Large-scale generation of functional mRNA-encapsulating exosomes via cellular nanoporation

Nature biomedical engineering, Article number: s41551-019-0485-1 (2019)
Presenter: Yu-Hsuan Huang       Date/Time: 2020/10/29, 16:10 -17:00
Commentator: Chu-An Wang, Ph.D.       Location: Room 601, Med College Building

Background:

Recently, cell-secreted extracellular vesicles (EVs), such as exosomes ranging from 40–150 nm, have emerged as promising carriers for nucleic-acid-based therapeutics. However, there is poor delivery and negatively charged molecules into cells. Even though there had developed a variety of techniques, such as Lipofectamine 2000 and electroporation, still might had toxicity or immunogenicity, manufacturing issues such as quality control and high cost, and their inability to penetrate into blood-brain barrier. The most important issue is the insufficient quantities of exosome.

Objective/Hypothesis:

The aim of this research project is to efficiently involve a high abundance of mRNAs into exosomes for targeting transcriptional manipulation and therapy.

Results:

For the purposes of this study, the authors developed a cellular nanoporation (CNP) biochip to stimulate cells to produce and release exosomes. The author used CNP generates large quantities of EVs loaded with transcribed mRNAs, they found that the cellular mechanism underlying CNP-triggered exosome release through HSP-p53-TASP6 signalling pathway. To evaluate the clinical utility of mRNA exosomes, they targeted the commonly mutated tumor-suppressor gene PTEN in PTEN-deficient human U87 glioblastoma cells and a mouse GL261 glioma model. They show that mRNA-containing exosomes can restore tumor suppressor function in orthotopically implanted PTEN-deficient brain gliomas, resulting in inhibition of tumor growth and prolonged animal survival.

Conclusion:

Large quantities of extracellular vesicles produced via cellular nanoporation, and loaded with endogenously transcribed therapeutic mRNAs and targeting peptides, promote therapeutic outcomes in vivo.