

Impact of Exosomes Serving as a Tool for Nano-Drug Delivery in Neurotherapeutics: Anti-Alzheimers

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ABSTRACT

Alzheimer's disease, being a chronic state progressive ND(neurodegenerative diseases), is characterised by abnormalities β -amyloid and impaired cognitive functions resulting in dementia. Exosomes (Nano-particles) have developed as a promising mediators of NDs in which they carry toxic particles between cells and transfer them. Hence, current review focuses primarily on the effects of exosomes in modulating mediators and promoting neuro-protection against NDs.

Key Words: Alzheimer's disease, miR-126-3p, Exosomes, neuro-therapeutics

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INTRODUCTION

Neurodegenerative disorders (NDs) are characterized as scope of interruptions in capacity or structure of the neurons or the nervous system. Such enduring dynamics may cause inability in thinking, cognition, movement and memory.[1] These days, the worldwide life expectancy has expanded, consequently; the related NDs are also rising.[2] as indicated by the WHO report on the top 10 reasons for worldwide demise.[3] Current medicines for NDs have significant adverse impacts, therefore, there is still interest to look for new techniques with reduced damages.[4] Presently, it has been recorded that specific protein abnormalities such as Amyloid (APP) precursor protein, tau protein, as well as α -synuclein leads to the development of NDs.[5] As such, nanotechnology, more explicitly, Nano medicine or pharmaceutical nanotechnology gives better medication delivery frameworks for NDs[6] resulting in management of it by improved monitoring, controlling, constructing, diagnosing, and treating at an atomic level.[7] Exosomes have advanced as a promising Neuro-

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therapeutics with evident roles in their peripheral neuronal regeneration and repair mechanism in terms of injury.[8]

ALZHEIMER'S DISEASE

AD is a chronic state progressive ND with a long pre- and present symptomatic period with no cure. AD is associated particularly with cognitive impairments which includes behavioural, social and work related dysfunctions which lead to death. In Alzheimer's disease, the activation of the microglia cells results

in beneficial effects during early stages as it induces phagocytosis and clearance of A β via microglial exosomes. The microglial miR-124-3p is known to be a critical mediator which modulates immunity and inflammation processes. The ApoE gene that is known for its role of A β disaggregation is targeted and inhibited by exosomal miR-126-3p in damaged neurons.

EXOSOMES

The vesicles present in the extracellular space of various cells in tissue culture are diverse, depending on its origin of the cells and their present state (e.g. transformed, stimulated, stressed etc.). Exosomes are generally secreted by various cell types and are present in body vehicles (such as urine, blood, amniotic fluid, CSF, malignant ascites etc). Exosomes usually contain various membrane proteins on their surfaces portraying as biomarkers in various pathological conditions.

Biogenesis of Exosomes

The exosomes are released by micro domains clathrin-coated (inward invaginations) on the surface plasma membrane. Proteins were properly categorized inside the cell and it is significant for neuronal wellbeing. The Exosomes are known to be indulged in toxic proteins spreading mechanism of NDs which can result in mutated or protein misfolding to serve as template oligomers formation.

Role of Exosomes In Neuroprotection

Various studies have proven the roles of exosomes such as nerve regeneration, neuronal protection and development resulting in release of exosomes by microglia⁵⁵, neurons⁵⁶, astrocytes⁵⁷, neural stem cells⁵⁸ and oligodendrocytes. Exosomes play a neuro-protective role in cases of injury and regeneration. The degradation of the accumulated toxic protein is mediated by two major proteins involving Ndfip1 and Nedd4. Stimulated by concerns of potential infective agents in donated blood, commercial enterprises have attempted to develop blood substitutes since the 1900s and also there are great and vital roles of engineering nanomaterials in this work [11].

Role of Exosomes In Neurotherapeutics

Exosomes when compared with liposomes has several advantages in delivery system. Liposomes being Ideal must evade immune responses and have a half-life longer for targeted drug release & amplified bioavailability. All these important properties are seen better functioned in exosomes. Exosomes has decreased immunogenicity with remarkable drug delivering properties. Sun et al provided the evidence of Exosomes being utilized for drug delivery. Evidences demonstrated the loading of exosomes with curcumin successfully which provided increased bioavailability along with increased solubility. Stimulated by concerns of potential infective agents in donated blood, commercial enterprises have attempted to develop blood substitutes since the 1900s.

DISCUSSION

There is an increase in quantifiable belongings around the globe, especially in neurodegenerative disorder in recent years. In previous findings of neurodegenerative disorders, the microglial exosomes are portrayed as a double-role weapon in development mechanism of A β abnormalities as well as neurodegeneration. Current biomedical imaging techniques including magnetic resonance imaging (MRI), positron emission tomography (PET), and computed X-ray tomography (CT) are vital in the diagnosis of various diseases. When inorganic nanoparticles are introduced into biological systems, their extremely small size and their exceptional physical and chemical properties make them useful probes for biological diagnostics.

CONCLUSION

In conclusion, our review focuses towards the nano-developing techniques towards various diseases including neuro-science. This review focuses towards Exosomes usage as a novel carrier in neuro-disorders treatment. Findings such as exosomal miR- 124-3p (of microglial) contributing towards neurodegeneration alleviation or enhancing the outcomes of cognition via ApoE signalling pathway can be taken further for targeting A β in AD. Altogether, exosomes can be a promising strategy

for targeted transporting of therapeutics in clinical application point of view.

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FIGURES

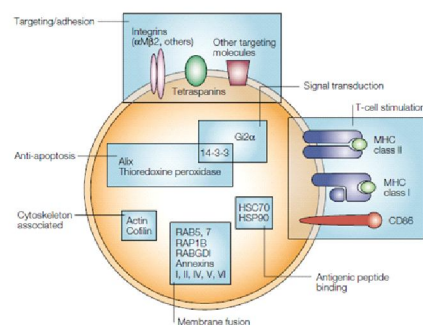


Figure 1: Diagrammatic representation of exosomes [31]

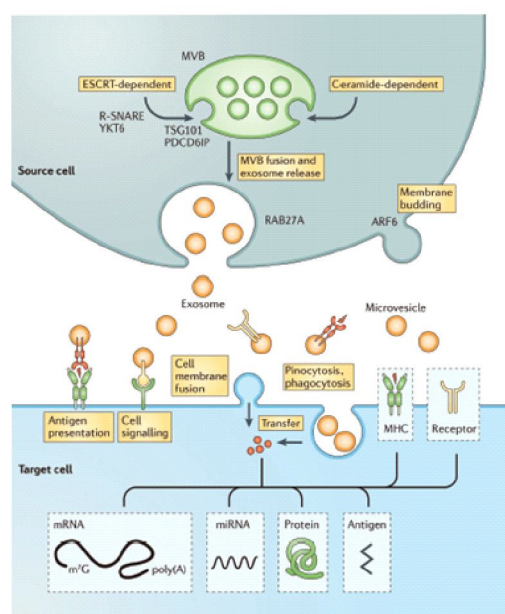


Figure 2: Mechanism Involved In Biogenesis Of Exosomes [43]

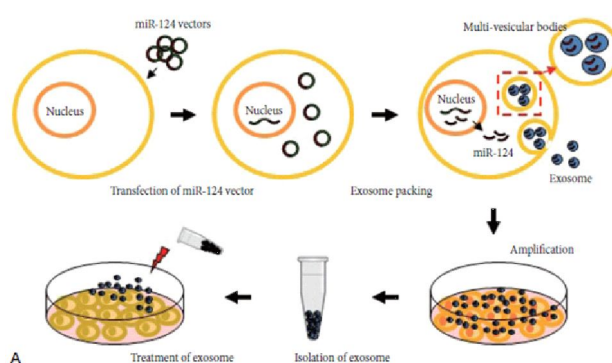


Figure 3: Generation of Exo-124. [76]