

Delivery of immunomodulatory RNAs using extracellular vesicles for anti-cancer immunotherapy

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Abstract

RNA-based therapeutics have become one of the most promising new classes of medicine in recent years. However, the delivery of RNA drugs is still challenging. We have shown that red blood cell extracellular vesicles (RBCEVs) are the ideal carriers for therapeutic RNAs because RNAs can be loaded readily into the EVs and delivered to cancer cells at high efficiency. RBCEVs are nontoxic, nonimmunogenic and devoid of DNA. Moreover, RBCEVs can be produced in a large quantity from donated blood. Here, we describe new development of RBCEVs for the delivery of immunomodulatory RNAs (immRNAs) that acts as RIG-I agonists. We demonstrate that immRNA-loaded RBCEVs induce RIG-I cascade activation, type I IFN production, and immunogenic cell death in breast cancer cells. Intratumoral administration of immRNA in RBCEVs significantly suppresses tumor growth of mammary breast cancer, and induces immune cell infiltration and tumor cell apoptosis mediated by RIG-I activation, turning the ‘cold’ tumors ‘hot’. Furthermore, we demonstrate that intrapulmonary delivery of immRNA-loaded RBCEVs modified with EGFR-targeting nanobodies actively enhances the potency of immRNA, leading to suppression of tumor metastasis and elevated tumor-specific immune responses in metastatic EGFR-positive breast cancer mouse models. Thus, delivery of RIG-I agonists using RBCEVs is a promising approach for anti-cancer immunotherapy.

Biography

Dr Minh Le graduated from NUS with a Bachelor’s degree in Life Sciences and a Ph.D. degree in Computational and Systems Biology, under the guidance of Prof. Bing Lim and Prof. Harvey Lodish. She was trained as a postdoctoral fellow with Prof. Judy Lieberman at Boston Children’s Hospital for 5 years and worked at City University of Hong Kong as an Assistant Professor for 4 years before returning to NUS. Dr Le is well recognised for her contributions to the field of microRNAs, extracellular vesicles and cancer biology. Her group has recently developed a strategy to harness extracellular vesicles from red blood cells for delivery of RNA drugs. This drug delivery platform is the foundation for her start-up company, Carmine Therapeutics. She is also an associate/deputy editor of JEV and JExBio. She has recently received the NUS Alumni award, Falling Walls Venture, and Graduate Mentor of the Year award.