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Peptide-Conjugated Vascular Endothelial Extracellular Vesicles Encapsulating Vinorelbine for Lung Cancer Targeted Therapeutics

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Abstract: Lung cancer is one of the major cancer types and poses challenges in its treatment, including lack of specificity and harm to healthy cells. Nanoparticle-based drug delivery systems (NDDSs) show promise in overcoming these challenges. While conventional NDDSs have drawbacks, such as immune response and capture by the reticuloendothelial system (RES), extracellular vesicles (EVs) present a potential solution. EVs, which are naturally released from cells, can evade the RES without surface modification and with minimal toxicity to healthy cells. This makes them a promising candidate for developing a lung-cancer-targeting drug delivery system. EVs isolated from vascular endothelial cells, such as human umbilical endothelial-cell-derived EVs (HUVEC-EVs), have shown anti-angiogenic activity in a lung cancer mouse model; therefore, in this study, HUVEC-EVs were chosen as a carrier for drug delivery. To achieve lung-cancer-specific targeting, HUVEC-EVs were engineered to be decorated with GE11 peptides (GE11-HUVEC-EVs) via a postinsertional technique to target the epidermal growth factor receptor (EGFR) that is overexpressed on the surface of lung cancer cells. The GE11-HUVEC-EVs were loaded with vinorelbine (GE11-HUVEC-EVs-Vin), and then characterized and evaluated in in vitro and in vivo lung cancer models. Further, we examined the binding affinity of ABCB1, encoding P-glycoprotein, which plays a crucial role in chemoresistance via the efflux of the drug. Our results indicate that GE11-HUVEC-EVs-Vin effectively showed tumoricidal effects against cell and mouse models of lung cancer.

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