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Exosome-mediated drug delivery for treatment of pulmonary metastases

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Exosomes have recently come into focus as natural nanoparticles for use as drug delivery vehicles because they lack many drawbacks inherent to other nanoformulations. Many potentially useful chemotherapeutics possess undesirable attributes such as low solubility in aqueous solutions, immunogenicity, or inefficient accumulation in target cancer cells due to multidrug resistance (MDR) mechanisms. Our objective was to assess the feasibility of an exosome-based drug delivery platform for a potent chemotherapeutic agent, paclitaxel (PTX), to treat MDR cancer. Herein, we developed and compared different methods of loading exosomes released by macrophages with PTX and characterized their size, stability, drug release, and *in vitro* antitumor efficacy. A reformation of exosomes upon sonication resulted in high loading efficiency, and sustained drug release. Importantly, incorporation of PTX into exosomes increased cytotoxicity more than 50 times in drug resistant MDCKMDR1 (Pgp+) cells. Furthermore, exoPTX demonstrated significantly greater cytotoxicity against all cell lines tested, as compared to Taxol and PTX. The biodistribution and antitumor effects of exoPTX were further evaluated in a model of murine Lewis lung carcinoma pulmonary metastases. Our studies demonstrated nearly complete co-localization of airway-delivered exosomes with cancer cells, and a potent anticancer effect in this mouse model. Overall, exoPTX holds a significant potential for the delivery of various chemotherapeutics to treat drug resistant cancers.

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