Engineered extracellular vesicles for safe and efficient sonodynamic cancer therapy

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Sonodynamic therapy (SDT), wherein sonosensitizers irradiated with ultrasound (US) produce cytotoxic reactive oxygen species (ROS), can eradicate deep-seated tumors owing to the deep tissue penetration of US. To enhance the clinical translation of sonodynamic cancer therapy, the development of nanocarriers capable of selectively delivering sonosensitizers to tumor tissues without systemic toxicity is crucial. Extracellular vesicles, a type of naturally occurring nanoparticles, have emerged as safe and versatile nanocarriers for targeted delivery of sonosensitizers into tumors. In this study, extracellular vesicles were engineered and loaded with various sonosensitizers to achieve cancer-specific SDT and pH/US-responsive drug release. In vivo study using tumor-xenograft mouse revealed that engineered extracellular vesicles significantly suppressed tumor growth under US irradiation without inducing systemic toxicity. Our findings demonstrate that sonosensitizer-loaded extracellular vesicles combined with US have great potential for safe and targeted cancer therapy.