment. The clinical use of several passively targeted nanosystems resulted in improved quality of care for patients. However, the therapeutic efficacy of these systems is not superior to the original drugs. Moreover, despite extensive investigations into actively targeted nanocarriers, numerous barriers still remain before their successful clinical translation, including sufficient blood-stream circulation time and efficient tumor targeting. The combination of synthetic nanomaterials with biological elements (e.g., cells, cell membranes, and macromolecules) is presently the cutting-edge research in cancer nanotechnology. The features provided by the biological moieties render the particles with prolonged bloodstream circulation time and homotopic targeting to the tumor site. Moreover, cancer cell membranes serve as sources of neoantigens, useful in the formulation of nanovaccines. In this chapter, we will discuss the advantages of biohybrid nanosystems in cancer chemotherapy, immunotherapy, and combined therapy, as well as highlight their preparation methods and clinical translatability.
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