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Unveiling the Role of Exosomes and microRNAs in Cancer Biology by Sparking Breast Cancer; An Editorial Perspective on the Horizon of Precision Oncology

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This review highlights recent advances in understanding the roles of non-coding RNAs, particularly microRNAs (miRNAs), and extracellular vesicles, such as exosomes, in cancer biology. These molecules are central to intercellular communication, tumorigenesis, metastasis, and therapeutic resistance. Exosomes, nanoscale vesicles secreted by cells, carry oncogenic cargos that reshape distant microenvironments, suppress immunity, and promote metastasis. Breast cancer (BC), the most common cancer among women, serves as a model for exploring exosome-based diagnostics, therapeutics, and biological insights.

miRNAs, small non-coding RNAs, regulate gene expression post-transcriptionally and act as tumor suppressors or oncogenes depending on their targets. For example, miR-320a and miR-142 inhibit BC progression, while miR-21 promotes metastasis. Encapsulated within exosomes, miRNAs serve as biomarkers and functional effectors. Exosomal miRNAs like miR-21, miR-155, and miR-10b are upregulated in BC patients and correlate with tumor stage and prognosis. Unique miRNA fingerprints in circulating exosomes also help distinguish BC subtypes (e.g., luminal, triple-negative, HER2-positive) via liquid biopsies.

Exosomes facilitate intercellular communication by transferring cargo, including miRNAs, to recipient cells, modulating the tumor microenvironment (TME). Engineered exosomes show promise in delivering tumor-suppressive miRNAs to reverse epithelial-mesenchymal transition (EMT), restore chemosensitivity, and reactivate immune surveillance. Beyond biomarkers, exosomes act as dynamic ecosystem engineers by transforming fibroblasts into cancer-associated fibroblasts (CAFs) and polarizing macrophages toward immunosuppressive phenotypes.

Clinically, exosome-based liquid biopsies enable real-time monitoring of treatment response and early relapse detection. Exosome-based vaccines and engineered exosomes as nanocarriers for targeted drug delivery represent revolutionary approaches. Challenges remain in standardizing isolation methods, scaling production, and addressing regulatory and ethical concerns. Nevertheless, exosomes hold immense potential for precision medicine, offering innovative diagnostic tools and therapies in oncology.

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INTRODUCTION

The field of cancer research has rapidly advanced in recent years, particularly in understanding the critical roles of non-coding RNAs (such as microRNAs (miRNAs)) and extracellular vesicles (such as exosomes). These molecules are the key players in intercellular communication, tumorigenesis, metastasis, and even therapeutic resistance. Several articles have been published in the Multidisciplinary Cancer Investigation (MCI) journal to shed light on various aspects of miRNA biology and their possible applications in cancer progression. These studies have also yielded compelling insights for further exploration of their functional mechanisms.

Exosomes and Cancer Intelligence

Exosomes are nanoscale extracellular vesicles that are secreted as cellular debris. They have a lot of applications in therapy, diagnosis, and prognosis of cancer, such as colorectal cancer [1], pancreatic ductal adenocarcinoma (PDAC) [2], renal cell carcinoma (RCC) [3], glioblastoma [4], and multiple myeloma (MM) [5]. Depending on the cellular source from which the exosomes were secreted, they can have different characteristics because they are the same as their parent cell but lack a nucleus. For example, exosomes derived from natural killer (NK) cells can have a cytotoxic property similar to that of NK cells and ultimately act naturally in the immune system [6]. Studies on these cancers agree on the fact that exosomes carry oncogenic cargos that can reshape distant niches, suppress immunity, confer drug resistance, and prepare new sites for metastasis by switching off immune cells. Since cancer cells especially produce and release these messenger particles in unusually large amounts, it could be ideal to decode the universal language of exosomal signaling. Contemporary, exosomes are recognized as master regulators of intercellular communication, modulation of tumor microenvironment (TME), and systemic propagation of disease. Out of all the cancers that are influenced by exosomes, breast cancer (BC) has played a pivotal role in proving the applicability of exosome-based diagnostics, therapeutics, and biological insight. BC is the most common cancer and the second leading cause of death among women. It is one of the most challenging diseases in oncology due to its biological complexity, heterogeneity, and intricate molecular interactions. This disease results from disruptions in regulatory gene and protein networks, which could lead to profound alterations in cellular processes such as proliferation, differentiation, apoptosis, invasion, and metastasis. Among these factors, miRNAs and gene interaction networks play a critical role in the development and progression of breast cancer. These findings unveil the intricate regulatory networks governed by miRNAs in maintaining cellular homeostasis and preventing malignant transformation. It's noteworthy that breast cancer is not merely a passive recipient of exosomal influence; on the contrary, it exhibits a cascade of exosome-mediated reprogramming that can illuminate broader principles in cancer biology, especially via miRNAs.

The miRNAs: From Diagnosis to Therapy

MicroRNAs are small, non-coding RNA molecules that post-transcriptionally regulate gene expression. They often act as tumor suppressors or oncogenic microRNAs (oncomiRs), depending on their target mRNAs. Janghorban et al. predicted that hsa-miR-320a acts as a tumor suppressor miRNA. It prevents the activation of several genes that are involved in the process of cell growth and proliferation-related pathways in breast cancer. [7]. MiR-142 has been demonstrated to play a critical role in inhibiting cell growth, migration, invasion, and metastasis by targeting various genes and pathways. [8]. OmcomiRs have also been shown to promote cell proliferation, metastasis, and tumor progression in BC. In this regard, Ghebati-Maleki mentioned miR-21, which acts as an immunosuppressive and pro-metastatic moiety in BC [9]. In another study, Sedighi et al. identified a novel miRNA within the SNHG21 locus, emphasizing the importance of bioinformatics and experimental validation in discovering new miRNAs with potential roles in cancer [10].

MicroRNAs encapsulated within exosomes can serve as both biomarkers and functional effectors. Exosomal miR-21, miR-155, miR-10b, and miR-1246 are shown to be consistently upregulated in the

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serum of BC patients. These observations could be correlated with tumor stage, metastasis, and poor prognosis. However, aside from the generic exosomal miRNAs of BCs, the tumour's hormone-receptor (ER/PR) and HER2 status can leave a unique "extra" miRNA fingerprint in circulating exosomes; detection of this non-miRNA fingerprint can allow clinicians to distinguish luminal, triple-negative, or HER2-positive subtypes of BC from a simple blood test instead of a tissue biopsy [11].

A Spark in the Dark: The relationship between miRNAs and Exosomes

As mentioned, exosomes facilitate intercellular communication by transferring their cargo to recipient cells, thereby modulating the TME. But the true frontier in possible exosome application lies in their potential for therapeutic reprogramming. Similar to mesenchymal stem cell (MSC)-derived exosomes, which carry miR-375 or miR-146b, can suppress glioma growth [4] and inhibit renal carcinoma proliferation [3]. Exosomes have already been engineered in preclinical models to deliver tumor-suppressive miRNAs (e.g., let-7a, miR-34a, and miR-200c) to breast tumors. These exosomes can reverse epithelial-mesenchymal transition (EMT), restore chemosensitivity, and reactivate immune surveillance. Moreover, exosomes excreted by breast cancer stem cells (BCSTs) can deliver specific long non-coding and circular RNAs (lncRNAs) (e.g., H19, MALAT1) to preserve stem-cell properties and induce relapse. This mechanism has also been observed in glioblastoma and colorectal tumors [1, 4]. This shared behavior highlights a core principle that exosomes carry the essential programs of malignancy, and BC offers the most accessible system to decipher them.

The connection of miRNAs and extracellular vesicles is very complex, as these vesicles act as "protective carriers" and protect miRNAs from degradation by enzymes in the extracellular space (such as RNase). The miRNAs, which are packaged inside exosomes, are referred to as exosomal microRNAs or exomiRs. More profoundly, exosomal miRNAs are not mere passengers, and they could act as biological drivers. For instance, exosomal miR-122 from BC cells can reprogram stromal metabolism in pre-metastatic niches by suppression of glucose uptake in non-tumor cells. This effectively "starves" the microenvironment to favor cancer cell colonization, similar to the way glioblastoma reprograms metabolism through exosomal miR-1246 [4]. However, this is usually less common due to the high sensitivity of miRNAs to degradation. Although modulation of the TME is not explicitly mentioned in the studies discussed here, the role of exosomes in the transport of miRNAs is implied through their capacity to affect distant tissues and promote metastasis. For example, Bhat et al. explored the diagnostic utility of miRNAs in various cancers, indirectly pointing to their presence in bodily fluids via exosomal transport [12]. Moreover, the dysregulation of specific miRNAs has been linked to cancer progression and prognosis. Indeed, dysregulation of miRNAs has been investigated in various cancers, demonstrating their potential as biomarkers and therapeutic targets. Identification of miRNA signatures associated with specific cancer types provides a promising avenue for personalized medicine, enabling more precise diagnosis and treatment strategies.

Beyond Biomarkers: Exosomes as Dynamic Ecosystem Engineers

BC exosomes do more than shuttle miRNAs, and they orchestrate ecosystems. They can transform fibroblasts into cancer-associated fibroblasts (CAFs), polarize macrophages toward immunosuppressive M2 phenotypes, and even impair dendritic cell maturation. Interestingly, paralleling mechanisms have been observed in MM and PDAC. [2, 5]. These exosomes have been shown to carry immune checkpoint ligands like PD-L1 that can directly induce T-cell exhaustion. This discovery can redefine the resistance to immunotherapy. The spark ignited by BC in exosome research is not isolated; on contrary, it is catalytic. Lessons from RCC (exosomal caveolin-1) [3], PDAC (adrenomedullin-induced diabetes) [2], MM (heparanase-driven exosome secretion) [5], and glioblastoma (hypoxia-induced miR-301a) all feed into a unified framework for understanding exosomal pathobiology [4]. Conversely, innovations in breast cancer—such as exosome barcoding, single-vesicle profiling, and miRNA circuit engineering—will radiate outward, transforming oncology as a whole.

The Clinical Horizon: Liquid Biopsies, Vaccines,

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and Smart Nanocarriers

The future of BC management could be revolutionized by novel exosome-based clinical approaches. Exosome-based liquid biopsies now enable real-time monitoring of treatment response, minimal residual disease, and early relapse—far surpassing the sensitivity of CA15-3 or CEA. Platforms detecting GPC1+ exosomes (pioneered in pancreatic cancer [2]) or CD24+/EpCAM+ vesicles are being adapted for breast cancer subtyping and early detection. Even more revolutionary is the rise of exosome-based vaccines. Dendritic cell-derived exosomes (DEXs) loaded with breast tumor antigens (e.g., HER2, MUC1, NY-ESO-1) can elicit potent, durable T-cell responses—building on successes in melanoma and MM [5]. When combined with immune adjuvants (e.g., IL-12, STING agonists), these acellular vaccines may overcome the immunologically "cold" nature of many breast tumors. Finally, engineered exosomes are emerging as next-generation nanocarriers. Surface-modified with HER2-targeting affibodies or iRGD peptides, they deliver chemotherapeutics, siRNAs, or CRISPR components directly to tumor cells—bypassing multidrug resistance and minimizing off-target toxicity. Their natural biocompatibility and blood–brain barrier penetration (demonstrated in glioblastoma models [4]) also position them to tackle brain metastases, a devastating complication in HER2+ and triple-negative breast cancer.

CONCLUSION

In conclusion, the contributions from these studies collectively enhance our understanding of how miRNAs and exosomes interact to influence cancer biology. Future research should focus on elucidating the precise mechanisms by which exosomes deliver miRNAs to target cells and how this process can be harnessed for clinical applications. As we continue to unravel the complexities of these molecular interactions, the potential for developing innovative diagnostic tools and targeted therapies becomes increasingly tangible. BC has long been a bellwether in oncology. Today, investigations on BC treatment pave the way for cancer treatment by studying exosomes and their miRNAs, and they shed light on the very architecture of cancer communication. Yet challenges such as standardization of isolation, scalability of production, regulatory pathways for engineered exosomes, and ethical frameworks for data-rich liquid biopsies remain to be dealt with in the future. These limitations demand interdisciplinary convergence between oncologists, bioengineers, AI specialists, and regulatory scientists. As we stand at the threshold of exosome-augmented precision medicine, one truth is clear: the smallest vesicles carry the largest promise. And in their cargo, we may finally decode the language of cancer and learn to speak back.

CONFLICT OF INTEREST

The author declare that they have no conflict of interest.

ETHICS APPROVAL

Not applicable.

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