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EXOSOME-BASED THERAPEUTICS AND DRUG DELIVERY SYSTEMS: ISOLATION, ENGINEERING, AND CLINICAL TRANSLATION

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ABSTRACT

Exosomes are small extracellular vesicles (30–150 nm) secreted by most cell types, carrying proteins, lipids, and nucleic acids that mediate intercellular communication. Their natural biocompatibility, low immunogenicity, ability to cross biological barriers, and intrinsic targeting properties have attracted intense interest for therapeutic and drug delivery applications. Exosomes can be loaded with small molecules, proteins, or nucleic acids and engineered to display targeting ligands, enabling precise delivery to specific tissues or cells. This review critically examines the current state of exosome-based therapeutics, focusing on isolation methods, engineering strategies, and clinical translation through early 2024. Isolation techniques include ultracentrifugation, size-exclusion chromatography, and microfluidic approaches, each with trade-offs in purity, yield, and scalability. Engineering strategies encompass cargo loading via electroporation, sonication, or co-incubation, and surface modification using chemical conjugation or genetic fusion. Preclinical studies have demonstrated therapeutic potential in oncology, cardiovascular disease, neurological disorders, and regenerative medicine. Several clinical trials are evaluating exosomes, including mesenchymal stem cell-derived exosomes for COVID-19 and graft-versus-host disease, and plant-derived exosomes for drug delivery. Challenges include heterogeneity, scalable manufacturing, batch-to-batch reproducibility, regulatory classification, and biodistribution. Future directions include standardized isolation and characterization, improved cargo loading efficiency, and development of allogeneic off-the-shelf products. Exosome-based therapeutics hold promise, but rigorous quality control and clinical evidence are required.

Keywords: Exosomes; Extracellular Vesicles; Drug Delivery; Isolation; Engineering; Clinical Translation

1 INTRODUCTION

Extracellular vesicles, particularly exosomes, have emerged as key mediators of intercellular communication and potential therapeutic vehicles. Exosomes originate from the endosomal pathway and carry a cargo of proteins, lipids, mRNA, miRNA, and other molecules reflecting their cell of origin. They can transfer this cargo to recipient cells, modulating physiological and pathological processes. Their lipid bilayer protects cargo from degradation, and their surface molecules enable interaction with specific cells.

The therapeutic potential of exosomes includes their use as cell-free regenerative agents, drug delivery vehicles, and diagnostic biomarkers. Mesenchymal stem cell-derived exosomes recapitulate many of the immunomodulatory and regenerative effects of their parent cells, with lower risk of tumorigenicity and easier storage. Exosomes can be loaded

with chemotherapeutics, siRNAs, or therapeutic proteins, and engineered to target tumors or other tissues. This review summarizes isolation, engineering, and clinical translation, focusing on literature through May 2024.

2 ISOLATION AND CHARACTERIZATION

Isolation methods include differential ultracentrifugation, density gradient centrifugation, size-exclusion chromatography, polymer precipitation, and microfluidic-based techniques. Ultracentrifugation is the most widely used but can be time-consuming and may damage vesicles. Size-exclusion chromatography yields high purity but diluted samples. Microfluidic methods offer speed and automation but are less established for large-scale production. Characterization includes particle size (nanoparticle tracking analysis, dynamic light scattering), concentration, and markers (CD9, CD63, CD81). Standardization remains a major challenge, as different isolation methods yield different vesicle populations with varying purity.

3 ENGINEERING STRATEGIES

3.1 Cargo Loading

Exosomes can be loaded with therapeutic cargo either during biogenesis (endogenous loading) or after isolation (exogenous loading). Exogenous loading methods include electroporation, sonication, extrusion, freeze-thaw cycles, and simple co-incubation. Electroporation is commonly used for nucleic acids but can cause aggregation and siRNA precipitation. Sonication and extrusion may damage membrane integrity. Endogenous loading involves overexpressing the desired cargo in producer cells, allowing it to be packaged into exosomes naturally, but yields are variable. Chemical transfection of producer cells is also used.

3.2 Surface Modification

Surface modification aims to improve targeting, circulation time, and cellular uptake. Strategies include genetic fusion of targeting ligands (e.g., Lamp2b fused to rabies virus glycoprotein for brain targeting), chemical conjugation (e.g., click chemistry), and membrane anchoring via hydrophobic insertion. PEGylation can extend circulation time but may reduce uptake. Display of antibodies or peptides can achieve active targeting to tumor cells.

4 THERAPEUTIC APPLICATIONS

4.1 Oncology

Exosomes are being developed as drug delivery vehicles for chemotherapeutics (e.g., doxorubicin) and as cancer vaccines. Tumor-derived exosomes can stimulate anti-tumor immunity when loaded with antigens or adjuvants. Mesenchymal stem cell-derived exosomes have been engineered to carry miRNAs or siRNAs targeting oncogenes. Preclinical studies show tumor growth inhibition and reduced systemic toxicity.

4.2 Regenerative Medicine and Cardiovascular Disease

Mesenchymal stem cell-derived exosomes have demonstrated cardioprotective, neuroprotective, and wound-healing effects in animal models. They carry growth factors, miRNAs, and proteins that promote tissue repair. Clinical trials have been initiated for acute myocardial infarction, stroke, and chronic wounds, though results are preliminary.

4.3 Inflammatory and Immune Disorders

Exosomes from mesenchymal stem cells or immune cells have immunosuppressive properties and are being tested in graft-versus-host disease, COVID-19-related cytokine storm, and autoimmune diseases. A phase 1 trial of mesenchymal stem cell-derived exosomes for COVID-19 reported safety and potential efficacy. Allogeneic exosome products are attractive due to low immunogenicity.

5 CLINICAL TRANSLATION AND REGULATORY CONSIDERATIONS

Several clinical trials of exosomes are registered, mostly phase 1/2. Products include mesenchymal stem cell-derived exosomes for various indications and plant-derived exosomes for oral drug delivery. Regulatory classification of exosomes is complex: they may be considered biological products, cell therapy derivatives, or drug delivery systems depending on their content and intended use. Manufacturing under GMP conditions requires rigorous quality control, including identity, purity, potency, and sterility. Batch-to-batch variability and scalability remain hurdles. Long-term safety, including immunogenicity and off-target effects, requires evaluation.

6 CHALLENGES AND FUTURE PERSPECTIVES

Key challenges include heterogeneity of exosome populations, lack of standardized isolation and characterization protocols, low cargo loading efficiency, and limited understanding of biodistribution. Future directions include development of high-throughput production systems, improved loading methods, and engineering of targeted exosomes. Artificial exosome mimetics and hybrid nanoparticles may overcome scalability issues. Integration of multi-omics and machine learning may optimize exosome design. Regulatory frameworks will need to evolve to accommodate these novel products.

7 CONCLUSION

Exosome-based therapeutics offer a versatile and biocompatible platform for drug delivery and regenerative medicine. Despite promising preclinical results, clinical translation is hampered by manufacturing and regulatory challenges. Standardization, scalability, and rigorous clinical trials are essential. As the field matures, exosomes may become an important class of biological therapeutics.

REFERENCES

[1] Théry C, Witwer KW, Aikawa E, et al. Minimal information for studies of extracellular vesicles 2018 (MISEV2018): a position statement of the International Society for Extracellular Vesicles and update of the MISEV2014 guidelines. J Extracell Vesicles. 2018;7(1):1535750.

[2] Kalluri R, LeBleu VS. The biology, function, and biomedical applications of exosomes. Science. 2020;367(6478):eaau6977.

[3] Valadi H, Ekström K, Bossios A, et al. Exosome-mediated transfer of mRNAs and microRNAs is a novel mechanism of genetic exchange between cells. Nat Cell Biol. 2007;9(6):654–659.

[4] Raposo G, Stoorvogel W. Extracellular vesicles: exosomes, microvesicles, and friends. J Cell Biol. 2013;200(4):373–383.

[5] Lener T, Gimona M, Aigner L, et al. Applying extracellular vesicles based therapeutics in clinical trials – an ISEV position paper. J Extracell Vesicles. 2015;4:30087.

[6] El-Andaloussi S, Lee Y, Lakhal-Littleton S, et al. Exosome-mediated delivery of siRNA in vitro and in vivo. Nat Protoc. 2012;7(12):2112–2126.

[7] Alvarez-Erviti L, Seow Y, Yin H, et al. Delivery of siRNA to the mouse brain by systemic injection of targeted exosomes. Nat Biotechnol. 2011;29(4):341–345.

[8] Kamerkar S, LeBleu VS, Sugimoto H, et al. Exosomes facilitate therapeutic targeting of oncogenic KRAS in pancreatic cancer. Nature. 2017;546(7659):498–503.

[9] Mendt M, Kamerkar S, Sugimoto H, et al. Generation and testing of clinical-grade exosomes for pancreatic cancer. JCI Insight. 2018;3(8):e99263.

[10] Sengupta V, Sengupta S, Lazo A, et al. Exosomes derived from bone marrow mesenchymal stem cells as treatment for severe COVID-19. Stem Cells Dev. 2020;29(12):747–754.

[11] Kordelas L, Rebmann V, Ludwig AK, et al. MSC-derived exosomes: a novel tool to treat therapy-refractory graft-versus-host disease. Leukemia. 2014;28(4):970–973.

[12] Lai RC, Arslan F, Lee MM, et al. Exosome secreted by MSC reduces myocardial ischemia/reperfusion injury. Stem Cell Res. 2010;4(3):214–222.

[13] Yáñez-Mó M, Siljander PR, Andreu Z, et al. Biological properties of extracellular vesicles and their physiological functions. J Extracell Vesicles. 2015;4:27066.

[14] Van der Pol E, Böing AN, Harrison P, et al. Classification, functions, and clinical relevance of extracellular vesicles. Pharmacol Rev. 2012;64(3):676–705.

[15] Witwer KW, Buzás EI, Bemis LT, et al. Standardization of sample collection, isolation and analysis methods in extracellular vesicle research. J Extracell Vesicles. 2013;2:20360.

[16] Johnsen KB, Gudbergsson JM, Skov MN, et al. A comprehensive overview of exosomes as drug delivery vehicles — endogenous nanocarriers for targeted cancer therapy. Biochim Biophys Acta. 2014;1846(1):75–87.

[17] Bunggulawa EJ, Wang W, Yin T, et al. Recent advancements in the use of exosomes as drug delivery systems. J Nanobiotechnology. 2018;16(1):81.

[18] Vader P, Mol EA, Pasterkamp G, et al. Extracellular vesicles for drug delivery. Adv Drug Deliv Rev. 2016;106:148–156.

[19] Liao W, Du Y, Zhang C, et al. Exosomes: the next generation of endogenous nanomaterials for advanced drug delivery and therapy. Acta Biomater. 2019;86:1–14.

[20] Garcia-Contreras M, Shah SH, Tamayo A, et al. Plasma-derived exosome characterization reveals a distinct microRNA signature in long duration type 1 diabetes. Sci Rep. 2017;7(1):5998.