Deep Science Publishing, 2025
https://doi.org/10.70593/978-93-7185-537-2_7

Chapter 7: Exosomes and Biomimetic Nanoparticles: Natural Nanocarriers for Breast Cancer

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Abstract

Breast cancer is one of the leading causes of cancer associated morbidity worldwide as conventional therapies are often limited by drug resistance and metastatic spread. These challenges observed with conventional therapies underscore the need of innovative systems for drug delivery that can overcome the challenges associated with conventional therapies. Exosomes are derived from cellular endosomal pathways and act as natural nanocarriers and have emerged as a promising approach for targeted therapy because of their inherent biomimetic properties and unique biogenesis. These have the ability of cell-cell communication and exhibit organotropism which makes them superior candidates in delivery therapeutic agents in oncology. Biomimetic nanoparticles are inspired from exosomes, but they offer several advantages in cancer therapy like improved tumor penetration, dual targeting capability, and reduced off-target as they are made of advanced design strategies. Various studies from literature survey indicate the superiority of exosomes over synthetic nanoparticles because of targeting specificity and biocompatibility, though challenges related to scalability and standardization persist. Recent advancements in oncology have led to the development of exosome-based delivery systems of nucleic acids and chemotherapeutic agents and multimodal approaches integrating photothermal and immunotherapy modalities. Preclinical studies related to exosome-coated porous silicon nanoparticles have demonstrated significant potential and several clinical trials are underway. Major challenges are related to the large-scale production, isolation procedures and regulatory guidelines. This chapter provides a comprehensive overview on exosomes and biomimetic nanoparticles as natural nanocarriers for breast cancer therapy.

Keywords: *Breast Cancer, Drug delivery system, Exosomes, Nanocarriers, Nanoparticles.*

1 Introduction

Breast cancer is one of the most diagnosed forms of cancer and is the leading cause of mortality in women worldwide which pose a threat to the health of the women globally (Wang & Wu, 2023). The cases of breast cancer in females are increasing constantly in all regions of the world (Smolarz *et al*., 2022). According to the reports of Cancer Statistics 2020, breast cancer alone is 30% of cancer found in females with approximate 276,480 new cases and around 42,000 estimated deaths (Sieger *et al*., 2021). Breast cancer alone comprises of 36 of total oncological patients worldwide which is a huge number and poses threat to the health of female worldwide. Majority of the cases of breast cancer are seen in females of developed countries, the major factor is the lifestyle which includes poor diet, excessive stress, nicotinism, and less physical activity (Bellanger *et al*., 2018).

The highest incidence rate of breast cancer is seen in Belgium and among the continents, the highest incidence rate is prevalent in Australia (Global Cancer observatory). Projections regarding the global burden of breast cancer worldwide is terrifying, by 2050 it is estimated that there can be 3.2 million new cases of breast cancer and around 1.1 million deaths annually due to breast cancer (Press release IARC). In countries with low and medium income, the incidence of breast cancer is further expected to increase mainly due to westernization of lifestyle which includes delay in pregnancies, reduced breastfeeding, lack of physical activity and poor diet (Porter, 2008).

Using immunohistological techniques, breast cancer can be divided into four principal molecular subtypes based on the expression of estrogen receptor, progesterone receptor, human epidermal growth factor (HER2), these four subtypes of breast cancer are Luminal A BC (ER+ and/or PR+, and HER2-), Luminal B BC (ER+ and/or PR+, and HER2+), HER2 BC (ER-, PR-, and HER2+), and triple-negative BC (TNBC) (ER-, PR-, and HER2-) (Burguin *et al*., 2021).

The standard treatment regimen for breast cancer includes a combination of surgery, radiotherapy, chemotherapy, and targeted therapies including monoclonal antibodies, small-molecule inhibitors, antibody-drug conjugates, and immunotherapy (Menon *et al*., 2025). Research on novel advancement such as ablation therapy and immune checkpoint inhibitors is going on, despite all these scientific advances in the field of breast cancer treatment, several clinical limitations persist that have impact on patient outcomes (Xiong *et al*., 2025). The standard treatment procedures for breast cancer are associated with side effects such as immunosuppression, fatigue, and cardiotoxicity which can affect quality of life (Salata *et al*., 2021). Another major challenge is the heterogeneity of cancer, such as TNBC lacks estrogen, progesterone, and HER2 receptor which limits the use of hormonal therapies and hence chemotherapy remains the only option (American Cancer society). Other than these, resistance is the major issue observed with

cancer therapy, it may be due to genetic mutation, alteration of drug metabolism, activation of alternative signaling pathways and many more (Kim *et al*., 2025).

Metastasis means a process in which a primary tumor develops into a distal secondary tumor and leads to failure of conventional treatment. This process allows cancer cells to invade and survive in circulation (Park *et al*., 2022). Cancer stem cells are key contributors to both drug resistance and metastasis as they can self-renew and differentiate (Zhang *et al*., 2021). Due to all these challenges, focus is shifting towards finding new treatment methods with advanced technologies, in this regard, exosomes and biomimetic nanoparticles are gaining attention as they offer advantages such as biocompatibility, ability to cross biological barriers and low immunogenicity.

This chapter provides a comprehensive overview on exosomes and biomimetic nanoparticles as natural nanocarriers for breast cancer therapy, providing a detailed overview of biogenesis and composition of exosomes, advantages of exosomes over synthetic carriers, role of exosomes in pathogenesis and diagnosis of breast cancer, its role in therapeutic delivery of chemotherapeutic agents along with the role of biomimetic nanoparticles in breast cancer. Fig **7**.1 shows the graphical abstract for the chapter.

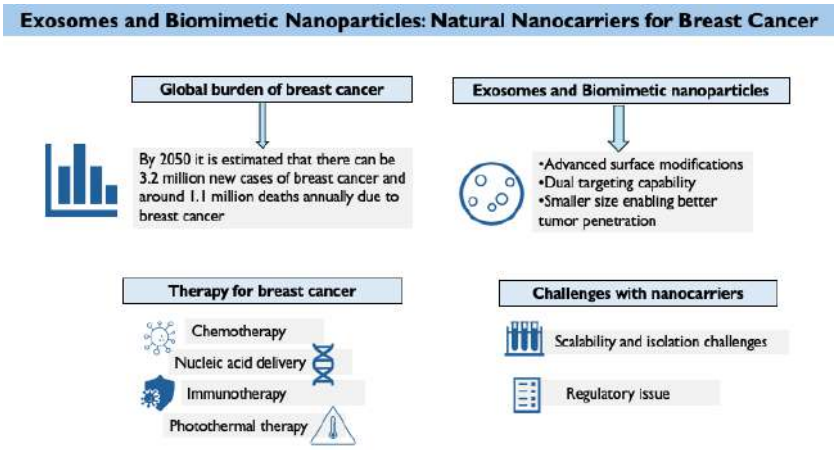

Fig 7.1 Graphical abstract: Exosomes and biomimetic nanoparticles: Natural Nanocarriers for breast cancer

2 Exosomes in Breast Cancer

2.1 Biogenesis and composition (proteins, nucleic acids, lipids)

Exosomes are cellular vesicles of 30-150 nm in diameter up to 200 nm. They originate from endocytic pathway (Piombino *et al*., 2021). Biogenesis of exosomes involve formation of early endosomes, maturation into multivesicular bodies and ultimately fusion with plasma membrane to release vesicles which are known as exosomes (Wang

et al., 2021). Exosomes employed for breast cancer therapy are composed of a range of proteins such as tetraspanins, integrins, and heat shock proteins, nucleic acids such as DNA, mRNA, non-coding RNAs and many more. They also contain lipids such as cholesterol, sphingomyelin, and ceramide (Kumar *et al*., 2022). Exosomes are responsible for intercellular communication between cancer cells and tumor microenvironment. This cell-cell communication can occur at various stages of breast cancer metastasis (Liu *et al*., 2021). The genetic material present in exosomes allows transfer of biological information across cell (Zha *et al*., 2017). Compared to other methods for cancer therapy, exosomes have low immunogenicity, high compatibility and very low chances of accumulation in tissues that can cause toxicity, hence exosomes are emerging as natural bio nanocarrier for targeted delivery (Weaver *et al*., 2022).

2.2 Advantages of exosomes

Various advantages of exosomes in breast cancer therapy includes biomimetic nature, immune evasion, and organotropism. These benefits are explained in detail below:

2.2.1 Biomimetic properties

As exosomes are derived from plasma membrane of parent cells, they have inherent biomimetic properties which allows them to deliver cargo to targe cells easily. In case of breast cancer, exosomes can deliver therapeutic agent to tumor cells through surface membrane protein and cell receptor interaction which helps in overcoming drug resistance that may be associated with p-glycoprotein (Zeng *et al*., 2025).

2.2.2 Immune evasion

Exosomes are composed of bilayer structure and have endogenous surface proteins which prevents cargo from degradation and have the capacity to evade recognition and removal by immune system and thus transport functional components to target cells (Zhou *et al*., 2020).

2.2.3 Organotropism

Exosomes can show organotropism, which means it can home to specific organs. Drug loaded exosomes can mix well with exosomes in metastatic organ via organotropism (Xie *et al*., 2021).

2.3 Advantages of exosomes over synthetic nanoparticles

Although researchers have cracked manufacturing process and stability concerns for nanoparticles, yet exosomes are superior in nature as they offer biocompatibility, cell targeting and immune evasion though some challenges associated with isolation and

scalability are there. Table 7.1 shows various key difference between exosomes and synthetic nanoparticles.

Table 7.1 Comparison between exosomes vs synthetic nanoparticles

Features	Exosomes	Synthetic nanoparticles
Origin	Natural, derived from extracellular vesicles	Artificial, derived from polymers
Biocompatibility	Highly biocompatible as these have endogenous origin	Depends on the nature of material used for fabrication
Stability	Stable in biological fluids	Varies depending on the nature of material used
Modification potential	Genetic modification possible	Only physical/chemical modifications possible
Off-target effects	Very less off-target effect due to natural targeting	Higher off-target toxicity
Immunogenicity	Low due to autologous nature	Comparatively high due to the nature of material used
Stability in circulation	Highly stable due to natural membrane properties	May face rapid clearance unless PEGylated
Cost and scalability	High cost due to complexity of purification, scalability is variable to batches	Cost-effective and scalable production
Clinical translation	Emerging but currently limited by isolation, standardization, and scalability.	Several types already approved but issues with toxicity
Examples in breast cancer	Paclitaxel, doxorubicin exosomes, Anti-miRNA-142-3p	Gold nanoparticles, mesoporous silica nanoparticles

2.4 Exosomes in breast cancer pathogenesis and diagnosis

2.4.1 Exosomes in breast cancer pathogenesis

Exosomes are critically involved in the breast cancer pathogenesis as they promote breast cancer progression, metastasis as well as drug resistance through different mechanisms. These extracellular vesicles function as vehicles of intercellular communication in the tumor microenvironment, stimulate oncogenic transformation and promote cancer cell survival (Liu *et al.*, 2021).

Exosomes secreted by cancer cells promote breast cancer progression by transferring oncoproteins, nucleic acids and lipids to surrounding cells (Kalluri & LeBleu, 2020). These molecular cargos have the ability to reprogram host cells resulting in increased proliferation, invasion and metastatic capability. For example, exosomes originating from breast cancer cells are able to transfer oncogenic miRNAs, including miR-21 and miR-155, that enhance cell survival and prevent apoptosis in recipient cells (Asgari &

Rezaie, 2021; Zhang & Yu 2019). Also, exosomes can transport matrix metalloproteinases (MMPs) which induce extracellular matrix degradation leading to golden river for cancer cell invasion and metastasis (Thuault *et al*., 2022).

Exosomal communication between cancer cells and various stromal cells including fibroblasts immune cells and endothelial cells significantly influences tumor microenvironment. Breast cancer-derived exosomes convert normal fibroblasts into cancer-associated fibroblasts that subsequently proactively support tumor growth very aggressively and angiogenesis (Maia *et al*., 2018; Kalluri & LeBleu, 2020). Exosomes modulate immune cell function effectively promoting immunosuppression by inhibiting activation of T-cells and expanding regulatory T-cells rapidly (Zhau *et al*., 2022).

Exosomes contribute significantly to pre-metastatic niche formation by priming distant organs for colonization metastatically with considerable efficacy. Breast cancer-derived exosomes get taken up quickly by cells in distant organs inducing hectic pro-inflammatory responses and creating a super favorable environment for circulating tumor cells establishing secondary tumors. Specific integrins and other adhesion molecules facilitating organ-specific metastatic patterns are transferred during this complex process somehow rather rapidly (Yusn *et al*., 2021).

2.4.2 Exosomes in breast cancer diagnosis

Exosomes have surfaced as stellar biomarkers for breast cancer diagnosis and prognosis largely because of stable presence in bodily fluids (Ahmad 2022). Exosome-based diagnostics commonly known as liquid biopsy boasts significant advantages over traditional methods involving tissue biopsy invasively (Qiu *et al*., 2025).

Exosomes swirling in blood and saliva bear distinct molecular fingerprints that differentiate between healthy folks and those afflicted with breast cancer. Tumor molecular characteristics are reflected in signatures comprising specific proteins nucleic acids and diverse lipid compositions found therein (Nonaka *et al*., 2017). Elevated levels of specific microRNAs like miR-21 and miR-210 in exosomes circulating systemically have been linked with breast cancer diagnosis and grim outcomes (Rhim *et al*., 2022; Wu, 2020).

Proteomic analysis of exosomes reveals presence of breast cancer-specific proteins such as HER2 and EGFR alongside various tumor-associated antigens (Piombino *et al*., 2021). Quantification of proteins in exosomes provides valuable info about tumor classification and predicting response to treatment accurately nowadays. Exosomal protein profiles facilitate distinction between various breast cancer subtypes thereby enabling bespoke treatment regimens somewhat effectively nowadays (Rontogianni *et al*., 2019).

The dynamic nature of exosomal content makes them excellent candidates for real-time monitoring of disease progression and treatment response. Tumor evolution and development of drug resistance along with metastatic progression get reflected in alterations of exosomal cargo quite frequently. Temporal monitoring capability proves particularly valuable in clinical settings where repeated biopsies pose significant risks or are downright impractical for patients (Azmi *et al*., 2013).

2.5 Exosomes as therapeutic drug delivery system for breast cancer

2.5.1 Drug Delivery Systems

Exosomes show considerable promise as therapeutic delivery vectors for breast cancer treatment owing largely to inherent biocompatibility and ability to traverse biological barriers quite effectively. Exosomes being utilized in breast cancer treatment involve delivery of various therapeutic agents such as chemotherapeutics and nucleic acids remarkably (Li *et al*., 2013).

2.5.1.1 Chemotherapeutics (e.g., doxorubicin, paclitaxel)

Chemotherapeutic agents are extensively studied cargo for exosome-based drug delivery systems being developed rapidly for treating breast cancer patients effectively nowadays. Doxorubicin has been loaded into exosomes successfully via various funky methods including electroporation and chemical conjugation readily nowadays. Doxorubicin encapsulated inside exosomes has shown great efficacy and less cardiotoxicity (Bisht *et al*., 2025).

It can easily overcome the various limitations associated with chemotherapeutic agents such as poor penetration, and other side effects (Tian *et al*., 2014; Toffoli *et al*., 2015).

Paclitaxel is an important chemotherapeutic agent for breast cancer has been delivered using this delivery system (Nehate *et al*., 2014). Paclitaxel's hydrophobic nature makes formulation challenging with conventional drug delivery systems, but exosomes offer a natural solution owing to lipid bilayer structure. Various preclinical models have shown that Paclitaxel exosomes system can increase antitumor efficacy (Huang *et al*., 2023).

Loading method choice hinges on physicochemical properties of drug and its intended therapeutic use largely within specific medical contexts obviously (Huang *et al*., 2023).

2.5.1.2 Nucleic acids (siRNA, miRNA)

Nucleic acid-based therapeutics represent a promising approach for breast cancer treatment by targeting specific oncogenes or restoring tumor suppressor functions. Exosomes provide an excellent platform for nucleic acid delivery due to their natural

ability to transport genetic material and their capacity to protect nucleic acids from degradation (Yadav *et al*., 2017)

Small interfering RNA (siRNA) delivery through exosomes has shown significant potential in breast cancer therapy. Exosome-delivered siRNA targets various oncogenic drivers such as HER2 and EGFR with reduced protein expression enhancing cancer cell mortality significantly. Exosomes naturally home in on tumor cells maximizing therapeutic efficacy substantially while off-target effects get minimized effectively (Palakurthi *et al*., 2024). Exosome-mediated microRNA therapy has surprisingly emerged as quite a potent strategy for treating breast cancer effectively nowadays. Anti-miRNA molecules can stop the progression of cancer by inhibiting specific oncogenes (Hironaka *et al*., 2022; Klicka *et al*., 2022). The major advantage of exosome-mediated nucleic acid delivery is enhanced cellular uptake, great tissue penetration and many more (Nordmeier *et al*., 2021).

2.5.2 Engineered Exosomes

The natural function of exosome can be increased via structurally engineering exosomes which can improve the therapeutic efficacy and specificity also. It also increases the loading capacity for cargo materials (Choi *et al*., 2021).

2.5.2.1 Genetic modifications

CRISPR-Cas9 tech has revolutionized the era of exosome engineering because it enables accurate genetic mods inside a lot o producer cell types. Exosomes can be loaded with specific therapeutic genes or targeting sequences during biogenesis through this somewhat unorthodox approach effectively. CRISPR-modified exosomes can be engineered rather cleverly to ferry gene-editing components inside cells targeting some nasty oncogenes (Aslan *et al*., 2024). Overexpression of tumor-suppressive miRNAs in producer cells constitutes a potent alternative strategy for genetic modification effectively. Genetically engineered cells overexpress specific miRNAs like miR-34a or miR-200c resulting in exosomes enriched heavily with such therapeutic molecules (Zuo *et al*., 2020). Therapeutic miRNAs are loaded consistently at high levels via this approach thereby significantly enhancing antitumor effects very effectively indeed. Genetic tweaks can be employed rather slyly to beef up exosome targeting properties via overexpression of specific surface receptors or proteins. Engineering producer cells overexpress folate receptors or HER2-targeting molecules can improve tumor-targeting specificity of resulting exosomes substantially in many cases (Sun *et al*., 2025).

2.5.2.2 Surface conjugation (antibodies, peptides)

Peptide conjugation offers another approach for exosome targeting enhancement. Cell-penetrating peptides can be conjugated to exosomes to improve their cellular uptake,

while tumor-targeting peptides can enhance their specificity for cancer cells. The use of pH-sensitive or enzyme-cleavable linkers in peptide conjugation allows for controlled release of therapeutic cargo in the tumor microenvironment (Wang *et al*., 2024; Armstrong *et al*., 2025).

Exosomes can be modified superficially by conjugation of targeting molecules thereby substantively enhancing therapeutic potential through a versatile approach. Specific antibodies or peptides get attached to exosomal surface thereby markedly improving ability to recognize target cells quite effectively. Exosomes conjugated with antibody have yielded ostensibly promising results in therapy of breast cancer remarkably well lately. Exosomes that are conjugated with antibodies specific for breast cancer can produce good therapeutic outcomes. It can also increase the specificity by binding with exosomes. It involves biochemical means to increase the targeting and is considered somewhat unconventional approach. Conjugation with peptides using pH-sensitive linkers increases the controlled release of therapeutics in the tumor microenvironment (Wang *et al*., 2020; Alas *et al*., 2021).

2.5.3 Multimodal Therapy

Nowadays, exosomes have possessed various kinds of systems that can easily integrate multiple therapeutic modalities which render this system to be a great advancement in the field of breast cancer treatment approach. Multimodal therapy melds disparate treatment modalities achieving synergistic effects thereby surmounting drug resistance and markedly improving outcomes for patients (Bardhan *et al*., 2010).

2.5.3.1 Photothermal/photoacoustic combinations

Exosome-based drug delivery paired with photothermal therapy has surfaced as a rather promising multimodal strategy for tackling breast cancer. Loading exosomes with chemotherapeutic agents alongside photothermal agents like gold nanoparticles or near-infrared dyes is core part of this strategy (Lim *et al*., 2011). Near-infrared laser irradiation triggers photothermal agents generating localized hyperthermia that directly kills cancer cells and boosts release of chemotherapeutic drugs.

PTT is combined with exosome-based system to yield various benefits such as deep penetration and effective release of chemotherapeutic agents. Localized heating effect disturbs the tumor vasculature and thus improves distribution of the drug. Photoacoustic combinations is one the most novel approaches which represents multimodal therapeutic strategy, producing ehnaced release of drug for tumor penetration (Liu *et al*., 2023; Raikwar *et al*., 2022).

2.5.3.2 Immunotherapy synergies

Exosomes combined with immunotherapeutic agents has opened the way for breast cancer treatment nowadays. Exosomes containing chemotherapeutic agents and immunotherapeutic produces synergistic effects producing high antitumor activity. Exosomes can be bioengineered rather cleverly to ferry various immunomodulatory molecules or cytokines and some potent immune checkpoint inhibitors. Exosomes naturally interact with various immune cells rather effectively making them ideal candidates for delivering immunotherapy quite successfully nowadays. Such an approach can help overcome immunosuppressive tumor microenvironments and significantly enhance effectiveness of various conventional cancer treatments remarkably well. Exosome-based drug delivery paired with CAR-T cell therapy signifies a potentially potent synergy in emerging immunotherapies quite remarkably nowadays. Exosomes deliver supportive factors enhancing CAR-T cell function and persistence while carrying therapeutic agents sensitizing tumor cells immune attack rather effectively (Yin *et al*., 2021; Tong *et al*., 2022).

3 Biomimetic nanoparticles in breast cancer

Nanoparticle based delivery of anti-tumor agents holds promise for cancer treatment, but the major limitations are inadequate drug targeting and limited biocompatibility. Hence, biomimetic nanoparticles made of cell membrane components have emerged as interesting area of research because these are biocompatible, have low toxicity and allows precise targeting (Zhang *et al*., 2024). These biomimetic nanoparticles differ from conventional synthetic nanoparticles in that they have coating of cell membrane components over inner core which enables them to evade the reticuloendothelial system while synthetic nanoparticles do not possess this specific characteristic (Kroll *et al*., 2017). Biomimetic nanoparticles can be classified into following three types: cell membrane coated, natural protein based, and targeting ligand (Issaka & Amu-darko, 2025). According to the sources of cell membrane, biomimetic nanoparticles can be classified into the following categories: red blood cell membrane coated nanoparticles, white blood cell membrane coated nanoparticles, platelet membrane coated nanoparticles, stem cell membrane coated nanoparticles, and hybrid membrane coated nanoparticles (Zhang *et al*., 2024). Biomimetic nanoparticles are made in such a way that they can mimic the biological entities because they are coated with various cell derived membranes (Issaka & Amu-darko, 2025). The design principles of biomimetic nanoparticles consist of surface modification which has been discussed in detail below:

3.1 Surface modification

Surface modification of the nanoparticles using cell membrane derived components, proteins, ligands, is used to mimic biological features. Surface modification allows prolong circulation, enhanced bioavailability, immune evasion and tumor specific

targeting. Surface modification can be done using a variety of components; natural protein-based biomimetic nanoparticles involve surface modification through serum albumin, ferritin protein cage; the surface of nanoparticles with targeting ligands involve surface modification using monoclonal antibodies, folic acid, aptamers, tumor penetrating peptides; while the surface of cell membrane coated nanoparticles are modified by coating it with RBC, WBC, platelets, immune cell membrane (Beh *et al*., 2021; Yu *et al*., 2022). Table **7**.2 shows various types of cell-membrane coated biomimetic nanoparticles.

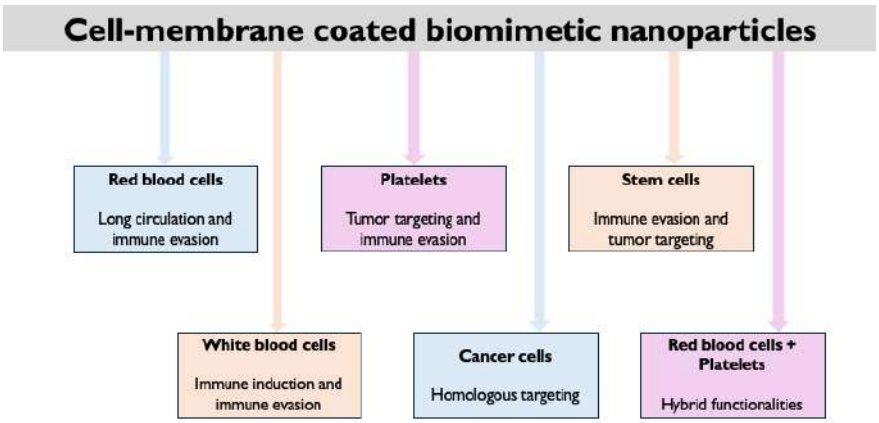

Fig 7.2 Types of Cell-membrane coated biomimetic nanoparticles

3.2 Key advantages over synthetic carriers

The key advantages of biomimetic nanoparticles over synthetic carriers are as follows:

3.2.1 Enhanced tumor penetration

Biomimetic nanoparticles are composed of natural membrane coatings which facilitate them to interact with tumor microenvironment and traverse biological membranes in an effective manner. Using this methodology, therapeutic agents can be easily delivered to areas regions which are poorly vascularized or hypoxic in nature (Beh *et al*., 2021).

3.2.2 Reduced off-target effects

This is one of the most key advantages of biomimetic nanoparticles over synthetic carriers as they mimic the surface of host cells and evade recognition by the immune system, in this way they get to be accumulated at the tumor site for longer period. Healthy cells are unable to uptake them as they have mimicked the surface of host cells

and therefore systemic toxicity gets reduced because off-target effects are reduced (Guo *et al*., 2025).

3.2.3 Dual targeting (EPR effect + ligand-receptor interactions)

Biomimetic nanoparticles use dual targeting involving EPR (Enhanced permeability and retention effect) and ligand-receptor interaction. Due to their nature of leaky vasculature, biomimetic nanoparticles accumulate in tumor tissues and by surface functionalization, active targeting is enabled by ligand-receptor interaction thereby increasing uptake by cancer cells rather than normal cells (Shih *et al*., 2022). Fig. 7.3 shows key advantages of biomimetic nanoparticles over synthetic nanocarriers.

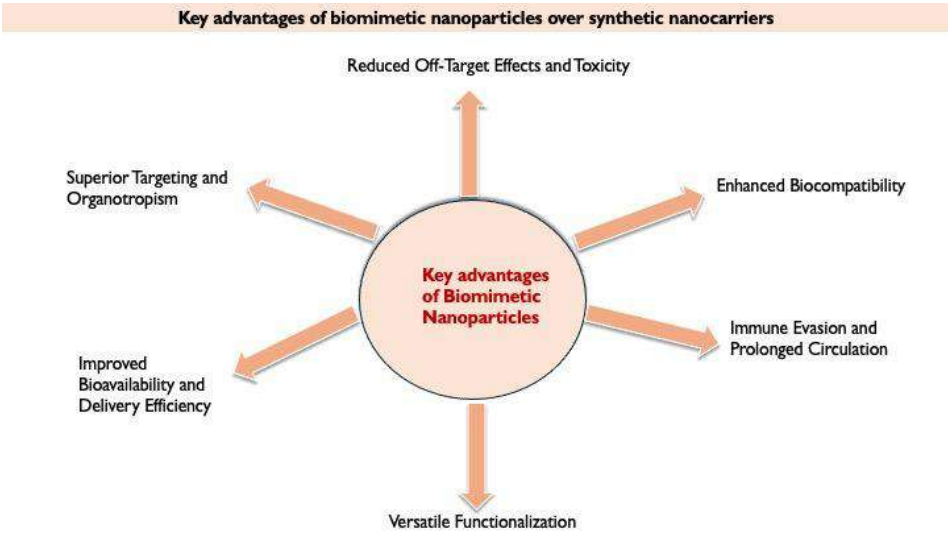

Fig. 7.3 Key advantages of biomimetic nanoparticles over synthetic nanocarriers

4 Preclinical and clinical advances

4.1 Preclinical studies

Table 7.2: Preclinical studies on application of exosomes and biomimetic nanoparticles in breast cancer

Title of study	Name of cells	Intervention	Result	Conclusion	References
Therapeutic Effect of Camel Milk and Its Exosomes on MCF7 Cells	MCF7 breast cancer cells	camel milk and its exosomes	Reduction in breast tumor progression shown by high apoptosis	Profound anticancer effect was found possibly by induction of apoptosis	(Badawy *et al*., 2018)

In Vitro and In Vivo			(indicated by high caspase-3 activity, inhibition of oxidative stress (decrease in iNOS gene expression) and increased activity of SOD, and CAT		
Exosome-mediated delivery of functionally active miRNA-142-3p inhibitor reduces tumorigenicity of breast cancer in vitro and in vivo	miR-142-3p and miR-150 in 4T1 and TUBO breast cancer cell lines.	exosomes isolated from bone marrow-derived mesenchymal stem cells	Reduction in miR-142-3p and miR-150 levels and increase in APC and P2X7R target genes	Favorable vehicle to deliver LNA-anti-miR-142-3p	(Naseri *et al*., 2018)
Plasma exosomes stimulate breast cancer metastasis through surface interactions and activation of FAK signalling	MDA-MB-231 and MCF-7 cell lines.	Plasma exosomes	Increase in migration and transwell invasion	Stimulation of metastasis promoting activity of breast cancer cells	(Shtam *et al*., 2019)
Stimuli-sensitive biomimetic nanoparticles for the inhibition of breast cancer recurrence and pulmonary metastasis	4 T1-luc	Doxorubicin biomimetic nanoparticles	Enhanced targeting and release efficacy	Enhanced therapeutic efficacy	(Yang *et al*., 2024)
Biomimetic Targeted Theranostic Nanoparticles	EpCAM)-positive MCF-7 breast	RBC membrane-cloaked nanoparticles	Enhanced cytotoxic efficacy and prolonged	Helpful in diagnosis of breast cancer	(Marshall *et al*., 2022)

for Breast Cancer Treatment	cancer cells	release

4.2 Clinical trials

Table 7.3 shows the clinical studies related to applications of exosomes and biomimetic nanoparticles in breast cancer. This information has been accessed from https:clinicaltrials.gov/

Table 7.3: Clinical studies on application of exosomes and biomimetic nanoparticles in breast cancer

Title of the study	**NCT ID**	**Indication**	**Intervention/therapy**	**Status of study**
Exosome as the Prognostic and Predictive Biomarker in EBC Patients	NCT05955521	Triple Negative Breast Cancer HER2-positive Breast Cancer	Exosome and ctDNA evaluation	Ongoing
Feasibility of Exosome Analysis in Cerebrospinal Fluid During the Diagnostic Workup of Metastatic Meningitis (Exo-LCR) (Exo-LCR)	NCT05286684	Breast cancer	Exosome based therapy	Completed
A Study to Measure the Expression of the HER2-HER3 Dimer in Tumour and Blood (Exosomes) Samples From Patients With HER2 Positive Breast Cancer Receiving HER2 Targeted Therapies	NCT04288141	HER2+ Breast Cancer	HER2-directed exosome therapy	Ongoing

Paclitaxel Albumin-Stabilized Nanoparticle Formulation in Treating Patients of Different Ages with Metastatic Breast Cancer	NCT00609791	Breast cancer	Paclitaxel albumin-stabilized nanoparticle formulation	Ongoing
Nanoparticle Albumin-Bound (Nab) Paclitaxel/ Cyclophosphamide in Early-Stage Breast Cancer	NCT00629499	Breast cancer	Nab paclitaxel	Completed

5 Current Challenges

5.1 Scalability of exosome production

The issues related with the scalability of exosome production and purification remains a major challenge because exosomes are mainly isolated from cell culture media or though methods like ultracentrifugation, size-exclusion chromatography, ultrafiltration etc (Cecchinn *et al*., 2023). Exosomes produced with these methods have low yield and purity. For scalable production techniques which gives high yield of exosomes are desired to scale up the process (Kim *et al*., 2024). Investment in scalable production technology such as bioreactor can help in facilitating large-scale manufacturing of exosomes making them more feasible for clinical use (Palakurthi *et al*., 2024).

5.2 Standardization of isolation/characterization

Isolation of exosomes from biological fluids is a complex process and it gets complicated further due to the presence of overlapping size particles in the biological fluids such as lipoproteins and microvesicles (Li *et al*., 2019). Conventional methods for isolation of exosomes such as ultrafiltration, ultracentrifugation, polymer-based precipitation and many more costs high and produces low yield which impose a great challenge (Ludwig *et al*., 2019). Also, there is lack of standardized protocols for isolation and characterization of exosomes which makes it difficult for clinical translation (Ayala *et al*., 2019).

6 Future Directions

6.1 Hybrid systems: Exosome-nanoparticles composites

Hybrid systems have come over as a novel technology to actively enhance the functionalities, these hybrid systems of exosome-nanoparticles are widely known by the name; hybridosomes. These hybrid exosome-nanoparticles composites can show immunomodulatory properties and possess natural targeting (Chan *et al*., 2022). This hybrid-nanoparticle composite approach cam also increase the half-life of exosomes in the blood stream of humans (Soltanmohammadi *et al*., 2024). In this study, exosome-based hybrid nano system has been developed to target triple negative breast cancer (TNBC). For this purpose, Mesenchymal stem cell exosome-coated drug-loaded polymeric nanoparticles were prepared using microfluidics methods to deliver doxorubicin in TNBC. The results of the study suggested that this hybrid framework was more helpful in tumor accumulation of drug as compared to synthetic nanoparticles (Joshi *et al*., 2023). Fig. **7**.4 shows various strategies to prepare hybrid exosome-nanoparticles composites.

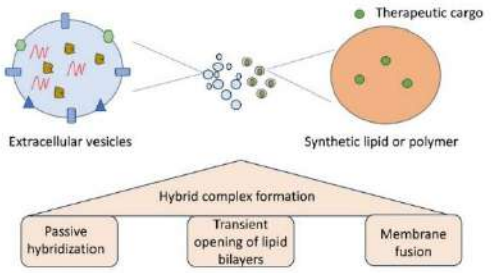

Fig. 7.4 Hybrid Exosome-nanoparticles composites

Conclusion

Exosomes and biomimetic nanoparticles address many limitations associated with conventional therapies for breast cancer making them a transformative frontier in breast cancer. They can mimic natural cell processes as they are made of biological components only which allows them to target specific cells with high specificity, immune evasion and efficient delivery. This nature of exosomes reduces the chances of off-target specificity and hence therapeutic efficacy increases. These nanocarriers are also able to deliver a wide range of cargo materials including nucleic acids, proteins, immunomodulators and most importantly chemotherapeutic agents. Despite of all the advantages offered by these natural bio nanocarriers, challenges regarding isolation, scalability, and standardisation persist. For regulatory assurance, there is need of further clinical studies. Also, due to the heterogeneity of breast cancer and tumor microenvironment, tailored therapy for individual cancer patients is paving the way for individualized therapy. Integration of artificial intelligence, synthetic biology, and bioengineering can be a useful approach in accelerating innovation in this field.

Acknowledgement
The authors would like to express their sincere gratitude to *Deep Science Publisher* and the editorial team of this book for their invaluable support in the final publication process and for providing the opportunity to contribute to this esteemed volume.
Conflicts of Interest
The authors declare that there are no conflicts of interest related to this work.
Funding Source
No funding was received for the preparation of this book chapter.
Author Contribution
All authors have contributed equally to the conception, preparation, and completion of this book chapter.

References

Ahmad, A. (2022). Exosomes in cancer diagnosis and therapy. *International Journal of Molecular Sciences, 23*(17), 9930. *https://doi.org/10.3390/ijms23179930*

Alas, M., Saghaeidehkordi, A., & Kaur, K. (2021). Peptide-drug conjugates with different linkers for cancer therapy. *Journal of Medicinal Chemistry, 64*(1), 216–232. *https://doi.org/10.1021/acs.jmedchem.0c01530*

American Cancer Society. (2024). *Breast cancer facts & figures 2024–2025*. *https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/breast-cancer-facts-and-figures/2024/breast-cancer-facts-and-figures-2024.pdf*

Armstrong, A., Coburn, F., Nsereko, Y., & Al Musaimi, O. (2025). Peptide-drug conjugates: A new hope for cancer. *Journal of Peptide Science, 31*(8), e70040.

Asgari, R., & Rezaie, J. (2021). Differential expression of serum exosomal miRNAs in breast cancer patients and healthy controls. *Advanced Pharmaceutical Bulletin, 12*(4), 858.

Aslan, C., Zolbanin, N. M., Faraji, F., & Jafari, R. (2024). Exosomes for CRISPR-Cas9 delivery: The cutting edge in genome editing. *Molecular Biotechnology, 66*(11), 3092–3116. *https://doi.org/10.1007/s12033-023-00932-7*

Ayala-Mar, S., Donoso-Quezada, J., Gallo-Villanueva, R. C., Perez-Gonzalez, V. H., & González-Valdez, J. (2019). Recent advances and challenges in the recovery and purification of cellular exosomes. *Electrophoresis, 40*(23–24), 3036–3049.

Azmi, A. S., Bao, B., & Sarkar, F. H. (2013). Exosomes in cancer development, metastasis, and drug resistance: A comprehensive review. *Cancer Metastasis Reviews, 32*(3–4), 623–642. *https://doi.org/10.1007/s10555-013-9441-9*

Badawy, A. A., El-Magd, M. A., & AlSadrah, S. A. (2018). Therapeutic effect of camel milk and its exosomes on MCF7 cells in vitro and in vivo. *Integrative Cancer Therapies, 17*(4), 1235–1246. *https://doi.org/10.1177/1534735418786000*

Bardhan, R., Chen, W., Bartels, M., Perez-Torres, C., Botero, M. F., McAninch, R. W., Contreras, A., Schiff, R., Pautler, R. G., Halas, N. J., & Joshi, A. (2010). Tracking of multimodal therapeutic nanocomplexes targeting breast cancer in vivo. *Nano Letters, 10*(12), 4920–4928.

Beh, C. Y., Prajnamitra, R. P., Chen, L. L., & Hsieh, P. C. (2021). Advances in biomimetic nanoparticles for targeted cancer therapy and diagnosis. *Molecules, 26*(16), 5052. *https://doi.org/10.3390/molecules26165052*

Bellanger, M., Zeinomar, N., Tehranifar, P., & Terry, M. B. (2018, June 8). Are global breast cancer incidence and mortality patterns related to country-specific economic development and prevention strategies? *Journal of Global Oncology*. *https://doi.org/10.1200/JGO.18.00006*

Bisht, A., Avinash, D., Sahu, K. K., Patel, P., Das Gupta, G., & Kurmi, B. D. (2025). A comprehensive review on doxorubicin: Mechanisms, toxicity, clinical trials, combination therapies and nanoformulations in breast cancer. *Drug Delivery and Translational Research, 15*(1), 102–133. *https://doi.org/10.1007/s13346-024-01648-0*

Burguin, A., Diorio, C., & Durocher, F. (2021). Breast cancer treatments: Updates and new challenges. *Journal of Personalized Medicine, 11*(8), 808. *https://doi.org/10.3390/jpm11080808*

Cecchin, R., Troyer, Z., Witwer, K., & Morris, K. V. (2023). Extracellular vesicles: The next generation in gene therapy delivery. *Molecular Therapy, 31*(5), 1225–1230.

Chan, M. H., Chang, Z. X., Huang, C. Y., Lee, L. J., Liu, R. S., & Hsiao, M. (2022). Integrated therapy platform of exosomal system: Hybrid inorganic/organic nanoparticles with exosomes for cancer treatment. *Nanoscale Horizons, 7*(4), 352–367.

Choi, H., Choi, Y., Yim, H. Y., Mirzaaghasi, A., Yoo, J. K., & Choi, C. (2021). Biodistribution of exosomes and engineering strategies for targeted delivery of therapeutic exosomes. *Tissue Engineering and Regenerative Medicine, 18*(4), 499–511.

Guo, J., Pan, X., Wu, Q., *et al*. (2025). Bio-barrier-adaptable biomimetic nanomedicines combined with ultrasound for enhanced cancer therapy. *Signal Transduction and Targeted Therapy, 10*, 137. *https://doi.org/10.1038/s41392-025-02217-8*

Hironaka-Mitsuhashi, A., Takayama, S., Jimbo, K., Suto, A., Shimomura, A., & Ochiya, T. (2022). Clinical application of microRNAs in breast cancer treatment. *Archives of Breast Cancer*, 20–31.

Huang, L., Wu, E., Liao, J., Wei, Z., Wang, J., & Chen, Z. (2023). Research advances of engineered exosomes as drug delivery carrier. *ACS Omega, 8*(46), 43374–43387.

International Agency for Research on Cancer. (2020). Global Cancer Observatory. *https://gco.iarc.fr/* (accessed June 1, 2020)

International Agency for Research on Cancer. (2025, February 24). Breast cancer cases and deaths are projected to rise globally (Press release No. 361). *https://www.iarc.who.int/wp-content/uploads/2025/02/pr361_E.pdf*

Issaka, E., & Amu-Darko, J. N. (2025). Biomimetic nanoparticles for cancer therapy: A review of recent advances, applications, and bottlenecks. *Biomedical Materials & Devices, 3*(1), 193–215.

Joshi, R., Lampe, J., Vishwanatha, J. K., & Ranjan, A. P. (2023). Exosome-based hybrid nanosystem for targeted TNBC therapy. *Cancer Research, 83*(7_Supplement), 832.

Kalluri, R., & LeBleu, V. S. (2020). The biology, function, and biomedical applications of exosomes. *Science, 367*(6478), eaau6977. *https://doi.org/10.1126/science.aau6977*

Kim, H. I., Park, J., Zhu, Y., *et al*. (2024). Recent advances in extracellular vesicles for therapeutic cargo delivery. *Experimental & Molecular Medicine, 56*, 836–849. *https://doi.org/10.1038/s12276-024-01201-6*

Kim, J., Harper, A., McCormack, V., Sung, H., Houssami, N., Morgan, E., Mutebi, M., Garvey, G., Soerjomataram, I., & Fidler-Benaoudia, M. M. (2025). Global patterns and trends in breast cancer incidence and mortality across 185 countries. *Nature Medicine, 31*(4), 1154–1162. *https://doi.org/10.1038/s41591-025-03502-3*

Klicka, K., Grzywa, T. M., Mielniczuk, A., Klinke, A., & Włodarski, P. K. (2022). The role of miR-200 family in the regulation of hallmarks of cancer. *Frontiers in Oncology, 12*, 965231.

Kroll, A. V., Fang, R. H., & Zhang, L. (2017). Biointerfacing and applications of cell membrane-coated nanoparticles. *Bioconjugate Chemistry, 28*(1), 23–32.

Kumar, D. N., Chaudhuri, A., Aqil, F., Dehari, D., Munagala, R., Singh, S., Gupta, R. C., & Agrawal, A. K. (2022). Exosomes as emerging drug delivery and diagnostic modality for breast cancer: Recent advances in isolation and application. *Cancers, 14*(6), 1435.

Li, X., Corbett, A. L., Taatizadeh, E., Tasnim, N., Little, J. P., Garnis, C., Daugaard, M., Guns, E., Hoorfar, M., & Li, I. T. S. (2019). Challenges and opportunities in exosome research: Perspectives from biology, engineering, and cancer therapy. *APL Bioengineering, 3*(1), 011503. *https://doi.org/10.1063/1.5087122*

Lim, Z. Z., Li, J. E., Ng, C. T., Yung, L. Y., & Bay, B. H. (2011). Gold nanoparticles in cancer therapy. *Acta Pharmacologica Sinica, 32*(8), 983–990.

Liu, T., Hooda, J., Atkinson, J. M., Whiteside, T. L., Oesterreich, S., & Lee, A. V. (2021). Exosomes in breast cancer—mechanisms of action and clinical potential. *Molecular Cancer Research, 19*(6), 935–945. *https://doi.org/10.1158/1541-7786.MCR-20-0952*

Liu, Z., Ai, K. & Yu, J. (Eds.). (2023). *Nanomaterials and multimodal tumor therapy*. Frontiers Media SA.

Ludwig, N., Whiteside, T. L., & Reichert, T. E. (2019). Challenges in exosome isolation and analysis in health and disease. *International Journal of Molecular Sciences, 20*(19), 4684.

Maia, J., Caja, S., Strano Moraes, M. C., Couto, N., & Costa-Silva, B. (2018). Exosome-based cell-cell communication in the tumor microenvironment. *Frontiers in Cell and Developmental Biology, 6*, 18.

Marshall, S. K., Angsantikul, P., Pang, Z., Nasongkla, N., Hussen, R. S. D., & Thamphiwatana, S. D. (2022). Biomimetic targeted theranostic nanoparticles for breast cancer treatment. *Molecules, 27*(19), 6473. *https://doi.org/10.3390/molecules27196473*

Menon, G., Alkabban, F. M., & Ferguson, T. (2025). Breast cancer. In StatPearls. StatPearls Publishing. *https://www.ncbi.nlm.nih.gov/books/NBK482286/*

Naseri, Z., Oskuee, R. K., Jaafari, M. R., & Forouzandeh Moghadam, M. (2018). Exosome-mediated delivery of functionally active miRNA-142-3p inhibitor reduces tumorigenicity of breast cancer in vitro and in vivo. *International Journal of Nanomedicine, 13*, 7727–7747.

Nordmeier, S., Ke, W., Afonin, K. A., & Portnoy, V. (2021). Exosome mediated delivery of functional nucleic acid nanoparticles (NANPs). In *Therapeutic RNA Nanotechnology* (pp. 539–564). Jenny Stanford Publishing.

Palakurthi, S. S., Shah, B., Kapre, S., Charbe, N., Immanuel, S., Pasham, S., Thalla, M., Jain, A., & Palakurthi, S. (2024). A comprehensive review of challenges and advances in exosome-

based drug delivery systems. *Nanoscale Advances, 6*(23), 5803–5826. *https://doi.org/10.1039/D4NA00501E*

Park, M., Kim, D., Ko, S., Kim, A., Mo, K., & Yoon, H. (2022). Breast cancer metastasis: Mechanisms and therapeutic implications. *International Journal of Molecular Sciences, 23*(12), 6806.

Piombino, C., Mastrolia, I., Omarini, C., Candini, O., Dominici, M., Piacentini, F., & Toss, A. (2021). The role of exosomes in breast cancer diagnosis. *Biomedicines, 9*(3), 312. *https://doi.org/10.3390/biomedicines9030312*

Porter, P. (2008). "Westernizing" women's risks? Breast cancer in lower-income countries. *New England Journal of Medicine, 358*(3), 213. *https://doi.org/10.1056/NEJMp0708138*

Qiu, P., Yu, X., Zheng, F., Gu, X., Huang, Q., Qin, K., Hu, Y., Liu, B., Xu, T., Zhang, T., & Chen, G. (2025). Advancements in liquid biopsy for breast cancer: Molecular biomarkers and clinical applications. *Cancer Treatment Reviews*, 102979.

Raikwar, S., Jain, A., Saraf, S., Bidla, P. D., Panda, P. K., Tiwari, A., Verma, A., & Jain, S. K. (2022). Opportunities in combinational chemo-immunotherapy for breast cancer using nanotechnology: An emerging landscape. *Expert Opinion on Drug Delivery, 19*(3), 247–268.

Rhim, J., Baek, W., Seo, Y., & Kim, J. H. (2022). From molecular mechanisms to therapeutics: Understanding microRNA-21 in cancer. *Cells, 11*(18), 2791. *https://doi.org/10.3390/cells11182791*

Rontogianni, S., Synadaki, E., Li, B., Liefaard, M. C., Lips, E. H., Wesseling, J., Wu, W., & Altelaar, M. (2019). Proteomic profiling of extracellular vesicles allows for human breast cancer subtyping. *Communications Biology, 2*, 325. *https://doi.org/10.1038/s42003-019-0570-8*

Salata, C., de Almeida, C. E., Ferreira-Machado, S. C., Barroso, R. C., Nogueira, L. P., Mantuano, A., Pickler, A., Mota, C. L., & de Andrade, C. B. V. (2021). Preliminary pre-clinical studies on the side effects of breast cancer treatment. *International Journal of Radiation Biology, 97*(7), 877–887. *https://doi.org/10.1080/09553002.2021.1919782*

Shih, C. P., Tang, X., Kuo, C. W., Chueh, D. Y., & Chen, P. (2022). Design principles of bioinspired interfaces for biomedical applications in therapeutics and imaging. *Frontiers in Chemistry, 10*, 990171. *https://doi.org/10.3389/fchem.2022.990171*

Shtam, T., Naryzhny, S., Samsonov, R., Karasik, D., Mizgirev, I., Kopylov, A., Petrenko, E., Zabrodskaya, Y., Kamyshinsky, R., Nikitin, D., & Sorokin, M. (2019). Plasma exosomes stimulate breast cancer metastasis through surface interactions and activation of FAK signaling. *Breast Cancer Research and Treatment, 174*(1), 129–141.

Siegel, R. L., Miller, K. D., Fuchs, H. E., & Jemal, A. (2021). Cancer statistics, 2021. *CA: A Cancer Journal for Clinicians, 71*(1), 7–33.

Smolarz, B., Nowak, A. Z., & Romanowicz, H. (2022). Breast cancer—epidemiology, classification, pathogenesis and treatment (review of literature). *Cancers, 14*(10), 2569.

Soltanmohammadi, F., Gharehbaba, A. M., Zangi, A. R., Adibkia, K., & Javadzadeh, Y. (2024). Current knowledge of hybrid nanoplatforms composed of exosomes and organic/inorganic nanoparticles for disease treatment and cell/tissue imaging. *Biomedicine & Pharmacotherapy, 178*, 117248.

Sun, W. Y., Lee, D. S., Park, J. H., Kim, O. H., Choi, H. J., & Kim, S. J. (2025). Utilizing miR-34a-loaded HER2-targeting exosomes to improve breast cancer treatment: Insights from an animal model. *Journal of Breast Cancer, 28*(3), 139–157. *https://doi.org/10.4048/jbc.2024.0262*

Thuault, S., Ghossoub, R., David, G., & Zimmermann, P. (2022). A journey on extracellular vesicles for matrix metalloproteinases: A mechanistic perspective. *Frontiers in Cell and Developmental Biology, 10*, 886381.

Tian, Y., Li, S., Song, J., Ji, T., Zhu, M., Anderson, G. J., Wei, J., & Nie, G. (2014). A doxorubicin delivery platform using engineered natural membrane vesicle exosomes for targeted tumor therapy. *Biomaterials, 35*(7), 2383–2390. *https://doi.org/10.1016/j.biomaterials.2013.11.083*

Tong, L., Zhang, S., Huang, R., Yi, H., & Wang, J. W. (2022). Extracellular vesicles as a novel photosensitive drug delivery system for enhanced photodynamic therapy. *Frontiers in Bioengineering and Biotechnology, 10*, 1032318.

Wang, J., & Wu, S. G. (2023). Breast cancer: an overview of current therapeutic strategies, challenge, and perspectives. *Breast Cancer: Targets and Therapy*, 721-730.

Wang, L., Zhou, X., Zou, W., *et al*. (2020). Exosomes containing miRNAs targeting HER2 synthesis and engineered to adhere to HER2 on tumor cells surface exhibit enhanced antitumor activity. *Journal of Nanobiotechnology, 18*, 153. *https://doi.org/10.1186/s12951-020-00711-5*

Wang, M., Liu, J., Xia, M., Yin, L., Zhang, L., Liu, X., & Cheng, Y. (2024). Peptide-drug conjugates: A new paradigm for targeted cancer therapy. *European Journal of Medicinal Chemistry, 265*, 116119.

Wang, X., Sun, C., Huang, X., Li, J., Fu, Z., Li, W., & Yin, Y. (2021). The advancing roles of exosomes in breast cancer. *Frontiers in Cell and Developmental Biology, 9*, 731062.

Weaver, J. W., Zhang, J., Rojas, J., Musich, P. R., Yao, Z., & Jiang, Y. (2022). The application of exosomes in the treatment of triple-negative breast cancer. *Frontiers in Molecular Biosciences, 9*, 1022725.

Wu, X. (2020). Expressions of miR-21 and miR-210 in breast cancer and their predictive values for prognosis. *Iranian Journal of Public Health, 49*(1), 21–29.

Xie, X., Lian, S., Zhou, Y., Li, B., Lu, Y., Yeung, I., & Jia, L. (2021). Tumor-derived exosomes can specifically prevent cancer metastatic organotropism. *Journal of Controlled Release, 331*, 404–415.

Xiong, X., Zheng, L. W., Ding, Y., *et al*. (2025). Breast cancer: Pathogenesis and treatments. *Signal Transduction and Targeted Therapy, 10*, 49. *https://doi.org/10.1038/s41392-024-02108-4*

Yang, D., Zhang, L., Ni, J., Ding, Y., Razzaq, A., Khan, Z. U., Iqbal, H., Alanazi, Y. F., Khan, N. U., & Wang, R. (2024). Stimuli-sensitive biomimetic nanoparticles for the inhibition of breast cancer recurrence and pulmonary metastasis. *International Journal of Pharmaceutics: X, 7*, 100252. *https://doi.org/10.1016/j.ijpx.2024.100252*

Yin, Z., Yu, M., Ma, T., Zhang, C., Huang, S., Karimzadeh, M. R., Momtazi-Borojeni, A. A., & Chen, S. (2021). Mechanisms underlying low-clinical responses to PD-1/PD-L1 blocking antibodies in immunotherapy of cancer: A key role of exosomal PD-L1. *Journal of Immunotherapy of Cancer, 9*(1), e001698. *https://doi.org/10.1136/jitc-2020-001698*

Yu, H., Wu, M., Chen, S., Song, M., & Yue, Y. (2022). Biomimetic nanoparticles for tumor immunotherapy. *Frontiers in Bioengineering and Biotechnology, 10*, 989881. *https://doi.org/10.3389/fbioe.2022.989881*

Yuan, X., Qian, N., Ling, S., Li, Y., Sun, W., Li, J., Du, R., *et al*. (2021). Breast cancer exosomes contribute to pre-metastatic niche formation and promote bone metastasis of tumor cells. *Theranostics, 11*(3), 1429–1445. *https://doi.org/10.7150/thno.45351*

Zeng, M., Hu, C., Chen, T., Zhao, T., & Dai, X. (2025). Advancements in cell membrane-derived biomimetic nanotherapeutics for breast cancer. *International Journal of Nanomedicine, 20*, 6059–6083. *https://doi.org/10.2147/IJN.S502144*

Zha, Q. B., Yao, Y. F., Ren, Z. J., Li, X. J., & Tang, J. H. (2017). Extracellular vesicles: An overview of biogenesis, function, and role in breast cancer. *Tumor Biology, 39*(2). *https://doi.org/10.1177/1010428317691182*

Zhang, L., & Yu, D. (2019). Exosomes in cancer development, metastasis, and immunity. *Biochimica et Biophysica Acta - Reviews on Cancer, 1871*(2), 455–468. *https://doi.org/10.1016/j.bbcan.2019.04.004*

Zhang, S., Zhang, X., Gao, H., Zhang, X., Sun, L., Huang, Y., Zhang, J., & Ding, B. (2024). Cell membrane-coated biomimetic nanoparticles in cancer treatment. *Pharmaceutics, 16*(4), 531. *https://doi.org/10.3390/pharmaceutics16040531*

Zhao, Y., Liu, L., Sun, R., Cui, G., Guo, S., Han, S., Li, Z., Bai, T., & Teng, L. (2022). Exosomes in cancer immunoediting and immunotherapy. *Asian Journal of Pharmaceutical Sciences, 17*(2), 193–205. *https://doi.org/10.1016/j.ajps.2021.12.001*

Zheng, Q., Zhang, M., Zhou, F., Zhang, L., & Meng, X. (2021). The breast cancer stem cells traits and drug resistance. *Frontiers in Pharmacology, 11*, 599965.

Zhou, X., Xie, F., Wang, L., *et al*. (2020). The function and clinical application of extracellular vesicles in innate immune regulation. *Cellular & Molecular Immunology, 17*, 323–334. *https://doi.org/10.1038/s41423-020-0391-1*

Zuo, L., Tao, H., Xu, H., Li, C., Qiao, G., Guo, M., Cao, S., & Liu, M. (2020). Exosomes-coated miR-34a displays potent antitumor activity in pancreatic cancer both in vitro and in vivo. *Drug Design, Development and Therapy, 14*, 3495–3507. *https://doi.org/10.2147/DDDT.S265423*