Recent Progress of Bioinspired Cell Membrane in Cancer Immunotherapy

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ABSTRACT: By modifying immune cells, immunotherapy can activate immune response to establish long-term immune memory and prevent tumor recurrence. However, their effectiveness is largely constricted by the poor immunogenicity, immune escape, and immune tolerance of the tumor. This is related to the characteristics of the tumor itself, such as genome instability and mutation. The combination of various nanocarriers with tumor immunotherapy is beneficial for overcoming the shortcomings of traditional immunotherapy. Nanocarriers coated by cell membranes can extend blood circulation time, improve ability to evade immune clearance, and enhance targeting, thus significantly enhancing the efficacy of immunotherapy and showing great potential in tumor immunotherapy. This article reviews the application research progress of different types of cell membrane–modified nanocarriers in tumor immunotherapy, immunotherapy combination therapy, and tumor vaccines, and provides prospects for future research.

KEYWORDS: Cell membrane, nanocarrier, biomimetic material, immunotherapy, tumor therapy

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Introduction

Presently, cancer remains one of the most significant factors threatening human health and is a major focus of the World Health Organization.[1] While surgery, radiation therapy (RT), and chemotherapy are still the primary clinical methods for treating tumors, their limitations, including poor targeting and obvious adverse reactions, cannot be denied. With the development of research, photothermal therapy (PTT), targeted therapy, immunotherapy, and combination therapy have gained increasing attention. Immunotherapy, in particular, has become popular as it can activate immune responses to inhibit tumor growth and establish long-term immune memory to prevent tumor recurrence.[2] Currently, immunotherapies used for tumors in the clinic include immune checkpoint inhibitors (ICBs), cytokine therapy, lymphocyte (Chimeric antigen receptor T cells, CAR-Ts) or macrophage (Chimeric antigen receptor macrophages, CAR-MS) therapy, and tumor vaccines.[3-6] It has great potential. Nevertheless, tumor immunotherapy still faces many challenges including treatment tolerance, heterogeneity of immune response, immune-related side effects, challenges of personalized therapy, continuity of the treatment and tolerance, and lack of early biomarkers. Solving these problems requires interdisciplinary research and in-depth cooperation to promote the scientific development of immunotherapy.[7] To improve the effectiveness of tumor immunotherapy and minimize the side effects, cell membrane–modified nanocarriers have emerged as a research hotspot owing to their favorable biocompatibility and low immunogenicity. Modification of nanocarriers by the internal cell membrane of the body can effectively retain their inherent advantages.

Cell membrane–modified nanocarriers exhibit immense potential for tumor immunotherapy. The cell membranes that can be used to modify nanocarriers include red blood cell membranes (RMs), blood platelet (PLT) membranes (PLTMs), white blood cell (WBC) membranes, tumor cell membranes, bacterial membranes, stem cell membranes, and hybrid fusion cell (FC) membranes. Each type of cell membrane has unique biological functions, yielding diversified functionalities of membrane-modified nanocarriers. For example, the nanocarriers can have a prolonged blood circulation time, improved ability to evade immune clearance, enhanced targeting, and other functions. Moreover, various inorganic or organic materials, such as silica nanoparticles (NPs), polymer NPs, melanin, and magnetic NPs, can serve as the inner core of the membrane coating (Figure 1).[8] The reasonably designed nanocarrier is more controllable and flexible, providing a novel platform for treating tumors. This review summarizes the research progress and applications of cell membrane–modified nanocarriers in tumor immunotherapy.

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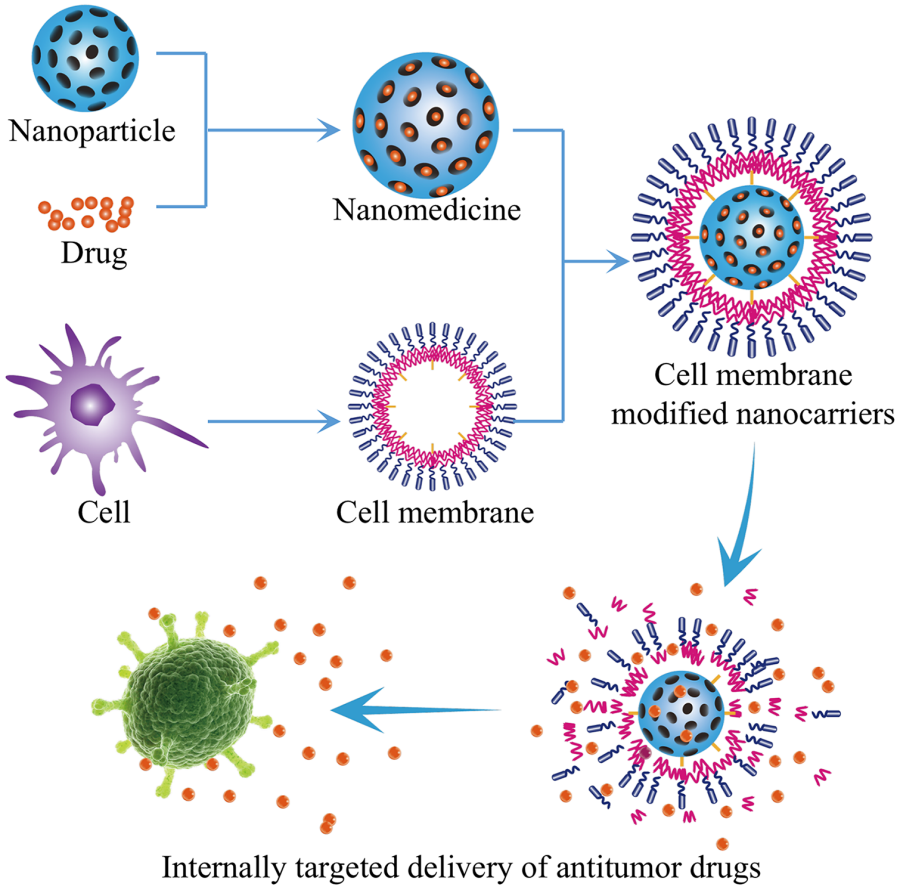

Figure 1. Schematic illustration of the preparation of cell membrane–coated nanocarriers. This typically involves the preparation of nanocomplex and membrane isolation followed by encapsulation of various types of nanocarrier cores with the membrane for cancer treatment.

Application of Cell Membrane

Red blood cell membrane–modified nanocarrier

Red blood cells (RBCs) are the most abundant cells in the blood and are responsible for oxygen transportation. Red blood cell membranes (RMs) have been widely used as surface modifications for drug carriers and are among the most established surface modification strategies.[9] The most remarkable feature of RMs is long-term circulation ability which is ascribed to the existence of special surface markers, such as cluster of differentiation 58 (CD58), CD59, and CD47 and their inherent physiological characteristics, providing the characteristics of immune evasion, flexibility, and high biocompatibility.[10-12] As a result, nanocarriers modified with RMs manifest excellent development prospects.

To enhance immunosuppression in the tumor microenvironment (TME) and increase tumor-infiltrating lymphocytes (TILs), Yang et al[13] modified nitric oxide poly (acrylamide-co-acrylonitrile-co-vinylimidazole)-S-nitrosothiols (PAAV-SNO) polymer that contains a near-infrared II (NIR-II) photothermal agent (IR1061) and the indoleamine 2,3-dioxygenase 1 (IDO-1) inhibitor 1-methyl-tryptophan (1-MT) using RMs. Through the combination of biomimetic red cell technology, PTT, and immunotherapy, the recruitment of $CD8^+$ cytotoxic T lymphocytes (CTLs) at tumor sites and the normalization of blood vessels were achieved, resulting in favorable curative outcomes for primary and metastatic breast cancer. In another work, Liang et al[14] developed a biomimetic formulation, black phosphorus quantum dot-RM nanovesicle (BPQD-RMNV) containing biomimetic BPQDs coated with RMs. The combination of BPQD-RMNV-mediated PTT with programmed cell death protein 1 (PD-1) antibody programmed cell death protein 1 (aPD-1) effectively inhibited the growth of basal-like breast tumors. In addition, RM-modified nanocarriers can also be used in combination with chemotherapy and immunotherapy for tumor treatment. For example, Song et al[15] investigated RM-based nano gel (hydroxypropyl-β-cyclodextrin acrylate and 2 opposite-charged chitosan derivatives) containing paclitaxel, which demonstrated a significant enhancement in antitumor activity. To address the problem of systemic and thermal toxicities, Ou et al[16] designed a nano-therapy system consisting of a poly-L-histidine (H)-grafted black phosphorus (BP) base core and an erythrocyte membrane (EM) shell (Figure 2A). This nanosystem containing an Ephrin-A2 receptor-specific peptide, interleukin (IL)-1α–silencing small interfering RNA, and paclitaxel provided an intelligent carrier for the combined treatment of tumors.

Tumor vaccine is one of the highly concerned focus nowadays. To improve dendritic cell (DC) targeting and antigen presentation efficiency, Guo et al[19] developed a PLGA NP wrapped by

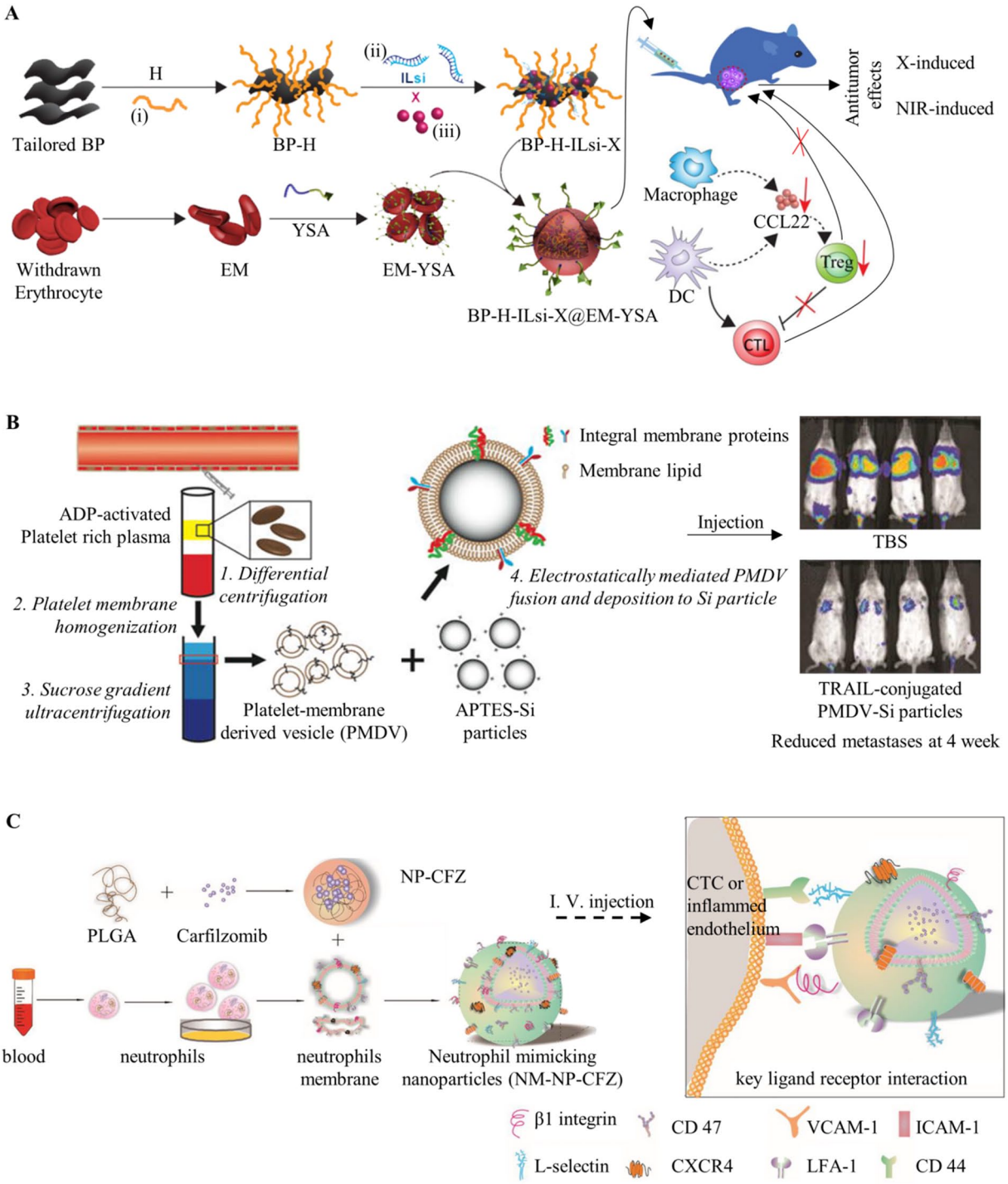

Figure 2. Application of blood cell for membrane-functionalized particles. (A). Schematic presentation of BP-H-ILsi-X@EM-YSA nanosystems using RBC. An intelligent all-in-one nanosystem was prepared using an ephrin-A2 receptor-specific peptide (YSA, targeting cancer cells) anchored EM as the "shell." The "core" contained (1) poly-L-histidine (H) grafted tailored BP as the near-infrared-stimulus core, (2) IL-1α–silencing small interfering RNA (ILsi) that abrogated IL expression resulting in restricted C-C motif chemokine ligand 22 (CCL22) secretion, and Treg cell accumulation to induce antitumor immune response, and (3) paclitaxel (X) that induced therapeutic effects. Adopted and revised with permission from Ou et al.[16] (B) Functionalization and characterization of PLTM-derived vesicle (PMDV)-coated Si particles (a) Schematic of preparing PLTM-coated Si particles. Longitudinal bioluminescence imaging at week 4 following injection detected reduced lung metastases in the experimental group compared with tris-buffered saline (TBS). Revised and reproduced with permission from Li et al.[17] (C) Illustration of neutrophil membrane–coated poly (lactic-co-glycolic acid) (PLGA) NPs loaded with carfilzomib (NM-NP-CFZ). NM-NP-CFZ was synthesized to target circulating tumor cell (CTC) in circulation and inflamed endothelial cells in the metastatic lesion where the interaction of (Leukocyte Function-associated Antigen-1) LFA-1 with intercellular cell adhesion molecule-1 (ICAM-1), CD44 with L-selectin, and β1 integrin with vascular cell adhesion molecule-1 (VCAM-1) was involved in the targeting and subsequent effect. Adopted and revised with permission from Kang et al.[18]

RM as a nano-vaccine. The research findings showed that the nano-vaccine could inhibit metastasis and prevent melanoma. In addition, the nano-vaccine augmented interferon-γ (IFN-γ) secretion and $CD8^+$ T-cell response. In another study, Reuven et al[20] designed an active cancer vaccine with anti-N-glycolylneuraminic acid (Neu5GC) antibodies loaded on RMs, which was experimentally proved to induce the production of anti-Neu5Gc IgG antibodies in mice and inhibit tumor growth.

Platelet membrane–modified nanocarrier

Platelets are small, irregularly shaped cells released by the mature megakaryocytes during cytoplasmic fragmentation in the bone marrow and are extremely important for the hemostatic function of the body. Due to the presence of CD47 protein and P-selectin on PLTMs,[21] nanocarriers modified with PLTMs can not only prolong blood circulation time and escape immune clearance but also have the ability of active targeting,[22] thereby, playing an important role in antitumor metastasis. There are associated antigens and functional proteins on PLTs, they are associated with immune defense and targeting of damaged vascular systems, while also responding to invasive microorganisms.[23] Given the above advantages, PLTM-modified nanocarriers are a promising targeted therapy for tumors.

Circulating tumor cells spread through the blood, causing tumor metastasis of distant organs. Circulating tumor cells exhibit distinct characteristics compared with the TME of solid tumors. Inspired by this, Li and co-workers synthesized activated PLTM-functionalized silica particles and bound the cancer-specific tumor necrosis factor-related (TNF-related) apoptosis-inducing ligand (TRAIL) on the surface (Figure 2B).[17] Although CTCs are protected by activated PLTs and fibrin deposition in blood circulation to avoid immune attacks, a nanocarrier disguised with PLTMs can transport anti-cancer drugs directly to CTC thrombosis. Furthermore, TRAIL offers the advantage of inducing apoptosis in cancer cells while presenting low toxicity to normal cells.[24,25] Mouse breast cancer experiments demonstrated that the nanocarriers were effective in reducing lung metastasis. Hu and co-workers developed PLGA NPs based on PLTM modification and loaded docetaxel in them.[26] Besides avoiding immune attacks and inhibiting tumor growth, the nanodrug delivery system was capable of reducing the damage caused by free docetaxel to blood vessels. Similarly, Wang designed porous NPs using PLTMs that were demonstrated to be more effective in tumor growth inhibition compared with bufalin preparations.[21] These findings suggest PLTMs as exceptionally promising materials in the preparation of tumor nano-vaccines.

White blood cell membrane–modified nanocarrier

White blood cells are a crucial part of the body's innate immune system that resists pathogen invasion.[27] These cells are not only found in blood and lymphatic vessels but also widely distributed throughout various tissues. White blood cell can be classified into 3 main categories based on their morphology, function, and location of origin: granulocyte, monocyte, and lymphocyte. Examples include macrophages, neutrophils, T lymphocytes, and natural killer cells. Tumors are often present in an inflammatory microenvironment, which can cause the tumor cells to overexpress various inflammatory factors. This, in turn, recruits various immune cells to the tumor site, although EM and PLTM-modified nanocarriers showed excellent performance in evading reticuloendothelium-mediated uptake and immune recognition monitoring. The immune cell membrane has specific surface markers (a variety of specific proteins and sugars), which makes the immune cell membrane unique functions. Therefore, it is of great research value to use different immune cells to build nanocarriers.

Macrophages are vital components of the human immune system and are widely distributed in the blood and tissues throughout the body. They function for identifying, engulfing, and eliminating foreign bodies such as bacteria and viruses.[28] Macrophage membrane–coated nanocarriers can play an important role in inducing both innate and acquired immune responses. For instance, Cao et al[29] developed macrophage membrane–modified EMTANSINE liposomes, which can improve the efficiency of drug delivery and significantly inhibit breast cancer lung metastasis. In addition, Zhang reported a NP (CSKC-PPIP/PTX@MA) wrapped in macrophage membrane that can control drug release step by step.[30] To better meet clinical needs, Liu et al[31] designed a macrophage membrane–covered laser-response variable nano-pharmaceutical (I-P@NPS@M) with good permeability, retention, and targeting. Advantageous properties, including good biocompatibility and immunomodulatory effects, make macrophages a promising material for the development of tumor vaccines. To optimize the immune response and minimize potential side effects of dendrobium devonianum polygonatum (DP), Zhang et al[32] developed a novel tumor vaccine by coating PLGA NPs (PLGA-DP/Ovalbumin (OVA)) with macrophage membranes, which demonstrated to effectively activate the immune response in mice. In addition, M1 macrophage membrane coating has better tumor-targeting ability. For example, the M1-macrophage cell-coated NPs ([C/I] BP@B-A(D)&M1 m) constructed by Hu et al,[33] can effectively inhibit the recurrence and metastasis of primary tumors, and are characterized by laser response, variable size, on-demand drug release, and prolonged circulation retention.

The DC membranes play a crucial role in antigen presentation and can specifically activate memory T cells and primary T cells. In addition, DCs are capable of releasing a wide range of cytokines, including costimulatory and adhesion molecules, which promote the interaction between DCs and T cells to regulate the adaptive immune response of the body.[34,35] In recent years, the DC tumor vaccine has made significant progress in prostate cancer and recurrent ovarian cancer.[36-39] Compared with the traditional DC vaccine, the "mini DC" vaccine prepared by the co-extrusion method is more clinically feasible.[40] Cheng et al used PLGA NPs loaded with IL-2 and

encapsulated with DC membrane. *In vivo* and *in vitro* experiments have demonstrated that this vaccine can effectively inhibit the growth and metastasis of ovarian cancer and activate the immune response of the entire body. Besides, it is easy to store and has a long shelf life.

As a host's first line of defense against invading pathogens, neutrophils are the most abundant type of granulocyte.[41] Neutrophils play a central role in the acute inflammatory phase. They can also target CTCs.[42] In the TME, neutrophils can interact with metastatic tumors and CTC through intercellular adhesion molecules.[43] Based on this property, Kang et al[18] designed neutrophil-coated PLGA NPs (NM-NP) that showed a profound cell binding affinity *in vitro* and CTC capture efficiency *in vivo* (Figure 2C). Interestingly, CFZ loaded by NM-NP could kill CTCs in the circulatory system and prevent early metastasis of tumor cells. Thus, nanocarriers based on neutrophil membrane can prevent tumor metastasis through a variety of different mechanisms.

Both T cells and NK cells are lymphocytes. First, T cells are an important type of lymphocyte with tumor-specific recognition ability and immune response, making them potentially applicable in cancer treatment. Given the limitations of traditional treatments, Ma et al[44] have constructed a new nanodrug delivery system that involves IR780-loaded mesoporous silica NPs coated with CAR-T cell membrane which specifically recognized Glypican-3 (GPC3) protein on the surface of liver cancer cells. This new drug delivery system has better immune targeting and photothermal antitumor ability. Due to the mutagenicity, heterogeneity, and immune escape of tumor cells, the dual-targeting strategy is more advantageous. Researchers constructed indocyanine green nanoparticles.[45] Next, natural killer (NK) cells are the most cytotoxic cells and can directly kill tumor cells.[46] They possess a variety of protein receptors including NKp46, CD226, and NKG2D, among others, that enable them to recognize and kill tumors.[34] Cai et al designed an allergy agent the 4,4′,4″,4‴-(porphine-5,10,15,20-tetrayl) tetrakis (benzoic acid) (TCPP) NPs coated with NK cell membrane (NK-NPs).[47] Nanoparticles coated with NK cell membrane can polarize M1 macrophages and produce an antitumor effect. In addition, after laser irradiation, NK-NPs can effectively inhibit tumor development and metastasis.

Moreover, nanocarriers can also be prepared using membranes from other important immune cells such as bone marrow–derived suppressor cells (MDSCs) and bone marrow–derived macrophages (BMDMs).[48,49] These novel approaches offer promising immunotherapeutic options for treating tumors.

Cancer cell membrane–modified nanocarrier

In recent years, tumor cells have become a major focus of research due to their distinctive characteristics. First, tumor cells are relatively easy to expand *in vitro* to obtain cell membranes. Second, tumor cell membranes can play important roles in immune activation, immune escape, and prolonging blood circulation time.[50] Finally, tumor cell membranes also have unique homologous binding properties.[50,51] These functions are primarily attributed to the surface proteins of tumor cell membranes, including N-cadherin, epithelial cell adhesion molecule (EpCAM), and galactose lectin-3.[52-55] Therefore, cancer cell membranes are a promising modification material for antitumor immunotherapy. When modified by tumor cell membranes, the carrier can not only promote immune response, targeted aggregation, and drug delivery but also has substantial potential in developing personalized tumor vaccines.

The tumor cell membrane can be modified by combining membrane core structure usually with various organic or inorganic materials, such as magnetic iron oxide nanoparticles (MNPs),[56] silica NPs (Figure 3A),[57,58] and PLGA NPs.[59-61] For example, B16-F10 cancer cell membrane–modified PLGA nanoparticles (CCNPs) can effectively deliver tumor-associated antigens to immune cells for processing and subsequent antigen-specific T-cell stimulation.[60] Similarly, it was demonstrated that PLGA NP coated with cancer cell membrane fractions (CCMFs) that contain intact membrane-associated proteins, including C-X-C chemokine receptor type 4 (CXCR4) and CD44, can reduce the migration and metastasis of tumor cells. These CCMF-PLGA NPs were capable of migrating to nearby lymph nodes and enhancing the percentage of $CD8^+$ and $CD4^+$ cytotoxic T-lymphocyte populations in the spleen and lymph nodes of immunized mice.[59] In addition, these nanocarriers showed the homologous targeting of cancer cells.

For most vaccines, immune adjuvants substantially enhance the immune response. Hence, when an adjuvant is injected into the body along with the antigen, it can significantly boost the immune response to the antigen. Currently, aluminum salt and Toll-like receptors (TLR) agonists, such as monophosphoryl lipid A (MPLA), CpG oligonucleotides, and R837, are the main clinically used immune adjuvants.[51,61-66] For the first time, PLGA NPs were loaded with immune adjuvant R837 and then coated with mannose-modified tumor cell membranes to prepare nano-vaccines (NP-R@M-M).[61] The resulting nano-vaccines facilitated the maturation of DCs and triggered an immune response. Similarly, the immunoadjuvant CpG can also promote the maturation of antigen-presenting cells. For instance, Kroll et al developed a novel nano-vaccine (CpG-CCNPs) by coating CpG-loaded PLGA nuclei (CpG-NPs) with B16-F10 mouse melanoma cell membrane. Nevertheless, several tumor vaccines that do not contain immune adjuvants have also demonstrated remarkable antitumor effects.[67,68] Personalized tumor vaccine has emerged as a promising area of research aimed at overcoming the limitations of low antigen immunogenicity and weak immune response. A personalized photothermal vaccine (Gel-BPQD-CCNVs) was prepared

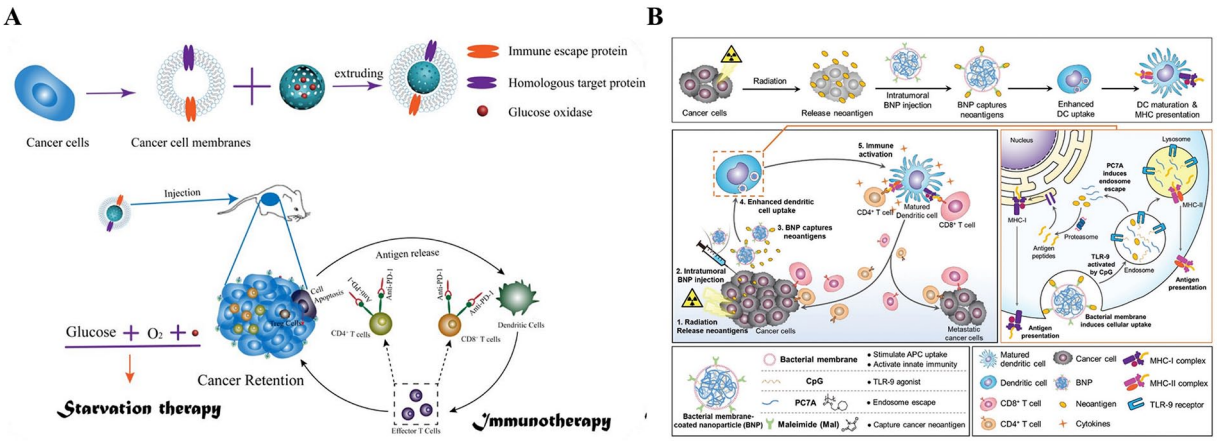

Figure 3. Application of tumor cell and bacterial for membrane-functionalized particles. (A) Schematic diagram of CMSN-Gox inducing antitumor immune response and enhancing anti-PD-1 immunotherapy. Adopted and revised with permission from Xie et al.[58] (B) Schematic diagram of *in situ* vaccine induced by bacterial membrane–coated nanoparticles (BNPs) combined with RT. Diagram of how BNP interacts with TME to enhance antigen presenting cell (APC) uptake and activation. Schematic diagram of *in situ* vaccine induced by BNP in combination with RT. The composition and the function of each component of BNP. Adopted and revised with permission from Patel et al.[62]

from the surgically removed tumor, which effectively activated DCs.[69] Furthermore, in combination with ICBs, photodynamic therapy, and "starvation therapy," the nanocarriers demonstrated complementary advantages and achieved better therapeutic outcomes.[57,58,61,64,65,68-70]

Bacterial membrane–modified nanocarrier

Bacterial membrane–modified nanocarriers have the characteristics of immune stimulation, prolonging cycle time, and tumor imaging.[71] The bacterial membrane-coated nanoparticles (BNPs) have also been employed in targeted drug delivery systems for antitumor therapy, as a wide range of bacterial-related membrane components can be used for immune stimulation or tumor-specific enrichment. Moreover, bacterial-mediated nanocarriers can migrate toward hypoxic tumor environments.[72] To enhance the immune response following systemic radiation therapy (RT) in immunologically "cold" tumors, Patel et al developed a BNP containing immune-activating PC7A/CpG polyplex. They extracted the bacterial membrane from a non-pathogenic strain (mycobacterium minor), which exhibited strong immunogenicity (Figure 3B).[62] After RT, BNP can capture cancer neoantigens, improve DC uptake, and promote antitumor T-cell responses. In addition, tumor immunotherapeutic agents constructed by using outer membrane vesicles of gram-negative bacteria exhibited promising potential in eradicating tumors with low toxicity.[73]

Hybrid cell membranes modified nanocarrier

The membranes of different types of cells have specific characteristics. The fusion of cell membranes is one of the simple and effective approaches to increasing the function of nanocarriers.[74] For example, when erythrocyte and PLTMs are fused, the protein marker molecules of the 2 membranes (CD235a, CD41, CD61, and CD44) remain on them.[22] Subsequently, Liu et al[75] proposed the concept of using DCs and tumor cell–derived FC bio-recombinant membranes (FM) for modifying tumor nano-vaccines. This offers a personalized treatment option for various tumors. In addition, various other types of membrane fusions are also reported, including tumor cell-Lactobacillus membrane, erythrocyte-cancer cell membrane, macrophage-tumor cell membrane, and multiple cell membrane fusion.[76-79] Consequently, FC membrane presents a promising technical advancement for the development of a multi-functional bionic drug delivery platform.

Other types of cell membranes modified nanocarrier

Stem cells are pluripotent cells with low immunogenicity and self-replicating ability that can target tumor cells, such as mesenchymal stem cells (MSCs), neural stem cells, and hematopoietic stem cells.[80] Nanocarriers modified by different types of stem cells can target different types of tumor cells. Moreover, MSC membranes possess a variety of receptors including cytokine receptors, growth factor receptors, cell-matrix receptors, chemokine receptors, and cell-cell interaction receptors.[81,82] To improve drug delivery efficiency and reduce the risk of vascular adverse reactions, Gao et al[83] developed a nanodelivery system (SCMGs) for mesenchymal dry cell membrane–modified gelatin nano gels. This system maintained the biological function and stability of dry cell membranes.

Clinical Application of Bionic Cell Membrane

Bionic membrane nanodelivery systems have become a pioneering technology in drug delivery, especially in the field of tumor immunotherapy. This innovative approach uses the properties of bionic membranes to precisely deliver therapeutic agents to target tissues or cells. In addition, it improves therapeutic efficacy while minimizing toxic side effects. In the specific clinical application of tumor immunotherapy, the bionic

membrane nanodelivery system demonstrates unique advantages: (1) drug delivery to the intratumoral TME: changes occurring within the TME, in addition to contributing to cancer immune escape.[84,85] It also affects the effectiveness of immunotherapy.[86,87] Potential in modulating the TME and enhancing immune cell activity is to improve the efficacy of tumor therapy. The bionic membrane nanodrug delivery system allows for more precise delivery of immune drugs to the immune microenvironment within the tumor by adjusting the properties of the NPs. This includes the lymph nodes, tumor mesenchyme, and other key immune sites within the tumor. Improve the effectiveness of the drug's action in the immune system. (2) Enhance immune cell infiltration into the tumor: The bionic membrane nanodrug delivery system can piggyback on immunomodulators. By adjusting the activity of immune cells, it prompts them to cross the tumor resistance barrier more effectively and increase the infiltration and killing effect on tumor cells.[88] (3) Precise release of immunostimulants: The nanodelivery system has the ability to release drugs under specific conditions. This makes it possible to release the immunostimulant when the immune cells come into contact with the tumor cells, improving the local effect of the treatment and avoiding the side effects caused by over-activation of the immune system.[89] (4) Individualized treatment strategy: Bionic membrane nanodrug delivery system can be individually adjusted according to the patient's tumor characteristics and immune status, and the treatment plan that best suits the patient's condition can be selected. This helps to improve the relevance and effectiveness of the treatment. (5) Multi-modal therapy: The system can be used not only for traditional immunotherapy but also combined with other treatment modalities such as radiotherapy and chemotherapy to form a multi-modal treatment strategy.[90] The comprehensive effect of the treatment can be further improved. (6) Interestingly, due to the preservation of the structure and function of the membrane, it can also be used for the diagnosis of clinical diseases.[91]

Although the bionic cell membrane has shown great advantages, but *in vitro* cell experiments, animal experiments, and other laboratory stage of research. Few have entered clinical trials. Among them, nanomimetic vaccines have high clinical translational significance. Sipuleucel-T is the first clinically approved cancer vaccine. It is able to prolong the survival of prostate cancer. There are also DC-derived exosomes that have been validated in clinical trials, like Dex.[84,92,93] Dex has been validated for its safety in advanced colorectal cancer, metastatic melanoma, and advanced non-small-cell lung cancer (NSCLC) in phase I clinical trials. In addition, there are many types of cell-derived cancer vaccines being tested in Phase I/II/III clinical trials with excellent translational potential.[94]

Conclusions and Prospect

With the continued progress of research, the options for intervention strategies for cancer are increasing. Immunotherapy will be an important research direction of antitumor therapy in the future. Numerous challenges are posed by tumor immunotherapy, such as immune tolerance, immune avoidance, and immunosuppression. In this regard, cell membrane–modified nanocarriers demonstrate important potential applications. These natural biofilms can evade the body's clearance mechanisms, overcome physiological barriers, and enable the nanocarrier to actively target and penetrate the tumor site. Moreover, the use of different nanomaterials and biofilms in a flexible combination allows personalized cancer treatment.

Despite the development and proven efficacy of numerous nanodrugs and nano-vaccines, translation from basic research to clinical trials has been challenging. Most studies have been confined to *in vitro* and mouse *in vivo* experiments. Primarily due to several challenges, only a handful of nano-vaccines have been approved by the US Food and Drug Administration. First of all, many technologies involved in cell membrane extraction and purification, characterization, and specific protein selection are still under development at this stage. Second, unlike tumor cells that multiply indefinitely outside the body, some cells are short-lived and difficult to obtain. Finally, the selection of nanomaterials requires consideration of charge, particle size, composition, antigen-carrying capacity, and interaction with body tissues. In conclusion, cell membrane–modified nanocarriers are in their infancy, but have a bright future in tumor therapy. To enable experimental clinical applications, it is essential to strengthen basic research, overcome technical challenges, and ensure quality and yield.

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Author Contributions

MZ, YW, and ZS contributed to article preparation. YL, HZ, and YW prepared the figures and tables. PL and YL revised the article. All authors approved the version of the article to be published.

Availability of Data and Materials

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REFERENCES

1. Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. *CA Cancer J Clin*. 2023;73:17-48. doi:10.3322/caac.21763
2. Mellman I, Coukos G, Dranoff G. Cancer immunotherapy comes of age. *Nature*. 2011;480:480-489. doi:10.1038/nature10673
3. Topalian SL, Drake CG, Pardoll DM. Immune checkpoint blockade: a common denominator approach to cancer therapy. *Cancer Cell*. 2015;27:450-461. doi:10.1016/j.ccell.2015.03.001
4. Garbers C, Heink S, Korn T, Rose-John S. Interleukin-6: designing specific therapeutics for a complex cytokine. *Nat Rev Drug Discov*. 2018;17:395-412. doi:10.1038/nrd.2018.45

5. Klichinsky M, Ruella M, Shestova O, et al. Human chimeric antigen receptor macrophages for cancer immunotherapy. *Nat Biotechnol*. 2020;38:947-953. doi:10.1038/s41587-020-0462-y
6. Meng Z, Zhang Y, Zhou X, Ji J, Liu Z. Nanovaccines with cell-derived components for cancer immunotherapy. *Adv Drug Deliv Rev*. 2022;182:114107. doi:10.1016/j.addr.2021.114107
7. O'Donnell JS, Teng MWL, Smyth MJ. Cancer immunoediting and resistance to T cell-based immunotherapy. *Nat Rev Clin Oncol*. 2019;16:151-167. doi:10.1038/s41571-018
8. Liu R, Luo C, Pang Z, et al. Advances of nanoparticles as drug delivery systems for disease diagnosis and treatment. *Chin Chem Lett*. 2023;34:107518. doi:10.1016/j.cclet.2022.05.032
9. Hu CM, Fang RH, Zhang L. Erythrocyte-inspired delivery systems. *Adv Healthc Mater*. 2012;1:537-547. doi:10.1002/adhm.201200138
10. Zhao YZ, Jia J, Li YB, Guo CX, Zhou XQ, Sun ZW. Effects of endosulfan on the immune function of erythrocytes, and potential protection by testosterone propionate. *J Toxicol Sci*. 2014;39:701-710. doi:10.2131/jts.39.701
11. Davis RM, Campbell JL, Burkitt S, et al. A Raman imaging approach using CD47 antibody-labeled SERS nanoparticles for identifying breast cancer and its potential to guide surgical resection. *Nanomaterials (Basel)*. 2018;8:953. doi:10.3390/nano8110953
12. Kulkarni A, Chandrasekar V, Natarajan SK, et al. A designer self-assembled supramolecule amplifies macrophage immune responses against aggressive cancer. *Nat Biomed Eng*. 2018;2:589-599. doi:10.1038/s41551-018
13. Yang Z, Gao D, Guo X, et al. Fighting immune cold and reprogramming immunosuppressive tumor microenvironment with red blood cell membrane-camouflaged nanobullets. *ACS Nano*. 2020;14:17442-17457. doi:10.1021/acsnano.0c07721
14. Liang X, Ye X, Wang C, et al. Photothermal cancer immunotherapy by erythrocyte membrane-coated black phosphorus formulation. *J Control Release*. 2019;296:150-161. doi:10.1016/j.jconrel.2019.01.027
15. Song Q, Yin Y, Shang L, et al. Tumor microenvironment responsive nanogel for the combinatorial antitumor effect of chemotherapy and immunotherapy. *Nano Lett*. 2017;17:6366-6375. doi:10.1021/acs.nanolett.7b03186
16. Ou W, Byeon JH, Soe ZC, et al. Tailored black phosphorus for erythrocyte membrane nanocloaking with interleukin-1alpha siRNA and paclitaxel for targeted, durable, and mild combination cancer therapy. *Theranostics*. 2019;9:6780-6796. doi:10.7150/thno.37123
17. Li J, Ai Y, Wang L, et al. Targeted drug delivery to circulating tumor cells via platelet membrane-functionalized particles. *Biomaterials*. 2016;76:52-65. doi:10.1016/j.biomaterials.2015.10.046
18. Kang T, Zhu Q, Wei D, et al. Nanoparticles coated with neutrophil membranes can effectively treat cancer metastasis. ACS Nano. 2017;11:1397-1411. doi:10.1021/acsnano.6b06477
19. Guo Y, Wang D, Song Q, et al. Erythrocyte membrane-enveloped polymeric nanoparticles as nanovaccine for induction of antitumor immunity against melanoma. *ACS Nano*. 2015;9:6918-6933.
20. Reuven EM, Leviatan Ben-Arye S, Yu H, et al. Biomimetic glyconanoparticle vaccine for cancer immunotherapy. *ACS Nano*. 2019;13:2936-2947. doi:10.1021/acsnano.8b07241
21. Wang H, Wu J, Williams GR, et al. Platelet-membrane-biomimetic nanoparticles for targeted antitumor drug delivery. *J Nanobiotechnology*. 2019;17:60. doi:10.1186/s12951-019
22. Dehaini D, Wei X, Fang RH, et al. Erythrocyte-platelet hybrid membrane coating for enhanced nanoparticle functionalization. Adv Mater. 2017;29:1606209. doi:10.1002/adma.201606209
23. Labelle M, Begum S, Hynes RO. Platelets guide the formation of early metastatic niches. *Proc Natl Acad Sci USA*. 2014;111:E3053-E3061. doi:10.1073/pnas.1411082111
24. von Karstedt S, Montinaro A, Walczak H. Exploring the TRAILs less travelled: TRAIL in cancer biology and therapy. *Nat Rev Cancer*. 2017;17:352-366. doi:10.1038/nrc.2017.28
25. Alizadeh Zeinabad H, Szegezdi E. TRAIL in the treatment of cancer: from soluble cytokine to nanosystems. *Cancers (Basel)*. 2022;14:5125. doi:10.3390/cancers14205125
26. Hu CM, Fang RH, Wang KC, et al. Nanoparticle biointerfacing by platelet membrane cloaking. *Nature*. 2015;526:118-121. doi:10.1038/nature15373
27. Zeng Z, Pu K. Improving cancer immunotherapy by cell membrane-camouflaged nanoparticles. *Adv Funct Mater*. 2020;30:2004397. doi:10.1002/adfm.202004397
28. Shapouri-Moghaddam A, Mohammadian S, Vazini H, et al. Macrophage plasticity, polarization, and function in health and disease. *J Cell Physiol*. 2018;233:6425-6440. doi:10.1002/jcp.26429
29. Cao H, Dan Z, He X, et al. Liposomes coated with isolated macrophage membrane can target lung metastasis of breast cancer. *ACS Nano*. 2016;10:7738-7748. doi:10.1021/acsnano.6b03148
30. Zhang Y, Cai K, Li C, et al. Macrophage-membrane-coated nanoparticles for tumor-targeted chemotherapy. *Nano Lett*. 2018;18:1908-1915. doi:10.1021/acs.nanolett.7b05263
31. Liu R, An Y, Jia W, et al. Macrophage-mimic shape changeable nanomedicine retained in tumor for multimodal therapy of breast cancer. *J Control Release*. 2020;321:589-601. doi:10.1016/j.jconrel.2020.02.043
32. Zhang Z, Li D, Li X, et al. PEI-modified macrophage cell membrane-coated PLGA nanoparticles encapsulating Dendrobium polysaccharides as a vaccine delivery system for ovalbumin to improve immune responses. *Int J Biol Macromol*. 2020;165:239-248. doi:10.1016/j.ijbiomac.2020.09.187
33. Hu C, Lei T, Wang Y, et al. Phagocyte-membrane-coated and laser-responsive nanoparticles control primary and metastatic cancer by inducing anti-tumor immunity. *Biomaterials*. 2020;255:120159. doi:10.1016/j.biomaterials.2020.120159
34. Gong P, Wang Y, Zhang P, et al. Immunocyte membrane-coated nanoparticles for cancer immunotherapy. *Cancers (Basel)*. 2020;13:77. doi:10.3390/cancers13010077
35. Oroojalian F, Beygi M, Baradaran B, Mokhtarzadeh A, Shahbazi MA. Immune cell membrane-coated biomimetic nanoparticles for targeted cancer therapy. *Small*. 2021;17:e2006484. doi:10.1002/smll.202006484
36. Gardner A, Ruffell B. Dendritic cells and cancer immunity. *Trends Immunol*. 2016;37:855-865. doi:10.1016/j.it.2016.09.006
37. Kantoff PW, Higano CS, Shore ND, et al. Sipuleucel-T immunotherapy for castration-resistant prostate cancer. *N Engl J Med*. 2010;363:363-411.
38. Bol KF, Schreibelt G, Gerritsen WR, de Vries IJM, Figdor CG. Dendritic cell-based immunotherapy: state of the art and beyond. *Clin Cancer Res*. 2016;22:1897-1906. doi:10.1158/1078-0432.CCR
39. Sabado RL, Balan S, Bhardwaj N. Dendritic cell-based immunotherapy. *Cell Res*. 2017;27:74-95. doi:10.1038/cr.2016.157
40. Cheng S, Xu C, Jin Y, et al. Artificial mini dendritic cells boost t cell-based immunotherapy for ovarian cancer. *Adv Sci (Weinh)*. 2020;7:1903301. doi:10.1002/advs.201903301
41. Chu D, Dong X, Shi X, Zhang C, Wang Z. Neutrophil-based drug delivery systems. Adv Mater. 2018;30:e1706245. doi:10.1002/adma.201706245
42. Cools-Lartigue J, Spicer J, McDonald B, et al. Neutrophil extracellular traps sequester circulating tumor cells and promote metastasis. *J Clin Invest*. 2013;123:3446-3458. doi:10.1172/JCI67484
43. Wculek SK, Malanchi I. Neutrophils support lung colonization of metastasis-initiating breast cancer cells. *Nature*. 2015;528:413-417. doi:10.1038/nature16140
44. Ma W, Zhu D, Li J, et al. Coating biomimetic nanoparticles with chimeric antigen receptor T cell-membrane provides high specificity for hepatocellular carcinoma photothermal therapy treatment. *Theranostics*. 2020;10:1281-1295. doi:10.7150/thno.40291
45. Han Y, Pan H, Li W, et al. T cell membrane mimicking nanoparticles with bioorthogonal targeting and immune recognition for enhanced photothermal therapy. *Adv Sci (Weinh)*. 2019;6:1900251. doi:10.1002/advs.201900251
46. Bassani B, Baci D, Gallazzi M, Poggi A, Bruno A, Mortara L. Natural killer cells as key players of tumor progression and angiogenesis: old and novel tools to divert their pro-tumor activities into potent anti-tumor effects. *Cancers (Basel)*. 2019;11:461. doi:10.3390/cancers11040461
47. Deng G, Sun Z, Li S, et al. Cell-membrane immunotherapy based on natural killer cell membrane coated nanoparticles for the effective inhibition of primary and abscopal tumor growth. *ACS Nano*. 2018;12:12096-12108. doi:10.1021/acsnano.8b05292
48. Zhou H, He H, Liang R, et al. *In situ* poly I:C released from living cell drug nanocarriers for macrophage-mediated antitumor immunotherapy. *Biomaterials*. 2021;269:120670. doi:10.1016/j.biomaterials.2021.120670
49. Yu G-T, Rao L, Wu H, et al. Myeloid-derived suppressor cell membrane-coated magnetic nanoparticles for cancer theranostics by inducing macrophage polarization and synergizing immunogenic cell death. *Adv Funct Mater*. 2018;28:1801389. doi:10.1002/adfm.201801389
50. Chen Z, Zhao P, Luo Z, et al. Cancer cell membrane-biomimetic nanoparticles for homologous-targeting dual-modal imaging and photothermal therapy. *ACS Nano*. 2016;10:10049-10057. doi:10.1021/acsnano.6b04695
51. Rao L, Bu LL, Cai B, et al. Cancer cell membrane-coated upconversion nanoprobes for highly specific tumor imaging. *Adv Mater*. 2016;28:3460-3466. doi:10.1002/adma.201506086
52. Yue XS, Murakami Y, Tamai T, et al. A fusion protein N-cadherin-Fc as an artificial extracellular matrix surface for maintenance of stem cell features. *Biomaterials*. 2010;31:5287-5296. doi:10.1016/j.biomaterials.2010.03.035
53. Osta WA, Chen Y, Mikhitarian K. EpCAM is overexpressed in breast cancer and is a potential target for breast cancer gene therapy. *Cancer Res*. 2004;64:5818-5824.
54. Iurisci I, Cumashi A, Sherman AA, et al. Synthetic inhibitors of galectin-1 and -3 selectively modulate homotypic cell aggregation and tumor cell apoptosis. *Anticancer Res*. 2009;29:403-410.
55. Nangia-Makker P, Hogan V, Raz A. Galectin-3 and cancer stemness. *Glycobiology*. 2018;28:172-181. doi:10.1093/glycob/cwy001
56. Zhu JY, Zheng DW, Zhang MK, et al. Preferential cancer cell self-recognition and tumor self-targeting by coating nanoparticles with homotypic cancer cell membranes. *Nano Lett*. 2016;16:5895-5901. doi:10.1021/acs.nanolett.6b02786

57. Wang H, Wang K, He L, Liu Y, Dong H, Li Y. Engineering antigen as photosensitiser nanocarrier to facilitate ROS triggered immune cascade for photodynamic immunotherapy. *Biomaterials*. 2020;244:119964. doi:10.1016/j.biomaterials.2020.119964
58. Xie W, Deng WW, Zan M, et al. Cancer cell membrane camouflaged nanoparticles to realize starvation therapy together with checkpoint blockades for enhancing cancer therapy. *ACS Nano*. 2019;13:2849-2857. doi:10.1021/acsnano.8b03788
59. Jin J, Krishnamachary B, Barnett JD, et al. Human cancer cell membrane-coated biomimetic nanoparticles reduce fibroblast-mediated invasion and metastasis and induce T-cells. *ACS Appl Mater Interfaces*. 2019;11:7850-7861. doi:10.1021/acsami.8b22309
60. Fang RH, Hu CM, Luk BT, et al. Cancer cell membrane-coated nanoparticles for anticancer vaccination and drug delivery. *Nano Lett*. 2014;14:2181-2188. doi:10.1021/nl500618u
61. Yang R, Xu J, Xu L, et al. Cancer cell membrane-coated adjuvant nanoparticles with mannose modification for effective anticancer vaccination. *ACS Nano*. 2018;12:5121-5129. doi:10.1021/acsnano.7b09041
62. Patel RB, Ye M, Carlson PM, et al. Development of an in situ cancer vaccine via combinational radiation and bacterial-membrane-coated nanoparticles. Adv Mater. 2019;31:e1902626. doi:10.1002/adma.201902626
63. Steinhagen F, Kinjo T, Bode C, Klinman DM. TLR-based immune adjuvants. *Vaccine*. 2011;29:3341-3355. doi:10.1016/j.vaccine.2010.08.002
64. Kroll AV, Fang RH, Jiang Y, et al. Nanoparticulate delivery of cancer cell membrane elicits multiantigenic antitumor immunity. *Adv Mater*. 2017;29:1703969. doi:10.1002/adma.201703969
65. Kang T, Huang Y, Zhu Q, et al. Necroptotic cancer cells-mimicry nanovaccine boosts anti-tumor immunity with tailored immune-stimulatory modality. *Biomaterials*. 2018;164:80-97. doi:10.1016/j.biomaterials.2018.02.033
66. Gan J, Du G, He C, et al. Tumor cell membrane enveloped aluminum phosphate nanoparticles for enhanced cancer vaccination. *J Control Release*. 2020;326:297-309. doi:10.1016/j.jconrel.2020.07.008
67. Fontana F, Shahbazi MA, Liu D, et al. Multistaged nanovaccines based on porous silicon@acetalated dextran@cancer cell membrane for cancer immunotherapy. *Adv Mater*. 2017;29:1603239. doi:10.1002/adma.201603239
68. Ochyl LJ, Bazzill JD, Park C, Xu Y, Kuai R, Moon JJ. PEGylated tumor cell membrane vesicles as a new vaccine platform for cancer immunotherapy. *Biomaterials*. 2018;182:157-166. doi:10.1016/j.biomaterials.2018.08.016
69. Ye X, Liang X, Chen Q, et al. Surgical tumor-derived personalized photothermal vaccine formulation for cancer immunotherapy. *ACS Nano*. 2019;13:2956-2968. doi:10.1021/acsnano.8b07371
70. Wang Z, Zhang F, Shao D, et al. Janus nanobullets combine photodynamic therapy and magnetic hyperthermia to potentiate synergetic anti-metastatic immunotherapy. *Adv Sci (Weinh)*. 2019;6:1901690. doi:10.1002/advs.201901690
71. Lim J, Koh VHQ, Cho SSL, et al. Harnessing the immunomodulatory properties of bacterial ghosts to boost the anti-mycobacterial protective immunity. *Front Immunol*. 2019;10:2737. doi:10.3389/fimmu.2019.02737
72. Paukner S, Stiedl T, Kudela P, Bizik J, Al Laham F, Lubitz W. Bacterial ghosts as a novel advanced targeting system for drug and DNA delivery. *Expert Opin Drug Deliv*. 2006;3:11-22.
73. Kim OY, Park HT, Dinh NTH, et al. Bacterial outer membrane vesicles suppress tumor by interferon-gamma-mediated antitumor response. *Nat Commun*. 2017;8:626. doi:10.1038/s41467-017
74. Chen HY, Deng J, Wang Y, Wu CQ, Li X, Dai HW. Hybrid cell membrane-coated nanoparticles: a multifunctional biomimetic platform for cancer diagnosis and therapy. *Acta Biomater*. 2020;112:1-13. doi:10.1016/j.actbio.2020.05.028
75. Liu WL, Zou MZ, Liu T, et al. Cytomembrane nanovaccines show therapeutic effects by mimicking tumor cells and antigen presenting cells. *Nat Commun*. 2019;10:3199. doi:10.1038/s41467-019
76. Jiang Q, Liu Y, Guo R, et al. Erythrocyte-cancer hybrid membrane-camouflaged melanin nanoparticles for enhancing photothermal therapy efficacy in tumors. *Biomaterials*. 2019;192:292-308. doi:10.1016/j.biomaterials.2018.11.021
77. Gong C, Yu X, You B, et al. Macrophage-cancer hybrid membrane-coated nanoparticles for targeting lung metastasis in breast cancer therapy. *J Nanobiotechnology*. 2020;18:92. doi:10.1186/s12951-020
78. Rao L, Wu L, Liu Z, et al. Hybrid cellular membrane nanovesicles amplify macrophage immune responses against cancer recurrence and metastasis. *Nat Commun*. 2020;11:4909. doi:10.1038/s41467-020
79. Wang D, Liu C, You S, et al. Bacterial vesicle-cancer cell hybrid membrane-coated nanoparticles for tumor specific immune activation and photothermal therapy. *ACS Appl Mater Interfaces*. 2020;12:41138-41147. doi:10.1021/acsami.0c13169
80. Stuckey DW, Shah K. Stem cell-based therapies for cancer treatment: separating hope from hype. *Nat Rev Cancer*. 2014;14:683-691. doi:10.1038/nrc3798
81. Wu HH, Zhou Y, Tabata Y, Gao J-Q. Mesenchymal stem cell-based drug delivery strategy: from cells to biomimetic. *J Control Release*. 2019;294:102-113. doi:10.1016/j.jconrel.2018.12.019
82. Zhang M, Cheng S, Jin Y, Zhang N, Wang Y. Membrane engineering of cell membrane biomimetic nanoparticles for nanoscale therapeutics. *Clin Transl Med*. 2021;11:e292. doi:10.1002/ctm2.292
83. Gao C, Lin Z, Jurado-Sánchez B, Lin X, Wu Z, He Q. Stem cell membrane-coated nanogels for highly efficient *in vivo* tumor targeted drug delivery. *Small*. 2016;12:4056-4062. doi:10.1002/smll.201600624
84. Guo X, Gao C, Yang DH, Li S. Exosomal circular RNAs: a chief culprit in cancer chemotherapy resistance. *Drug Resist Updat*. 2023;67:100937. doi:10.1016/j.drup.2023.100937
85. Xu Y, Xiong J, Sun X, Gao H. Targeted nanomedicines remodeling immunosuppressive tumor microenvironment for enhanced cancer immunotherapy. *Acta Pharm Sin B*. 2022;12:4327-4347. doi:10.1016/j.apsb.2022.11.001
86. Li S, Kang Y, Zeng Y. Targeting tumor and bone microenvironment: Novel therapeutic opportunities for castration-resistant prostate cancer patients with bone metastasis. *Biochim Biophys Acta Rev Cancer*. 2024;1879:189033. doi:10.1016/j.bbcan.2023.189033
87. Chen Z, Yue Z, Yang K, et al. Four ounces can move a thousand pounds: the enormous value of nanomaterials in tumor immunotherapy. *Adv Healthc Mater*. 2023;12:e2300882. doi:10.1002/adhm.202300882
88. Kang Y, Li S. Nanomaterials: Breaking through the bottleneck of tumor immunotherapy. *Int J Biol Macromol*. 2023;230:123159. doi:10.1016/j.ijbiomac.2023.123159
89. Zhu X, Li S. Ferroptosis, necroptosis, and pyroptosis in gastrointestinal cancers: the chief culprits of tumor progression and drug resistance. *Adv Sci (Weinh)*. 2023;10:e2300824. doi:10.1002/advs.202300824
90. Chen Z, Yue Z, Yang K, Li S. Nanomaterials: small particles show huge possibilities for cancer immunotherapy. *J Nanobiotechnology*. 2022;20:484. doi:10.1186/s12951-022
91. Liu H, Miao Z, Zha Z. Cell membrane-coated nanoparticles for immunotherapy. *Chin Chem Lett*. 2022;33:1673-1680. doi:10.1016/j.cclet.2021.10.057
92. Yang F, Shi K, Jia YP, Hao Y, Peng J-R, Qian Z-Y. Advanced biomaterials for cancer immunotherapy. *Acta Pharmacol Sin*. 2020;41:911-927. doi:10.1038/s41401-020
93. Li S. The basic characteristics of extracellular vesicles and their potential application in bone sarcomas. *J Nanobiotechnology*. 2021;19:277. doi:10.1186/s12951-021
94. Zhang J, Li X, Zhang Z, et al. Role of the RIP3-PGAM5-Drp1 pathway in aluminum-induced PC12 cells necroptosis. *Ecotoxicol Environ Saf*. 2023;270:115860. doi:10.1016/j.ecoenv.2023.115860