Neural Stem Cell-Derived Exosomes for Adult Neuroregeneration

Xu, Zhixuan (School: Dutch Fork High School)

Alzheimer's disease (AD) causes the gradual loss of neurons, which leads to memory and cognitive problems. Due to the inability to replace the lost neurons, current treatments cannot stop or reverse the progression of AD. One promising approach is to convert astrocytes into new neurons. However, delivering the drugs needed to trigger this conversion safely and effectively remains difficult due to the existence of the blood-brain barrier (BBB). In this study, the feasibility of using neural stem cell (NSC)-derived exosomes as carriers to convert astrocytes into neurons was investigated. Exosomes isolated from NSCs were characterized with Zeta sizer, transmission electron microscopy, and western immunoblotting. CHIR99021 and SB431542, which induce astrocyte to neuron conversion, were loaded into the exosomes and their loading efficiency was determined to be higher than 90%. Compared with liposomes, a traditional drug delivery platform, NSC-derived exosomes exhibited a significant higher efficacy in entering BBB endothelial cells, with a p-value < 0.0001. Drug release studies demonstrated that exosomes release minimal drugs in blood circulation while quickly releasing drugs in brain fluid conditions. MTT assays found that drug-loaded exosomes were non-toxic in tested concentration ranges for both BBB endothelial cells and astrocytes. Confocal microscopy revealed that the exosomes can effectively enter astrocytes and convert them into neurons, evidenced by the appearance of MAP2 and NeuN-positive cells after treatment. Overall, this project suggests that NSC-derived exosomes could offer a safe and effective approach to promote neuron regeneration in the brain, which opens a window for reversing the progression of AD.

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