Efficacy and safety of γ-PGA nanoparticles as vaccine carrier

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Recently, nanoscopic systems that incorporate therapeutic agents, and molecular targeting and diagnostic imaging capabilities are emerging as the next generation of functional nanomedicines to improve the outcome of drug therapeutics. Among the many nanoparticulate systems, micelle-like aggregates or nanoparticles formed with amphiphilic block- or graft- copolymers are currently being studied for possible application as protein carriers. We recently developed a technique to prepare uniform nanoparticles (γ-PGA NPs) using amphiphilic γ-PGA (γ-PGA-L-PAE), in which L-phenylalanine ethyl ester (L-PAE) is introduced as a hydrophobic residue into the α-position group carboxyl of poly(γ-glutamic acid) (γ-PGA) which is a biodegradable polymer derived from a natto mucilage. γ-PGA NPs are excellent vaccine carriers capable of delivering antigenic proteins to antigen-presenting cells (APCs) and eliciting potent immune responses based on antigen-specific cytotoxic T lymphocytes. In mice, subcutaneous immunization with γ-PGA NPs entrapping ovalbumin (OVA) more effectively inhibited the growth of OVA-transfected tumors than immunization with OVA emulsified using Freund's complete adjuvant. In addition, γ-PGA NPs did not induce histopathologic changes after subcutaneous injection or acute toxicity through intravenous injection. Importantly, γ-PGA NPs efficiently delivered entrapped antigenic proteins into APCs through cytosolic translocation from the endosomes, which is a key process of γ-PGA NP-mediated anti-tumor immune responses. These antigen-capturing APCs migrated to regional lymph nodes. Our results demonstrate that a γ-PGA NP system for antigen delivery will advance the clinical utility of vaccines against cancer.