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## ACCEPTED MANUSCRIPT

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## ABSTRACT

Standard of care for cancer is commonly a combination of surgery with radiotherapy or chemoradiotherapy. However, in some advanced cancer patients this approach might still remain inefficient and may cause many side effects, including severe complications and even death. Oncolytic viruses exhibit different anti-cancer mechanisms compared with conventional therapies, allowing the possibility for improved effect in cancer therapy. Chemotherapeutics combined with oncolytic viruses exhibit stronger cytotoxic responses and oncolysis. Here, we have investigated the systemic delivery of the oncolytic adenovirus and paclitaxel encapsulated in extracellular vesicles (EV) formulation that, *in vitro*, significantly increased the transduction ratio and the infectious titer when compared with the virus and paclitaxel alone. We demonstrated that the obtained EV formulation reduced the *in vivo* tumor growth in animal xenograft model of human lung cancer. Indeed, we found that combined treatment of oncolytic adenovirus and paclitaxel encapsulated in EV has enhanced anticancer effects both *in vitro* and *in vivo* in lung cancer models. Transcriptomic

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