Proceedings of the 6th World Congress on Recent Advances in Nanotechnology (RAN'21)
~~Lisbon, Portugal~~ Visual Conference – June 14 – 16, 2021
DOI: 10.11159/nddte21.04

Using Extracellular Vesicles for Brain Delivery of Therapeutic Proteins

Elena V Batrakova, PhD
The University of North Carolina
Chapel Hill, NC, United States
batrakov@email.unc.edu

Abstract

Increasing evidence suggests that extracellular vesicles (EVs) are promising natural nanocarriers that can be used for delivery of various types of therapeutics. We reported earlier engineered EV-based formulations for treatment of neurodegenerative diseases and cancer. Herein, we investigated the use of EVs for brain delivery of different therapeutic proteins, including a soluble lysosomal enzyme tripeptidyl peptidase-1, TPP1; a potent antioxidant, catalase, and glial cell-derived neurotrophic factor, GDNF. The therapeutic proteins were loaded into EVs using two methods: (i) transfection of EV-producing cells, macrophages, with drug-encoding plasmid DNA, or (ii) incorporation of the therapeutic protein into naive empty EVs. The second approach utilized sonication, or extrusion, or freeze-thaw cycles, or permeabilization of EVs membranes with saponin to achieve high loading efficiency. The utilized methods provided effective incorporation of functional therapeutic proteins into EVs. Notably, along with the enzyme, EVs released by pre-transfected macrophages contained drug-encoding *p*DNA. EVs significantly increased stability of the proteins against protease degradation and provided extraordinary drug delivery to target cells in *in vitro* and in vivo models of neurodegeneration. A robust accumulation of EVs carriers was detected in the inflamed brain. Finally, systemic administration of drug loaded EVs significantly increased neuronal survival and decreased neuroinflammation. We hypothesized that EV-based formulations have a potential to be a versatile strategy to treat different neurodegenerative disorders.