Polyanhydride nanoparticle vaccine platform delays tumor growth in an antigen specific model

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Statement of Purpose: Immunotherapies designed to direct the immune system to elimate malignancies is a growing area of research aimed at providing a safe and effective alternative and/or adjunct therapy to chemotherapeutic and surgical interventions. These approaches require the development of immunization regimens that induce efficacious cell-mediated immunity directed at antigens expressed by tumor cells. Particles consisting of polyanhydride copolymers based on 1,6-bis(*p*-carboxyphenoxy) hexane (CPH), and 1,8-bis(*p*-carboxyphenoxy)-3,6-dioxaoctante (CPTEG) have been shown to enhance dendritic cell activation, which in turn induces activation and proliferation of antigen-specific $CD4^+$ and $CD8^+$ T cells *in vitro* [1]. Polyanhydride particle-based vaccines have also been proven to be safe for the recipient, even when large doses are administered [2]. Here, we demonstrate that immunization of mice with a polyanhydride nanoparticle-based vaccine platform induced a potent immune response to a specific tumor-associated model antigen in order to control tumor progression *in vivo*. Specifically, we challenge immunized mice with a transgenic tumor cell line, expressing ovalbumin (Ova) as a target antigen, to determine if our vaccination strategy is effective.

Methods: C57BL/6 mice were vaccinated subcutaneously with either soluble Ova (2.0 mg), soluble Ova (1.75 mg) plus Ova encapsulated (0.25 mg) in 20:80 CPTEG:CPH nanoparticles, soluble Ova (2.0 mg) adjuvanted with Alum, or PBS. Six weeks post-vaccination, all mice in each group (n = 12) were challenged with a lethal dose of Ova-expressing EG7 tumor cells subcutaneously in the flank. The progression of the tumors was monitored three times per week over the course of the study. Individual mice were removed from study when their measured tumor volume reached 1000 mm^3. The study was terminated at 30 days after injection of the EG7-Ova tumor cells.

Results: Mice immunized once with a regimen consisting of soluble Ova and Ova encapsulated in 20:80 CPTEG:CPH nanoparticles exhibited delayed tumor growth during the course of our study when compared to mice immunized with soluble Ova adjuvanted with Alum, soluble Ova alone, or PBS (Fig. 1A). Mice that received the nanoparticle formulation also had improved survival rates when compared to mice immunized with other formulations (Fig. 1B).

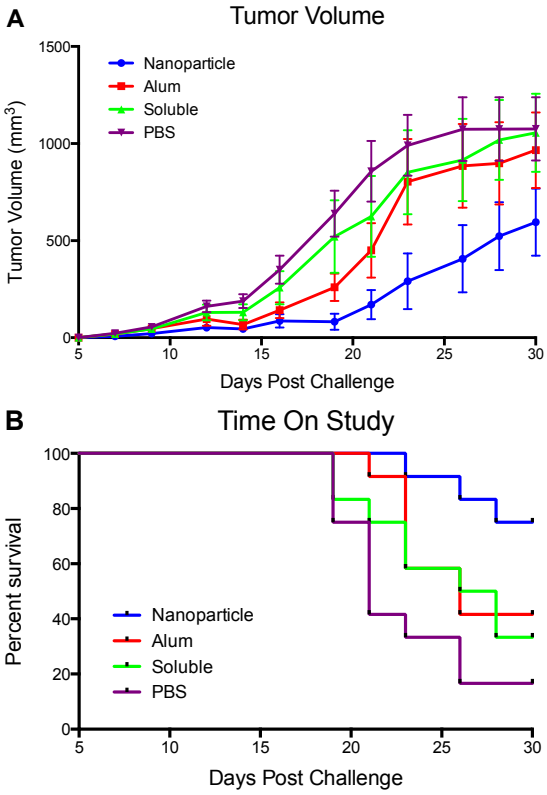

Figure 1. (A) Delayed tumor growth in mice immunized with the polyanhydride nanoparticle formulation. (B) Improved survival rates over the course of the study in mice immunized with the polyanhydride nanoparticle formulation.

Conclusions: We demonstrated that soluble Ova administered in combination with Ova encapsulated in polyanhydride nanoparticles enhanced anti-tumor immune responses. In turn, mice challenged with a lethal dose of tumor cells experienced delayed tumor growth and enhanced survival rates. Previously, our team has shown that immunization with polyanhydride nanoparticles enhances early antigen-specific $CD8^+$ T cell responses [3]. Polyanhydride nanoparticle-based vaccines may promote anti-tumor immunity by inducing robust cytotoxic T cell responses.

References:

[1] Torres et al. *Acta Biomater*. 2011; 7:2857-2864.
[2] Huntimer et al. *Adv Healthcare Mater*. 2012.
[3] Huntimer et al. *Proceed 9th World Biomat Congress*. 2012.