Inhalable Exosome-Based Dual Therapy: A Novel Strategy to Overcome Drug Resistance in Non-Small Cell Lung Cancer

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Non-small cell lung cancer (NSCLC) accounts for 85% of all lung cancers and can develop resistance to current therapies. This creates an urgent need for more effective and targeted treatments. The overexpression of microRNA-21 (miR-21) contributes to this resistance by promoting tumor growth and reducing the effectiveness of certain anticancer drugs, such as the third-generation epidermal growth factor receptor (EGFR) gene-targeting tyrosine kinase inhibitor (TKI) osimertinib (OSI). By enabling targeted, non-invasive delivery of therapeutic agents directly to tumor cells, exosome-based inhalable therapies offer a promising strategy to overcome drug-delivery challenges. In this study, we developed a targeted exosome-based inhalation therapy for NSCLC using exosomes derived from H1975 cells loaded with anti-miR-21 and OSI. This approach aims to suppress miR-21 expression while improving the delivery of OSI directly to cancerous cells. We used nanoparticle tracking analysis (NTA), transmission electron microscopy (TEM), zeta potential measurements, cumulative drug-release profiling, CCK-8 cell viability assay, qPCR, and fluorescence microscopy to characterize and evaluate the therapy. We expect that the combined exosome, OSI, and antimiR-21 treatment will achieve better delivery efficiency and therapeutic efficacy compared to OSI or antimiR-21 alone. Specifically, the therapy is expected to significantly reduce miR-21 expression and increase cancer cell death in H1975 cells. These findings may serve as a foundation for future research investigating exosome-based inhalation therapies as targeted delivery systems for overcoming drug resistance in NSCLC.

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