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To study anti-tau antibody loading and neuronal uptake efficiency of human bone marrow mesenchymal stem cells-derived extracellular vesicles

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Background: Despite significant progress in drug delivery issue, efficient central nervous system (CNS) delivery of neuro therapeutics remains challenging. Extracellular vesicles (EVs), part of normal cell-to-cell communication, were introduced recently as a transporter that can overcome biological barriers against CNS delivery. So these natural nanoliposomes are promising tools for delivery systems design, especially for CNS. In present study, we examine the efficiency of mesenchymal stem cell (MSC)-derived EVs for drug loading and neuronal uptake.

Methods: We isolated human bone marrow-derived mesenchymal stem cells (hBMSCs)-EVs by differential ultracentrifugation coupled to density gradient technique. The protein content of harvested vesicles was measured using a BCA Protein Assay Kit. Then vesicles were characterized by performing dynamic light scattering, transmission electron microscopy and Western blotting. We examined different drug loading methods (incubation, freeze and thaw and sonication) and comprise the loading efficiency using an ELISA procedure. Neuronal uptake of vesicles also was studied using PKH-26-labeled vesicles.

Results: We isolated the 114-nm size vesicles from the hBMSCs condition media that presented EV marker protein. Quantification using BCA Protein Assay revealed 30 × 106 hBMSCs could produce approximately 4000 µg extracellular vesicles. The results disclosed EVs loaded a significant amount of anti-tau antibody and neurons can uptake this loaded vesicles.

Summary/Conclusion: In our study, we designed a drug delivery method that can be used as a brain delivery system. So we loaded anti-tau antibody into hBMSC-EVs and then studied the neuronal uptake of these systems efficiently. The results disclosed EVs loaded a significant amount of anti-tau antibody and neurons can uptake this loaded vesicles.