



Nanovesicle mediated delivery of anticancer agents effectively regressed intrahepatic tumors in athymic mice

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Hepatocellular carcinoma (HCC) is the second most common cause of cancer-related deaths worldwide with rapidly growing incidence rates. The current therapeutic methods for HCC are not effective due to lack of efficient and targeted drug delivery system. We evaluated the efficacy of milk-derived nanovesicles (MNV) to deliver anticancer agents into HCC cells in culture as well as intrahepatic tumors induced in athymic nude mice. MNVs were isolated from commercial skim milk using ultracentrifugation and characterized with nanoparticle tracking analysis (NTA) and electron microscopy. MNVs were loaded with doxorubicin (dox-MNV), or anti-miR221 oligonucleotides (anti-miR221-MNV), purified by ultracentrifugation, and characterized using spectrophotometry and NTA. HepG2 cells in culture were treated with dox-MNV and anti-miR221-MNV and evaluated the rate of cell death. Intrahepatic tumors induced in athymic mice were injected with dox-MNV through tail vein and assessed tumor regression using in-vivo imaging system. Cellular uptake studies depicted plain and dox-MNV attained saturation within 4 h of treatment. Cell toxicity studies on HepG2 cells with MNV-dox at 1 μ M depicted around 20% cell death at 24 h, 50% at 48 h, and 80% at 72 h. HepG2 cells treated with fluorescent-tagged dox-MNV and anti-miR221-MNV exhibited nuclear disintegration and apoptosis within 48 hrs. Treatment of intrahepatic tumors with dox-MNV resulted in significant regression and increased survival rate. The results demonstrated that MNVs can be effectively used for successful delivery of anticancer agents into HCC cells and intrahepatic tumors. MNV mediated target delivery of anticancer agents could be an efficient modality for the treatment of malignant HCC and might produce a great impact on anticancer therapy.

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