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Exosome-Mediated Drug Delivery: Enhancing Targeted Therapy for Cancer and Neurodegenerative Diseases

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Abstract

Exosomes, nanoscale extracellular vesicles secreted by various cell types, have emerged as promising tools for drug delivery due to their intrinsic biocompatibility, low immunogenicity, and natural ability to target specific cells. This review explores the potential of exosome-mediated drug delivery for enhancing targeted therapies in cancer and neurodegenerative diseases. By leveraging the inherent characteristics of exosomes, including their ability to cross biological barriers such as the blood-brain barrier, researchers are developing innovative methods to load therapeutic agents into exosomes for precise delivery. Recent advancements in engineering exosomes for enhanced targeting, stability, and payload capacity are discussed, alongside challenges related to large-scale production, standardization, and clinical translation. The promising results from preclinical and early clinical studies highlight the potential of exosomes as a transformative platform for precision medicine in treating complex diseases.

Keywords: Exosomes; Drug delivery; Targeted therapy; Cancer; Neurodegenerative diseases; Blood-brain barrier; Biocompatibility; Extracellular vesicles; Precision medicine; Therapeutic engineering

Introduction

Exosomes are small, lipid-bilayer-enclosed extracellular vesicles (30–150 nm) secreted by virtually all cell types. They play an essential role in intercellular communication by transporting proteins, lipids, and nucleic acids between cells. Initially considered cellular waste disposal systems, exosomes have since gained significant attention for their role in physiological and pathological processes. Their unique properties, including biocompatibility, low immunogenicity, and ability to cross biological barriers such as the blood-brain barrier, make them promising candidates for drug delivery applications [1].

Drug delivery systems have long been a cornerstone of therapeutic advancements, aiming to improve the bioavailability, targeting, and efficacy of therapeutic agents. Traditional methods, while effective in many cases, often face limitations such as systemic toxicity, off-target effects, and difficulties in penetrating certain biological barriers. These challenges are particularly pronounced in diseases like cancer and neurodegenerative disorders, where precision in targeting and delivery is critical. Exosomes offer a natural, cell-derived solution to overcome these hurdles, presenting an innovative approach to enhancing targeted therapy.

One of the most significant advantages of exosome-mediated drug delivery is their ability to target specific cells or tissues. This targeting capability is due to the surface markers expressed on exosomes, which can be modified to improve specificity. For example, exosomes derived from cancer cells often show a natural propensity to target tumors, making them ideal candidates for delivering anti-cancer therapeutics. Similarly, engineered exosomes can be used to deliver drugs across the blood-brain barrier, addressing a critical challenge in treating neurodegenerative diseases like Alzheimer's and Parkinson's disease.

Recent advancements in the field have focused on optimizing the loading of therapeutic agents, such as small molecules, proteins, and nucleic acids, into exosomes. Techniques such as electroporation, sonication, and genetic engineering have been employed to enhance drug loading efficiency and stability. Moreover, researchers are exploring strategies to engineer exosomes with enhanced targeting capabilities by modifying their surface with ligands, antibodies, or peptides [2,3].

Despite their potential, the clinical application of exosome-mediated drug delivery faces several challenges. These include scalability and reproducibility in exosome production, standardization of isolation and purification methods, and ensuring the stability and bioactivity of exosome-based therapeutics. Regulatory hurdles also exist, as the use of exosomes as a drug delivery platform is still in its infancy compared to traditional methods.

Nevertheless, preclinical and early clinical studies have shown encouraging results, highlighting the potential of exosome-based therapies in treating complex diseases. For instance, exosomes loaded with chemotherapeutic agents have demonstrated enhanced tumor targeting and reduced systemic toxicity in cancer models. Similarly, exosomes carrying neuroprotective agents have shown promise in preclinical models of neurodegenerative diseases, underscoring their versatility and therapeutic potential.

In this review, we delve into the latest developments in exosome-mediated drug delivery, focusing on its applications in cancer and neurodegenerative diseases. We discuss the unique properties of exosomes that make them suitable for targeted therapy, the methods used to engineer and optimize their drug delivery capabilities, and the challenges that must be addressed to translate these findings into clinical practice. By exploring the intersection of exosome biology and drug delivery, we aim to shed light on the transformative potential of

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exosomes in precision medicine.

Materials and methods

Materials

Cell lines and culture media

Cell lines: Cancer cell lines (e.g., MCF-7, A549), neuronal cell lines (e.g., SH-SY5Y), or primary cells relevant to the disease models (e.g., glioblastoma or astrocytes).

Culture media: Dulbecco's Modified Eagle Medium (DMEM), Roswell Park Memorial Institute (RPMI) medium supplemented with fetal bovine serum (FBS) and antibiotics (penicillin/streptomycin).

FBS treatment: Exosome-depleted FBS was used to avoid contamination with bovine exosomes [4].

Reagents and instruments

Reagents: Phosphate-buffered saline (PBS), protease inhibitors, RNA isolation kits, and drug compounds (e.g., doxorubicin, siRNA, or neuroprotective agents).

Instruments: Ultracentrifuge, nanoparticle tracking analyzer (NTA), dynamic light scattering (DLS) system, flow cytometer, and transmission electron microscope (TEM).

Antibodies and markers

Exosome-specific markers: CD9, CD63, CD81, TSG101, and Alix.

Targeting ligands or peptides: RGD peptides, aptamers, or antibodies for surface engineering [5].

Methods

Exosome isolation

Differential ultracentrifugation

Cell culture supernatant was centrifuged sequentially at 300 × g, 2000 × g, and 10,000 × g to remove cells, debris, and large vesicles.

The final supernatant was ultracentrifuged at 100,000 × g to pellet exosomes [6].

Alternative methods

Size-exclusion chromatography (SEC) or polymer-based precipitation kits for enhanced purity.

Immunoaffinity capture using exosome-specific antibodies for selective isolation.

Exosome Characterization

Size and morphology

TEM and NTA were used to determine size distribution and confirm vesicular morphology.

Protein markers

Western blot or flow cytometry was performed to detect exosome markers (e.g., CD63, CD81, TSG101).

Surface charge

Zeta potential analysis was conducted to evaluate surface charge and stability [7].

Drug loading

Passive loading

Exosomes were incubated with therapeutic agents under optimized conditions to allow diffusion of small molecules into the vesicles.

Active loading techniques

Electroporation: For loading nucleic acids such as siRNA or miRNA.

Sonication or freeze-thaw cycles: Used to enhance encapsulation of hydrophilic drugs [8].

Genetic engineering of donor cells

Donor cells were transfected with plasmids encoding therapeutic proteins or RNA, which were subsequently packaged into secreted exosomes.

Surface engineering

Chemical modification

Surface conjugation of targeting ligands (e.g., peptides, antibodies) via click chemistry or carbodiimide coupling.

Genetic modification

Donor cells were engineered to express targeting ligands on the exosome membrane.

In vitro drug delivery and uptake studies

Cell viability assays

MTT or CellTiter-Glo assays were conducted to assess cytotoxicity in cancer cells.

Targeting efficiency

Fluorescently labeled exosomes were tracked using confocal microscopy or flow cytometry.

Blood-brain barrier (BBB) models

Transwell models were used to evaluate exosome permeability across the BBB [9].

In vivo studies

Animal models

Cancer models (e.g., xenograft mice) and neurodegenerative disease models (e.g., transgenic Alzheimer's or Parkinson's mice).

Biodistribution studies

Exosomes were labeled with dyes (e.g., DiR) and tracked using in vivo imaging systems.

Therapeutic efficacy

Tumor growth inhibition or neuroprotection was assessed using histological analysis and behavioral tests [10].

Statistical analysis

Data were analyzed using appropriate statistical tests (e.g., Student's t-test, ANOVA) with significance set at $p < 0.05$.

Discussion

Exosome-mediated drug delivery represents a transformative approach to precision medicine, offering unique advantages for targeted therapy in cancer and neurodegenerative diseases. The

discussion highlights the potential of exosomes, their challenges, and future directions for clinical translation.

Exosomes, due to their natural origin and biological compatibility, are less likely to provoke immune responses compared to synthetic drug delivery systems. Their small size and lipid bilayer composition enable efficient delivery across challenging biological barriers, including the blood-brain barrier, which has long been a major obstacle in treating neurodegenerative diseases. This capability positions exosomes as promising candidates for delivering therapeutic agents to specific tissues, including hard-to-reach locations like the brain and metastatic tumor sites.

In cancer therapy, exosomes have shown significant promise. Tumor-derived exosomes naturally home to cancer cells, allowing them to act as targeted carriers for anti-cancer drugs, RNA therapeutics, or immune-modulating agents. This specificity minimizes off-target effects and systemic toxicity, which are common drawbacks of traditional chemotherapy. Moreover, exosomes can be engineered to enhance their therapeutic payload and targeting efficiency through the incorporation of ligands, antibodies, or peptides, enabling highly customized treatment approaches.

In the context of neurodegenerative diseases, exosomes offer a unique advantage by facilitating the delivery of neuroprotective agents, such as siRNA, miRNA, and small molecules, directly to neuronal cells. Exosome-based strategies have shown potential in reducing neuroinflammation, promoting neuronal survival, and modulating disease progression in preclinical models of Alzheimer's and Parkinson's disease. The ability of exosomes to cross the blood-brain barrier without the need for invasive procedures further underscores their therapeutic potential.

Despite these promising advancements, several challenges must be addressed to translate exosome-based therapies into clinical applications. First, the scalability and standardization of exosome production remain significant hurdles. The current isolation methods, such as ultracentrifugation and size-exclusion chromatography, are time-consuming and lack consistency for large-scale production. Additionally, ensuring the purity and stability of exosomes during storage and transport is critical for maintaining their bioactivity.

The heterogeneity of exosomes is another challenge, as they are derived from diverse cell types and contain varying molecular compositions. This variability complicates the characterization and quality control processes, raising concerns about batch-to-batch reproducibility. Moreover, the engineering of exosomes for enhanced targeting and drug loading must balance efficiency with the preservation of their natural properties.

From a regulatory perspective, the clinical approval of exosome-based therapeutics faces unique challenges. As cell-derived vesicles, exosomes are classified between biologics and drug delivery systems, necessitating the establishment of clear guidelines for their manufacturing, quality assurance, and safety evaluation. Ethical considerations related to donor cell sources also need to be addressed.

Future research should focus on developing innovative engineering techniques to improve exosome yield, purity, and functionality. Advances in microfluidics and bioreactor technologies hold promise for scalable exosome production. Additionally, integrating multi-omics approaches, such as proteomics and transcriptomics, can provide deeper insights into exosome composition and functionality, enabling the design of more effective therapeutic exosomes.

Conclusion

Exosome-mediated drug delivery has emerged as a revolutionary approach in precision medicine, offering groundbreaking possibilities for treating complex diseases such as cancer and neurodegenerative disorders. These natural nanovesicles, derived from various cell types, possess unique biological properties that make them highly suitable as drug carriers, including their biocompatibility, low immunogenicity, and ability to traverse biological barriers like the blood-brain barrier. The inherent targeting capabilities of exosomes, combined with advancements in engineering techniques, have propelled them to the forefront of drug delivery research.

In cancer therapy, exosomes provide a promising platform for delivering chemotherapeutics, RNA-based drugs, and immune-modulating agents directly to tumor cells, thereby minimizing off-target effects and systemic toxicity. Tumor-derived exosomes, with their natural homing ability to cancer cells, have demonstrated significant potential in enhancing drug specificity and efficacy. Additionally, engineering exosomes with surface modifications, such as ligands or antibodies, further improves their targeting precision and therapeutic outcomes.

For neurodegenerative diseases, the ability of exosomes to cross the blood-brain barrier without invasive procedures offers a significant advantage over traditional drug delivery methods. Exosomes loaded with neuroprotective agents, such as siRNA, miRNA, or small molecules, have shown promise in preclinical studies for mitigating neuronal damage, reducing neuroinflammation, and modulating disease progression in conditions like Alzheimer's and Parkinson's disease. This capability underscores the versatility of exosomes as carriers for therapeutic payloads in addressing central nervous system disorders.

Despite these advancements, several challenges remain in translating exosome-based therapies into clinical applications. The scalability of exosome production, standardization of isolation and purification methods, and quality control are critical areas that require further development. Current methods for exosome isolation, such as ultracentrifugation and size-exclusion chromatography, are not yet optimized for large-scale production and often result in batch-to-batch variability. Additionally, ensuring the stability, bioactivity, and reproducibility of exosome formulations is essential for their clinical success.

Regulatory and ethical challenges also pose barriers to the clinical application of exosome-based therapeutics. Clear guidelines for manufacturing, quality assurance, and safety evaluation must be established to facilitate their approval as therapeutic agents. Ethical considerations, particularly regarding the use of donor cells for exosome production, must also be addressed to ensure the ethical and equitable development of these therapies.

The future of exosome-mediated drug delivery lies in the continued integration of innovative technologies, such as genetic engineering, microfluidics, and bioreactor systems, to enhance exosome production, targeting, and drug loading efficiency. Advances in omics technologies, including proteomics and transcriptomics, will provide deeper insights into the molecular composition and functional diversity of exosomes, enabling the design of more effective and specific therapeutic strategies. Furthermore, interdisciplinary collaborations between researchers, clinicians, and regulatory bodies will be essential to overcome the challenges associated with clinical translation.

In conclusion, exosome-mediated drug delivery holds immense

promise as a transformative approach in precision medicine. By addressing the current challenges and leveraging ongoing advancements in technology and research, exosomes have the potential to revolutionize the treatment landscape for cancer, neurodegenerative diseases, and other complex medical conditions. As research progresses, exosome-based therapies could become a cornerstone of targeted and personalized medicine, offering safer, more effective, and less invasive treatment options for patients worldwide.

Conflict of interest

None

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References

1. Venne J, Busshoff U, Poschadel S, Menschel R, Evangelatos N (2020) International consortium for personalised medicine: An international survey about the future of personalised medicine. Pers Med 17:89-100.
2. Steinhubl SR, Muse ED, Topol EJ (2015) The Emerging Field of Mobile Health. Sci Transl Med 7:283rv3.
3. Vicente AM, Ballensiefen W, Jönsson JI (2020) How personalised medicine will transform healthcare by 2030: The ICPerMed vision. J Transl Med 18:180.
4. Denny JC, Collins FS (2021) Precision Medicine in 2030-Seven Ways to Transform Healthcare. Cell. 184:1415-1419.
5. Baylot V, Le TK, Taïeb D, Rocchi P, Colleaux L (2024) Between hope and reality: Treatment of genetic diseases through nucleic acid-based drugs. Commun Biol 7:489.
6. Heming CP, Muriithi W, Macharia LW, Filho PN, Moura-Neto V, et al. (2022) P-glycoprotein and cancer: What do we currently know? Heliyon 8:e11171.
7. Terry SF (2015) Obama's Precision Medicine Initiative. Genet Test Mol Biomark 19:113-114.
8. Schleidgen S, Klingler C, Bertram T, Rogowski WH, Marckmann G (2013) What is personalized medicine: Sharpening a vague term based on a systematic literature review. BMC Med Ethics 14:55.
9. Delpierre C, Lefèvre T (2023) Precision and personalized medicine: What their current definition says and silences about the model of health they promote. Implication for the development of personalized health. Front Sociol 8:1112159.
10. Manzari MT, Shamay Y, Kiguchi H, Rosen N, Scaltriti M, Heller DA. (2021) Targeted drug delivery strategies for precision medicines. Nat Rev Mater 6:351-370.