Recent Developments of Exosome Therapeutic Approaches in Neurodegeneration

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***Abstract*—The neurodegenerative diseases, such as Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, and Huntington's disease, are characterized by gradual neuronal impairment and loss. Even with improved understanding of their pathophysiology, efficacious therapeutic approaches are still scarce. Exosomes.nano.vesicles of the extracellular compartment.have emerged as therapeutic hopefuls because they can cross the blood-brain barrier (BBB), are biocompatible, and can facilitate intercellular communication. Here, we review recent advancements in the development of exosomes as therapeutic delivery vehicles for molecules, regulators of neuroinflammation, and biomarkers for the diagnosis of neurodegenerative diseases. We also discuss the hurdles of taking exosome-based therapies from the bench to the bedside and suggest directions for future research.**

***Index. Terms*—Exosomes, neurodegeneration, Alzheimer's disease, Parkinson's disease, blood-brain barrier, biomarkers, drug delivery**

I. INTRODUCTION

Neurodegenerative diseases (NDs) constitute a category of chronic, progressive illnesses that are marked by selective neuronal degeneration in the CNS. Existing therapies are mostly symptom-relieving and are not focused on reversing or stopping disease advancement. The increasing interest in exosome-based therapies is due to their natural function in intercellular communication and their potential to transport bioactive molecules such as proteins, lipids, mRNA, and microRNA. Their inherent capacity to traverse the BBB makes them very attractive for CNS-focused therapies.

2. EXOSOMES: BIOLOGY AND MECHANISM OF ACTION

Exosomes are endosomal origin 30–150 nm vesicles secreted from the majority of cell types. They hold particular cargo from the parental cell and fulfill functions in immune response modulation, angiogenesis, and tissue repair. In the CNS, they are secreted by neurons, microglia, astrocytes, and oligodendrocytes and can transmit pathological or protective signals based on their source and context.

Key Functional Attributes
BBB Penetration Due to their lipid content and size, they are efficient at penetrating the BBB.
Cell-Specific Targeting Targeted delivery is made possible by engineering surface proteins.
Low Immunogenicity Being derived from autologous sources, exosomes have less potential to evoke immune responses.

III. EXOSOMES IN SPECIFIC NEURODEGENERATIVE DISEASES

3.1 Alzheimer's Disease (AD)

NSC- and MSC-derived exosomes have been identified to contain neuroprotective microRNAs like miR-29 and miR-132, which repress BACE1 expression and lower amyloid-beta (Aβ) deposition. Exosomes are also investigated as potential early biomarkers for AD detection because they transport tau and Aβ proteins that can be detected in blood or CSF.

3.2 Parkinson's Disease (PD)

Exosomes have also shown therapeutic value in inhibiting α-synuclein aggregation. For example, MSC-derived exosomes bearing siRNA against α-

synuclein mRNA showed potential in in vitro and in vivo models of PD. Exosomes can also be used to deliver neurotrophic factors such as GDNF (glial cell-derived neurotrophic factor) to induce survival of dopaminergic neurons.

3.3 Amyotrophic Lateral Sclerosis (ALS)
ALS-exosomes tend to contain disease-causing proteins like TDP-43 and SOD1. Therapeutic approaches propose to inhibit the delivery of these exosomes or employ artificially designed exosomes to deliver RNAi molecules to silence poisonous gene expressions. Adipose-derived MSC-derived exosomes have been found to be beneficial in delaying the progression of the disease in animal models.

3.4 Huntington's Disease (HD)
Exosome therapy in HD aims at the delivery of siRNA or antisense oligonucleotides to suppress mutant huntingtin (mHTT) genes. Exosomes derived from stem cells have shown neuroprotective properties in models of HD by enhancing mitochondrial activity and attenuating oxidative stress.

IV. EXOSOMES AS DRUG DELIVERY SYSTEMS

Exosomes are being engineered for targeted delivery of therapeutic entities, including:
RNA Therapeutics : delivery of miRNA, siRNA, and mRNA to regulate gene expression.
Proteins : Enzyme or neurotrophic factor delivery.
Small Molecules : Targeted and encapsulated delivery of anti-inflammatory or neuroprotective molecules.
Surface modifications like RVG peptides can be used to improve neuronal targeting. Scalable manufacturing, purity, and cargo loading efficiency are challenges.

V. EXOSOMES AS DIAGNOSTIC BIOMARKERS

Exosomes isolated from blood or CSF have emerged as a non-invasive source of biomarkers for the detection and monitoring of NDs at an early stage:
Increased Aβ42 and phosphorylated tau in exosomes derived from AD
Elevated α-synuclein in PD
Exosomal miRNAs as indicators of disease stage
Standardization of isolation and analysis methods is key to their clinical use.

VI. CHALLENGES AND FUTURE DIRECTIONS

Even with encouraging preclinical results, several challenges to clinical translation exist:

- Heterogeneity : Exosomes differ in size and cargo, which impacts reproducibility.
- Isolation and Characterization Scalable, standardized protocols are not available.
- Regulatory. Barriers Classification, manufacture, and quality control require clearer guidelines.

Future research must emphasize

- High-scale clinical trials to evaluate safety and efficacy
- Enhanced engineering approaches to cargo loading and targeting
- Combination of exosomes with other treatments, e.g., CRISPR/Cas9 or nanomedicine

VII. CONCLUSION

Exosomes provide a new and promising platform for the diagnosis and therapy of neurodegenerative disorders. Their intrinsic function to traverse the BBB, biocompatibility, and potential to carry different therapeutic molecules make them highly promising candidates for novel neurotherapies. Through additional research and standardization, exosome-based therapies could presently transform management of neurodegenerative diseases.

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