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Research Progress on the Therapeutic Effects of Exosomes on Tumors

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Abstract: With the deepening of medical research, many innovative research results have emerged in the field of cancer treatment, providing new possibilities for clinical treatment. Targeted drug delivery systems based on engineered exosomes show significant therapeutic advantages and application prospects because of their unique biological characteristics. In this paper, the biological characteristics of exosomes and their theoretical basis as drug carriers are described in detail. The regulation mechanism of exosomes in the tumor microenvironment was discussed, and the interaction between exosomes and tumor cells and immune cells was analyzed. The representative cases of exosomes in tumor diagnostic marker screening and clinical treatment were reviewed. In addition, the key scientific problems and technical challenges facing the clinical application of engineered exosomes are objectively analyzed, and their future development prospects are forecasted. It is hoped that it can provide more theoretical references for clinical translational research of engineered exosomes and promote the application and development of this technology in the field of tumor precision therapy.

Keywords: Exosome, cancer, diagnosis and treatment

1. Introduction

One of the main causes of death in the global is cancer, not only having a profound impact on human lifespan but also significantly reducing the quality of life for patients. Take lung cancer as an example, a malignant tumor originating from the bronchial or alveolar epithelium, its incidence accounts for more than one-tenth of all new cancer cases globally, and the number of deaths it causes is close to one-fifth of the total cancer deaths worldwide. Although traditional tumor treatment methods, such as radiotherapy, chemotherapy, radiotherapy, targeted therapy and surgery, have achieved certain results to some extent, they are often accompanied by significant side effects, drug resistance issues, and long-term adverse reactions. These problems not only limit the treatment effect but also expose patients to high risks and severe complications, while adversely affecting prognosis recovery. Therefore, seeking new tumor treatment strategies has become a key focus in current research fields.

In recent years, with the rapid development of synthetic biology, clinical medicine and gene editing technology, engineered exosomes have gradually demonstrated the potential to break through the limitations of traditional therapies, providing more precise and efficient solutions for cancer treatment. Currently, numerous studies are dedicated to using engineered exosomes as drug delivery systems in the clinical treatment of high-incidence cancers such as esophageal cancer, lung cancer, breast cancer

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and colon cancer. Research shows that exosomes have obvious advantages in enhancing drug efficacy and reducing side effects. However, despite their promising prospects, this field still needs to further improve exosome separation techniques, deeply explore their characteristics, and verify their safety and effectiveness in preclinical and clinical trial stages.

This article summarizes the structural features and biological roles of exosomes, analyzes their mechanism of action in the emergence and progression of tumors, and simultaneously explores their potential application value in clinical diagnosis and treatment.

2. Exosome structure and biological features

Exosomes are nanoscale vesicles released by cells, possessing unique biological features. These vesicles are surrounded by a lipid bilayer membrane and usually range in size from 30 to 200 nanometers in diameter. This structure protects various bioactive molecules contained within. Under transmission electron microscopy, exosomes typically appear as cup-shaped or round structures. They are primarily formed within multivesicular bodies (MVBs) inside cells and are expelled into the extracellular space when MVBs fuse with the plasma membrane. A variety of cell types, including stem cells, immune cells, and tumor cells, are capable of secreting exosomes. These vesicles contain a rich assortment of bioactive substances, such as proteins, lipids, mRNA, miRNA, long non-coding RNA, circular RNA, and DNA. The specific composition and amount of these components depend on the type of originating cells. Exosomes selectively encapsulate these molecules, which often results in significant differences in RNA content compared to their parent cells.

3. Exosome functions in tumor initiation and progression

Exosomes play a pivotal role in regulating the tumor microenvironment by influencing the behavior of other cells, modulating immunity, and promoting angiogenesis. By altering the tumor microenvironment, they contribute significantly to cancer initiation and progression. The tumor microenvironment (TME) refers to the internal milieu where tumors arise and thrive, encompassing tumor cells, non-tumor cells (such as immune cells, fibroblasts, and glial cells), microvessels, lymphatic vessels, extracellular matrix, and biomacromolecules.

3.1. Exosomes and tumor cells

Exosomes derived from tumor cells possess the capacity to transfer metastatic potential to recipient cells and establish a pre-metastatic niche for specific organs [1]. In metastatic subtypes of colon cancer, upregulated circLONP2 regulates the intracellular maturation of miR-17, and the elevated mature miR-17 is transferred to neighboring cells via exosomes, initiating metastasis and spreading metastatic capability at the primary site while accelerating tumor metastasis in distant organs [2]. Furthermore, research has demonstrated [3] that RNA-Seq analysis of exosomes secreted by chemotherapy- and radiotherapy-resistant dying tumor cells reveals substantial alterations in miRNAs. Among these, miR-194-5p regulates the cell cycle by inhibiting the transition from G1 to S phase and enhances the DNA damage response, thereby improving the survival of therapy-resistant clones (TRCs). This process also regulates the expression of E2F3, promoting tumor cell repopulation and reaggregation.

3.2. Exosomes and immune cells

Exosomes are integral to tumor immunity, exhibiting a multifaceted role by both enhancing anti-tumor immune responses and contributing to immune suppression. Exosomes could play a role in immunosuppression. Research indicates that ExoPD-L1 suppresses T cell immunity via various

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mechanisms, which can be described as hindering T cell activation by connecting either directly or indirectly with PD-1 receptors on T cells, facilitating tumor immune evasion, and thus driving tumor development [4]. The precise mechanism requires additional investigation.

In addition, exosomes also have immunogenicity and molecular transfer properties, which can activate the immune system and promote anti-tumor immune responses. Anti-tumor experiments with dendritic cell-derived exosomes have shown that exosomes derived from dendritic cells are rich in MHC class I molecules and tumor antigens, such as heat shock proteins, which are crucial for antigen presentation and T cell activation [5]. In vitro and in vivo studies have shown their ability to activate CD8+ T cells, which enhances anti-tumor immunity and suppresses tumor progression. Furthermore, experiments involving CAR-T cell-derived exosomes have indicated that upon stimulation by tumor antigens, CAR-T cells release a significant amount of exosomes [6]. These exosomes possess CAR on their surface and contain perforin/granzyme internally, enabling them to identify and destroy tumor cells. Notably, exosomes derived from HER2 CAR-T cells exhibit multiple cytokines similar to their parent CAR-T cells, including granzyme B, IL-17, and IL-2, thus preserving the functionality of CAR-T cells and allowing specific binding and penetration of HER-2 expressing target cells. Moreover, research has demonstrated that exosomes originating from MSLN-CAR-T cells can achieve a 52% to 66% inhibition of tumor growth and display dose-dependent effects in suppressing tumor development.

3.3. Exosomes and extracellular matrix

Exosomes derived from stromal cells also have the ability to promote or restrict tumor progression . During tumor metastasis, exosomes promote cytoskeletal remodeling, invasive pseudopodia formation, and increased migration through fibronectin, facilitating tumor metastasis. They also promote the degradation of the extracellular matrix through membrane-type matrix metalloproteinase (MT1-MMP), leading to the remodeling of the extracellular matrix and basement membrane, angiogenesis, and vascular permeability, thereby promoting tumor metastasis. Tumor metastasis is the main cause of cancer-related deaths. Many studies have identified the direct invasive role of exosomes in tumor metastasis and their specific effects in promoting metastasis by facilitating metastasis, transformation, and establishing pre-metastatic niches [7]. Additionally, exosomes derived from stromal cells can limit tumor progression by altering the tumor microenvironment. These exosomes contain matrix metalloproteinase-2 or MMP-2 enzymes, which can modify cell functions and provide the ability to restructure the tumor microenvironment, thereby restricting tumor progression [8].

4. Application of exosomes in tumor diagnosis

Exosomes, as biomarkers for liquid biopsy, can be used for the early detection and monitoring of tumors. The use of exosomes as diagnostic tools mainly involves the application of controllable exosomes rather than the utilization of the inherent characteristics of natural exosomes. The properties of the source cells of exosomes are often modified to generate exosomes with specific biological characteristics. Several studies have investigated the surveillance function of exosomes in cancer therapy and discovered that by examining the nucleic acids, proteins, and other elements within exosomes originating from tumor cells, it is possible to dynamically track the treatment outcomes and progression of tumors [9].

Exosomes can also be modified or functionalized by adding tumor-targeting ligands. In tumor drug development, biomarkers are widely used in conjunction with diagnostic methods for patient stratification. Biomarker screening and patient stratification strategies are crucial for addressing the high heterogeneity of cancer, as they can precisely identify patient groups most likely to benefit from

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molecular targeted drug therapy. Biomarker screening and patient stratification strategies play a vital role in promoting the clinical development and application of these drugs.

Overall, exosomes show great potential in tumor treatment, but their clinical application still needs to overcome technical and biological challenges.

5. Clinical application

Due to exosomes' low immunogenicity, great biocompatibility, and capacity to pass through various bio-barrier without being recognized and cleared by the host immunization system, have become ideal drug carriers. Exosomes-based medication delivery systems offer new approaches for treating cancer and there's hope that it can propel future clinical cancer therapy. As a small molecule drug delivery system, exosomes can delivery a varity of drugs. When using curcuin in cancer treatment, its low bioavailability, poor water solubility and rapid metabolism in the body significantly reduce its therapeutic effect. Aqil and other scientists used exosomes which extracted from milk to load curcmin. There research showed that the ExoCUR formulation is stable, facilitating transportation and storage and oral administration don't significantly alter its properties. Notably, exosomes effectively increased the tissue bioavailability of curcumin, and ExoCUR demonstrated high biological activity in anti-proliferation and anti-tumor effects. Through solvent extraction and UPLC analysis, the stability of CUR over time in the formulation of exosomes was determined. After six months of preservation at degress Celsius, the anti-proliferative effect of ExoCUR on lung cancer cells was similar to that of the formulation without long-term storage. Aqil and other scientsts' experiments indicated that compared to CUR, ExoCUR significantly increased the growth inhibition rate of various cancer cells, including H1299 lung cancer cells, A549 lung cancer cells, cervical cancer cells, and breast cancer cells, further confirming the advantages of exosome drug delivery systems over traditional therapies [10].

As a traditional chemotherapy drug Paclitaxel has significant efficacy against multiple solid tumors, but its negative effects are obvious. Incorporating hematological toxicity, neurotoxicity, cardiovascular toxicity, and possible changes in liver and renal function, along with other adverse reactions. The precise targeted transport ability of exosomes can reduce the damage of paclitaxel to normal tissues. Exo-PTX As a natural drug delivery system, can evade phagocytosis, exhibit excellent biocompatibility, and offer enhanced safety relative to conventional therapies [11]. They can be used as carriers to target paclitaxel to tumor tissues. In addition to more secure, in vitro drug release behavior analysis showed that Exo-PTX released paclitaxel faster in a simulated tumor microenvironment compared to normal body fluid. Moreover, Exo-PTX had a significantly higher inhibitory rate on HepG2 cells than the same dose of PTX. Here it is importent to pay attention to even when the paclitaxel content in Exo-PTX was zero, it still had an inhibitory effect on HepG2 cells [12]. The anti-tumor effect of paclitaxel-loaded exosomes was improved compared to traditional therapies.

Doxorubicin, an important drug for cancer treatment, has significant anti-tumor effects but also causes severe cardiomyopathy, renal burden, liver function problems, cognitive impairment in the brain, and even significant effects on the reproductive system [13]. Animal experiments have indicated that Exo-DOX can protect the cardiac function of mice. Meanwhile, the levels of hepatotoxicity biomarkers in the Exo-DOX group were much less than those in the free doxorubicin group, further demonstrating the possibility of Exo-DOX reducing the toxic side effects of doxorubicin treatment in patients [14].

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6. Challenges and solutions

Exosomes seem to be a double-edged sword. When utilized as a drug delivery system for cancer therapy, there is a certain risk of promoting metastasis. Exosomes can carry functional proteins, microRNAs, and other regulatory molecules, enhancing the invasive and metastatic ability of recipient cells, leading to the promotion of tumor metastasis during drug delivery. Some exosomes may naturally carry pro-survival signals or anti-apoptotic molecules, increase the proliferation activity of tumor cells and inhibite the apoptosis, resulting in uncontrolled tumor cell growth. Studies have shown that compared with exosomes derived from non-cancer-related fibroblasts, exosomes derived from esophageal cancer-related fibroblasts carry HOX transcript antisense RNA, which poses a risk of promoting the spread and invasion of cancer cells, accelerating the malignant phenotype of esophageal squamous cell carcinoma [15]. This further indicates that when designing exosome-based drug delivery systems for clinical cancer treatment, the source of exosomes must be strictly controlled, and research on potential pathogenic genes and metastasis-promoting and invasion-promoting molecules should be strengthened to avoid potential risks and increase the difficulty of clinical treatment.

Currently, the use of exosomes in cancer treatment is still in the laboratory stage, mainly focusing on animal experiments and basic research. The specific mechanism of action is not yet clear, and there is a lack of large-scale clinical data support. Treatment efficacy and safety have not been confirmed. As one of the core bottlenecks in the field of exosome-based cancer treatment, scientists need to perform comprehensive study on the mechanism of action of exosomes, optimize clinical models, and promote more efficient clinical trials. Governments and relevant institutions should also strengthen the regulation of engineered exosome preparation and quickly establish unified standards to promote the clinical application of exosome-related drugs. In summary, the potential of exosomes in cancer treatment is obvious, but further fundamental studies and clinical trials remain necessary to ascertain their safety and efficacy.

7. Conclusion

Considering the distinctive biological properties of exosomes, they play important roles in cell communication, tumor microenvironment remodeling, and immunomodulation. Exosomes provide intricate and significant functions within the human body. Exosomes secreted by immune cells have been shown to contribute to innate immunity by inhibiting tumor development, proliferation, and metastasis. Conversely, neoplastic cells can elude immune monitoring and promote immunological tolerance by using exosomes, which are secreted by tumor cells and can transfer bioactive molecules between other cells. Exosomes show great potential in tumor monitoring and treatment. Currently, with more and more research focusing on exosomes' usage in clinical practice, scientists are attempting to use them as biomarkers for liquid biopsy for early cancer detection. At the same time, exosome-based drug delivery systems offer new hope for cancer treatment. The application of exosomes in clinical practice will make more personalized cancer treatment possible. Cancer patients can be diagnosed more timely and accurately through exosome technology, which greatly increases the success rate of subsequent treatment. Moreover, cancer treatment methods based on exosomes will provide patients with treatments that have fewer side effects and better efficacy. However, exosomes with dual roles also face many challenges on the road to clinical application. There is a risk that exosomes may exacerbate cancer conditions, which further leads to a lack of clinical trials and makes it difficult to ensure the effectiveness and safety of exosome treatment. Therefore, further improving the basic research on exosomes, strengthening the detection and regulation of exosome-related drugs, and promoting the safe and standardized conduct of clinical trials have become the necessary path for the wide application of exosomes in clinical practice.

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Authors contribution

All the authors contributed equally and their names were listed in alphabetical order.

References

[1] *Hoshino A, Costa-Silva B, Shen TL, et al. Tumour exosome integrins determine organotropic metastasis[J]. Nature,2015,527(7578):329-335.*

[2] *Han K, Wang FW, Cao CH, et al. Circ LONP2 enhances colorectal carcinoma invasion and metastasis through modulating the maturation and exosomal dissemination of micro RNA-17[J]. Mol Cancer,2020,19(1):60.*

[3] *Tang Y, Zhang P, Wang Y, et al. The biogenesis, biology, and clinical significance of exosomal PD-L1 in cancer[J]. Front Immunol,2020,11:604.*

[4] *Morrissey SM, Yan J. Exosomal PD-L1: Roles in Tumor Progression and Immunotherapy. Trends Cancer. 2020 Jul;6(7):550-558.*

[5] *Exosomes as carriers to stimulate an anti-cancer immune response: A review[J]. Biochimica et Biophysica Acta (BBA) - Molecular Cell Research, 2025, 1869(2): 240070.*

[6] *Hu D, Yang R, Wang G, et al. Emerging strategies to overcome current CAR-T therapy dilemmas—exosomes derived from CAR-T cells[J]. International Journal of Nanomedicine, 2024, 19: 2773–2791.*

[7] *Milane L, Singh A, Mattheolabakis G, Suresh M, Amiji MM. Exosome mediated communication within the tumor microenvironment[J]. J Control Release, 2015,219:278-294.*

[8] *Mesenchymal Stem Cell Derived Exosomes in Cancer Progression, Metastasis and Drug Delivery: A Comprehensive Review[J]. PMC, 2018.*

[9] *Nam, G. H., Choi, Y., Kim, G. B., et al. Emerging Prospects of Exosomes for Cancer Treatment: From Conventional Therapy to Immunotherapy. Adv Mater , 2020;32:e2002440.*

[10] *[Aqil F,Munagala R,Jeyabalan J,et al. Exosomes for the Enhanced Tissue Bioavailability and Efficacy of Curcumin[J]. AAPS J,2017,19(6):1691-1702. doi:10.1208/s12248-017-0154-9.*

[11] *Liang L, Zhao L, Wang Y, Wang Y. Treatment for Hepatocellular Carcinoma Is Enhanced When Norcantharidin Is Encapsulated in Exosomes Derived from Bone Marrow Mesenchymal Stem Cells. Mol Pharm. 2021;18(3):1003-1013. doi:10.1021/acs.molpharmaceut.0c00976*

[12] *Liang Minjie, LIANG Leyi, ZHENG Zhaoguang, LI Yiqing, Mo Feilao, Zhao Ling, WANG Yan, Wang Ying. Optimization of drug delivery technology and in vitro antitumor effect of taxol exosomes [J]. New Chinese Medicines and Clinical Pharmacology, 2019,35(11):1759-1766. (in Chinese) DOI:10.19378/j.issn.1003-9783.2024.11.015.*

[13] *MOHAJERI M,SAHEBKAR A.Protective effects of curcumin against doxorubicin-induced toxicity and resistance:A review[J].Critical reviews in oncology hematology,2018,122:30-51.*

[14] *Wang JQ. Study on targeted treatment of osteosarcoma by engineered exosom-like delivery of adriamycin [D]. Chongqing medical university, 2024. DOI: 10.27674 /, dc nki. Gcyku. 2024.000012.*

[15] *Lu Jin, SHEN Jiangfeng, Han Guang, Chen Quan. Potential molecular mechanism of exosome lncRNA HOTAIR in malignant metastasis of esophageal cancer [J/OL]. Cellular and molecular immunology journal: 1-14. DOI: 10.13423 / j.carol carroll nki cjcmi. 009915.*