Optimizing Bacterial Outer Membrane Vesicles (OMVs) for mRNA-Based Immunogene Therapy

Ge, Jingyi (School: Raffles Institution)

Despite decades of medical advancement, cancer continues to claim about 10 million lives annually. mRNA therapeutics represent a promising approach for cancer immunotherapy, particularly because they enable the transient expression of immunostimulatory proteins while avoiding some nonspecific toxicities associated with conventional treatments like chemotherapy. However, the efficacy of mRNA therapeutics is limited by inefficient delivery to immune cells, and trade-offs between high transfection rates of viral vectors and safety of non-viral ones. Bacterial outer membrane vesicles (OMVs) have emerged as promising alternatives to traditional gene carriers due to their natural biocompatibility. They also possess immunostimulatory properties from the presence of pathogen-associated molecular patterns. This further activates innate immune pathways, potentially enhancing anti-tumor immune responses, and thereby complementing their role as vectors in immunotherapy. In this study, OMVs from E. Coli were isolated and then loaded with mRNA encoding interleukin-15 and its receptor alpha chain (IL-15/IL-15R alpha) via electroporation, with parameters optimized to improve mRNA encapsulation. After modification with mannose, uptake of modified OMVs (OMV-Man) was assessed with flow cytometry. Lastly, IL-15/IL-15R alpha expression in cells was quantified by ELISA. Cells treated with OMV-Man showed a 1.65-fold increase in IL-15/IL-15R level compared to unmodified OMVs ($p=0.0006$), demonstrating enhanced intracellular mRNA delivery and subsequently promoting downstream immune activities. By improving cellular uptake whilst maintaining safety, mannose-modified OMVs offer a promising platform for next-generation cancer treatment, combining targeted delivery with immunotherapy.

Awards Won:

Second Award of $2,400