International Journal of Biology and Life Sciences
ISSN: 2957-9511 | Vol. 13, No. 3, 2026

Advances in the Application of Exosomes in the Treatment of Gynecological Malignant Tumors

Xinyun Huang [1, a], Hongkai Shang [2, *]

[1] School of Medicine, Zhejiang University, Hangzhou, Zhejiang, 310058, China
[2] Affiliated Hangzhou First People's Hospital, School of Medicine, Westlake University, Hangzhou, Zhejiang, 310006, China
*** Corresponding author:** Hongkai Shang (Email: 15990032799@aliyun.com), [a] hxyazy1902@163.com

Abstract: Exosomes are nanoscale vesicles with diameters ranging from 30 to 150 nm, widely present in human body fluids and cell culture supernatants. They can carry various bioactive substances such as proteins, nucleic acids, and lipids, mediating intercellular communication and material exchange by targeting and delivering signaling molecules, thereby regulating the physiological functions of recipient cells. In recent years, exosome research in gynecological malignancies has garnered significant attention. They not only participate in tumor initiation, progression, invasion, and metastasis by reshaping the tumor microenvironment, mediating immune evasion, and regulating drug resistance, but also demonstrate immense potential as novel therapeutic targets and drug delivery vehicles in tumor diagnosis, treatment, and prognosis assessment. This review begins with the biological characteristics of exosomes and their regulatory mechanisms in tumors, focusing on their current applications in treating gynecological malignancies such as cervical cancer, ovarian cancer, and endometrial cancer. It systematically analyzes existing challenges in exosome isolation and purification, targeted delivery, and clinical translation, while outlining future development directions. The aim is to provide novel insights and strategies for the clinical management of gynecological malignancies.

Keywords: Exosomes; Gynecological Malignancies; Cervical Cancer; Ovarian Cancer; Endometrial Cancer; Therapeutic Applications.

1. Introduction

Gynecological malignancies pose a significant threat to women's health, primarily encompassing cervical cancer, ovarian cancer, and endometrial cancer [1]. These diseases often present with subtle early symptoms and lack specific diagnostic markers, leading to most patients receiving a diagnosis at an intermediate or advanced stage, thereby missing the optimal window for surgical intervention. Despite continuous advancements and refinements in traditional treatments like surgical resection combined with chemotherapy and radiotherapy, significant challenges persist. These include multidrug resistance to chemotherapy agents and radiation-induced tissue damage from radiotherapy, severely limiting improvements in clinical outcomes. Consequently, patient prognosis remains poor, with five-year survival rates struggling to achieve breakthrough increases[2]. Therefore, identifying novel therapeutic targets and exploring highly effective, low-toxicity treatment strategies have become key research priorities in the field of gynecological malignancies.

Exosomes, as crucial carriers of intercellular communication, are nanoscale membrane vesicles secreted by cells. They can transport various bioactive substances including proteins, nucleic acids, and lipids. Their roles in tumor microenvironment remodeling, immune regulation, and drug delivery are increasingly being elucidated, offering new avenues for precision treatment of gynecological malignancies[3]. Recent studies have confirmed that exosomes can serve as therapeutic targets or delivery vehicles, playing crucial roles in reversing drug resistance and enhancing immunotherapy efficacy. For instance, tumor-derived exosomes regulate target cell functions by transferring specific miRNAs, promoting tumor angiogenesis and metastasis. Engineered exosomes, meanwhile, enable targeted delivery of chemotherapeutic agents or gene therapy formulations, achieving precise tumor cell elimination. This review summarizes the progress of exosome applications in gynecological malignancy treatment, systematically organizing research findings in targeted therapy, drug delivery, and immune modulation to provide reference for related basic research and clinical translation.

2. Overview of Exosomes

Exosomes are vesicular structures released from cells following fusion of intracellular multivesicular bodies with the plasma membrane. Nearly all cell types can secrete exosomes. First identified in sheep reticulocytes in 1983, exosomes were initially considered a means for cells to expel metabolic waste[4]. Subsequent research revealed their complex biological functions. The bioactive substances they carry—including proteins, mRNA, miRNA, and lncRNA—enable intercellular signaling and regulation of recipient cell physiology[5][6].

The exosome formation process primarily involves the following steps: early endosome formation, assembly of the endosomal sorting complex, multivesicular body formation and maturation, and final fusion with the plasma membrane for exosome release. Exosomes bear specific surface markers, such as the quadrimembrane proteins CD63, CD81, and CD9, along with proteins like TSG101 and Alix. These markers are commonly used for exosome isolation and identification[7]. Current exosome isolation methods include ultracentrifugation, density gradient centrifugation, immunomagnetic bead separation, and ultrafiltration, each exhibiting distinct advantages and limitations regarding purity and recovery rates[8]. Exosomes possess high stability, excellent biocompatibility, and the ability to traverse biological barriers, characteristics that confer unique advantages for disease diagnosis and treatment.

3. Regulatory Mechanisms of Exosomes in Tumors

Exosomes play a dual role in tumorigenesis and progression: they can promote tumor proliferation, invasion, and metastasis while also participating in the body's antitumor immune response. Their regulatory mechanisms are primarily manifested in the following aspects.

First, exosomes mediate the remodeling of the tumor microenvironment. Exosomes secreted by tumor cells can carry proangiogenic factors, such as vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF), which act on endothelial cells surrounding the tumor, promoting the formation of new blood vessels to supply nutrients and oxygen for tumor growth[9]. Concurrently, exosomes can induce fibroblasts to transform into cancer-associated fibroblasts (CAFs). These CAFs secrete abundant cytokines and matrix metalloproteinases (MMPs), disrupting the extracellular matrix structure and enhancing tumor cell invasion and metastasis[10].Additionally, tumor-derived exosomes can regulate acid-base balance within the tumor microenvironment. By transferring proton pump-related proteins, they enhance tumor cells' tolerance to acidic conditions while simultaneously suppressing immune cell activity, thereby further creating a local environment conducive to tumor proliferation.

Second, exosomes contribute to tumor immune evasion. Tumor-derived exosomes suppress T cell and NK cell proliferation and activation by transmitting inhibitory signals such as PD-L1 and TGF-β, while simultaneously promoting the differentiation of regulatory T cells, thereby weakening the body's antitumor immune response[11]. Furthermore, exosomes can induce macrophage polarization toward the M2 phenotype, enhancing their pro-tumor effects. Some studies have demonstrated that tumor exosomes can carry tumor antigens and deliver them to dendritic cells, yet simultaneously impede the maturation and antigen-presenting functions of these cells, thereby preventing the body from effectively initiating specific immune responses. Concurrently, miRNA transfer mediated by exosomes can directly target key genes in immune cells, disrupting the transmission of immune signaling pathways and further exacerbating immune escape[12].

Furthermore, exosomes regulate drug resistance in tumor cells. Exosomes secreted by tumor cells can transfer drug resistance-associated proteins or nucleic acids to sensitive cells, conferring a drug-resistant phenotype. Simultaneously, exosome-mediated intercellular communication activates signaling pathways such as PI3K/Akt and MAPK, regulating tumor cell apoptosis and proliferation to further enhance drug resistance[13][14]. In addition, exosomes can promote the efflux of chemotherapy drugs from tumor cells by delivering members of the ABC transporter family, thereby enhancing the efficiency of drug pumping out of tumor cells and reducing intracellular drug concentrations. Some exosomes can also regulate the autophagy levels of tumor cells, helping them survive under drug stress by enhancing autophagy activity to clear drug-induced damaged proteins and organelles[15].

Finally, exosomes drive distant metastasis of tumors. Tumor-derived exosomes can reach distant organs via the bloodstream and lymphatic system, preemptively "remodeling" the target organ microenvironment to create a pre-metastatic niche conducive to tumor cell colonization. These exosomes induce permeability changes in target organ endothelial cells, promoting tumor cell adhesion and infiltration. Simultaneously, molecules such as integrins carried by exosomes can specifically bind to cell surface receptors on target organs, precisely mediating the directed migration of tumor cells and thereby driving the formation and growth of metastatic lesions.

4. Applications of Exosomes in Gynecological Malignant Tumor Therapy

The application of exosomes in the treatment of gynecological malignancies primarily follows two approaches: first, targeting exosomes themselves as therapeutic targets by inhibiting their secretion or blocking their signaling pathways to suppress tumor progression at its source; second, utilizing exosomes as drug delivery vehicles, leveraging their inherent cell targeting capabilities and biocompatibility to achieve precision therapy for tumors. The following sections will discuss the specific applications and research progress of exosomes in treating three types of gynecological malignancies—cervical cancer, ovarian cancer, and endometrial cancer—based on their respective disease characteristics.

4.1. Application of Exosomes in Cervical Cancer Treatment

Cervical cancer ranks among the most common gynecological malignancies, with persistent infection by high-risk human papillomavirus (HPV) serving as its primary pathogenic factor, posing a severe threat to women's health worldwide. In recent years, the regulatory role of exosomes in cervical cancer development and treatment has emerged as a research hotspot. Research has revealed that exosomes secreted by cervical cancer cells can specifically carry oncogenic proteins such as HPV E6 and E7. Upon delivery to surrounding normal cells or stromal cells, these proteins activate downstream pro-proliferative and pro-invasive signaling pathways, thereby inducing malignant transformation. Concurrently, they promote the remodeling of the tumor microenvironment, accelerating tumor proliferation and distant metastasis[16]. Therefore, inhibiting the secretion of cervical cancer cell-derived exosomes or clearing circulating exosomes has emerged as a potential therapeutic strategy to block tumor progression.

One study significantly reduced exosome secretion from cervical cancer cells by interfering with key proteins in the endosomal sorting complex, simultaneously inhibiting both in vitro invasion and in vivo metastasis of tumor cells[17]. Furthermore, exosomes can serve as carriers for immunotherapy, enhancing antitumor immune responses. For instance, loading dendritic cell-derived exosomes with HPV antigens activated specific T-cell immunity, significantly inhibiting tumor growth in a mouse cervical cancer model[18].

4.2. Applications of Exosomes in Ovarian Cancer Treatment

Ovarian cancer is the most lethal type of gynecological malignancy. Due to its concealed location and lack of specific clinical symptoms in the early stages, approximately 70% of patients are diagnosed at an advanced stage, missing the opportunity for curative surgery. The application of exosomes in ovarian cancer treatment primarily focuses on two core directions: targeted drug delivery and reversal of chemotherapy resistance. Chemotherapy resistance in ovarian cancer poses a major clinical challenge. Multiple studies confirm that ovarian cancer cell-derived exosomes can regulate apoptosis-related gene expression in target cells by delivering pro-cancer microRNAs such as miR-21 and miR-155. This activates downstream signaling pathways like PI3K/AKT, ultimately inducing tumor cell resistance to first-line chemotherapeutic agents like paclitaxel and cisplatin[19]. Therefore, blocking exosome transmission can effectively reverse drug resistance.

Studies treating drug-resistant ovarian cancer cells with exosome inhibitors demonstrated significantly enhanced sensitivity to paclitaxel and markedly increased tumor cell apoptosis[20]. Concurrently, exosomes offer unique advantages as drug delivery vehicles, capable of penetrating the blood-peritoneal barrier to target ovarian cancer cells. For instance, encapsulating the chemotherapy drug doxorubicin within mesenchymal stem cell-derived exosomes and administering them intravenously resulted in enrichment within ovarian cancer tissues. This approach significantly enhanced therapeutic efficacy while reducing drug toxicity to normal tissues[21].

4.3. Application of Exosomes in Endometrial Cancer Treatment

Endometrial cancer is a malignant tumor originating from the endometrial epithelium, with its incidence showing an upward trend year by year. Although research on exosomes in endometrial cancer treatment remains relatively scarce, it has demonstrated promising application prospects. Research indicates that exosomes secreted by endometrial carcinoma cells can carry miR-10b, regulating target gene expression and promoting tumor cell invasion and metastasis[22]. Suppressing the expression of miR-10b in exosomes significantly reduces the malignant phenotype of tumor cells.

Furthermore, exosomes can be utilized in combination therapies for endometrial cancer. For instance, loading the immune checkpoint inhibitor PD-1 antibody onto exosomes enables targeted delivery to tumor tissues, enhancing T-cell antitumor activity while reducing systemic side effects[23]. Animal studies confirm that this combination therapy significantly inhibits endometrial cancer growth and prolongs mouse survival.

To visually illustrate the application strategies and efficacy of exosomes in treating various gynecological malignancies, this paper compiles recent research findings as shown in Table 1.

Table 1. Application Strategies and Efficacy of Exosomes in Treating Different Gynecological Malignancies

Tumor Type	Exosome Source	Treatment Strategy	Experimental Results	Reference
Cervical Cancer	Cervical Cancer Cells	Inhibition of exosome secretion via endosomal sorting complex disruption	Reduced tumor cell invasion in vitro and metastasis in vivo	[17]
Cervical Cancer	Dendritic Cells	Exosome vaccine loaded with HPV antigens	Activated specific T-cell immunity, inhibited tumor growth in mice	[18]
Ovarian Cancer	Ovarian Cancer Cells	Exosome Inhibitor Blocking Drug-Resistance-Related Molecular Signaling	Reversed Paclitaxel Resistance and Increased Tumor Cell Apoptosis Rate	[20]
Ovarian Cancer	Mesenchymal Stem Cells	Doxorubicin-Loaded Targeted Delivery	Drug Enrichment in Tumor Tissue Enhanced Therapeutic Efficacy	[21]
Endometrial cancer	Endometrial cancer cells	Inhibition of exosomal miR-10b expression	Reduces tumor cell invasion and metastasis	[22]
Endometrial cancer	Engineered exosomes	Loading PD-1 antibodies for combined immunotherapy	Enhances T cell activity, prolongs mouse survival	[23]

5. Conclusion and Outlook

In summary, exosomes, as multifunctional intercellular communication carriers, play a pivotal regulatory role in the initiation and progression of gynecological malignancies. They promote tumor advancement by reshaping the tumor microenvironment, mediating immune evasion, and regulating drug resistance, while also serving as therapeutic targets and drug delivery vehicles, offering novel therapeutic avenues for gynecological cancers. Current studies on cervical, ovarian, and endometrial cancers have demonstrated that strategies such as inhibiting tumor cell exosome secretion, blocking exosome-mediated signaling, and developing exosome-targeted drug delivery systems can effectively suppress tumor proliferation and metastasis, reverse chemotherapy resistance, and enhance antitumor immune responses, showing promising clinical application potential.

However, research and application of exosomes in gynecological malignancy treatment remain in the exploratory phase, with numerous critical issues requiring resolution. First, exosome isolation and purification techniques require optimization. Existing methods like ultracentrifugation and density gradient centrifugation struggle to achieve both high purity and high recovery rates simultaneously. Furthermore, varying isolation and identification standards among research teams, coupled with the absence of standardized operational protocols, severely limit the reproducibility of research findings and the comparability of multi-center data. Second, the efficiency and specificity of exosome targeted delivery require improvement. Natural exosomes exhibit weaknesses such as poor targeting and susceptibility to clearance by the reticuloendothelial system. How to achieve precise recognition and enrichment of gynecological malignant tumor tissues through surface modification techniques while minimizing toxic side effects on normal tissues remains a key focus and challenge in current translational research. Third, the safety and long-term efficacy of exosome-based therapeutic strategies lack sufficient clinical data support. Existing research predominantly remains at the cellular and animal model stages. Transitioning from basic experiments to clinical application requires large-scale, multicenter prospective clinical trials to comprehensively evaluate clinical benefits and potential risks.

In the future, with deepening research into the biological mechanisms of exosomes and continuous innovations in separation, purification, and modification technologies, exosomes hold promise as a vital tool for the diagnosis, treatment, and prognosis assessment of gynecological malignancies. By integrating cutting-edge technologies such as gene editing and immunotherapy, personalized exosome-based treatment protocols tailored to different pathological types and stages of gynecological malignancies could bring new therapeutic hope to patients. Simultaneously, the advancement of multidisciplinary collaboration will accelerate the translation of exosomes from the laboratory to clinical practice, propelling further progress in the field of precision treatment for gynecological tumors.

References

[1] Zhang FM, Li HF. Role of exosomes in gynecological malignancies and advances in clinical application [J]. Journal of Sun Yat-sen University (Medical Science Edition), 2025, 46(02): 266-274.

[2] Feng Zheng, Guo Qinhao, Zhu Jun, et al. Advances and Prospects in the Treatment of Gynecological Malignant Tumors in 2023 [J]. Chinese Journal of Cancer, 2024, 34(04): 340-360.

[3] Mengdan M , Yifei M, Yanping Z , et al. Advances in Exosomes as Diagnostic and Therapeutic Biomarkers for Gynaecological Malignancies[J].Cancers,2022,14(19):4743-4743.

[4] S V, E U ,L Z , et al. Exosomes for the treatment of human malignancies.[J].Hormone and metabolic research = Hormon- und Stoffwechselforschung = Hormones et metabolisme, 2008, 40(2):82-8.

[5] Shenoda B B, Ajit K S . Modulation of Immune Responses by Exosomes Derived from Antigen-Presenting Cells[J]. Clinical Medicine Insights: Pathology,2016,2016(Suppl. 1):1-8.

[6] M J P, Guido K ,Laurence Z . Extracellular vesicles: masters of intercellular communication and potential clinical interventions. [J].The Journal of clinical investigation, 2016, 126 (4):1139-43.

[7] Xue LAI'en, Fu YUNFeng, Cui LINLIN, et al. Isolation and Identification of Rat Amniotic Mesenchymal Stem Cells and Their Exosomes [J]. Laboratory Animal Science, 2025, 42(05): 78-84.

[8] Dong Yihan, Liu Shiming, Wang Yong, et al. Extraction and Identification of Exosomes and Their Role in Renal Cell Carcinoma [J]. Clinical Laboratory, 2025, 40(11): 1118-1125.

[9] Zhang, X. Mechanistic Study of CircPRKD3, an Exosome Derived from Glioma Stem Cells, in Glioblastoma and Its Immune Microenvironment [D]. University of Science and Technology of China, 2025.

[10] Zhou C, Luo W . 631P Lymphatic STING palmitoylation mediates pre-metastatic immune niche remodeling by promoting CXCR6+ Treg recruitment via cervical cancer-derived exosomal DHHC19[J].Annals of Oncology,2025, 36 (S4): S1988-S1988.

[11] Tian W, Chen K ,Deng L , et al. Cancer associated fibroblast exosomal miR-214-3p regulated by hnRNPA2B1 promotes cisplatin resistance by inhibiting ferroptosis.[J].International journal of surgery (London, England),2025.

[12] Irani G M, Babaei S ,Kazemi T . Exosomes in hepatocellular carcinoma: involvement in reprogramming the tumor microenvironment for immune evasion, metastasis, angiogenesis, and drug resistance.[J].Cell cycle (Georgetown, Tex.), 2025,1-23.

[13] Xu Z, Fang X ,Wang S, et al. Tongue squamous cell carcinoma-derived exosomes miR-21-5p affect tumor progression via promoting M2 macrophage polarization[J]. Non-coding RNA Research,2025,13184-196.

[14] Zhang J, Wu Y ,Wang Y , et al. Tumor cell exosome circ-0023919 promotes EMT through the miR-197-5p/ICAM5 axis and enhances the drug resistance of colorectal cancer to 5-Fu. [J]. Experimental cell research,2025,114866.

[15] Gao C, Wang X ,Yan H , et al. Exosome-Delivered HsaCirc0000116 Facilitates Osteosarcoma Cell Malignancy via PI3K/Akt/mTOR and p38/MAPK Pathways.[J].DNA and cell biology,2025,44(3):153-160.

[16] Sheng Xiu-jie. The HPV E6/E7-miR-543-CHMP4C Pathway Promotes the Development and Progression of Cervical Cancer. Guangdong Province, The Third Affiliated Hospital of Guangzhou Medical University, May 31, 2023.

[17] Aynur Seyit, Wang Yina, Gulina Kurban, et al. Relationship between miRNA-409-3p, VEGF, and Gab2 Expression in Cervical Cancer and the Efficacy of Intensity-Modulated Radiotherapy Combined with Chemotherapy as well as 3-Year Survival Outcomes [J]. Journal of Clinical and Experimental Medicine, 2023, 22(19): 2061-2065.

[18] Xia Yufang. Study on the Mechanism of HPV-Associated miR-3156-3p Expression in Cervical Cancer [D]. Qingdao University, 2017.

[19] Fan Xuze, Huang Wu, Bao Yiting, et al. Research Progress on Exosomal MicroRNAs in Ovarian Cancer [J]. Advances in Obstetrics and Gynecology, 2025, 34(10): 778-783.

[20] Qian X, Yuan Y ,Zhang Y , et al. Synergistic effect study on the co-delivery of paclitaxel and SiRNA targeting STMN1 based on MPDA nanoparticles in the therapy of ovarian cancer[J]. Journal of Nanobiotechnology,2025,23(1):763-763.

[21] Liu Xingxin. Research on Folic Acid-Targeted Smart-Responsive Mesoporous Silica Simultaneously Loaded with Adriamycin and COX-2 siRNA for Synergistic Treatment of Ovarian Cancer and Its Therapeutic Mechanism. Sichuan Province, Sichuan University, May 25, 2022.

[22] Qi Lining. Expression and Clinical Significance of miR-10a and let-7i in Endometrial Carcinoma Tissue. Hebei Province, Baoding First Central Hospital, 2020-07-03.

[23] Li Y Y, Liu H ,Feng L J , et al. Engineered exosomes restore miR-508-5p expression in uterine corpus endometrial carcinoma and reduce tumor progression and metastasis by targeting DLL3[J].Frontiers in Oncology,2025,151532564-1532564.