Single Dose Tetanus Vaccine Based on Polyanhydride Microspheres

Matt J. Kipper[1], Jennifer Wilson[2], Michael Wannemuehler[2], and Balaji Narasimhan[1]
[1]Department of Chemical Engineering, Iowa State University
[2]Department of Veterinary Microbiology and Preventive Medicine, Iowa State University

Single dose vaccines have major implications for the effectiveness of mass immunization programs. The development of single dose vaccines is fraught with a complex combination of clinical and engineering challenges. Several health organizations have listed the development of single dose vaccines as one of the "grand challenges" of human health worldwide. We describe the results of an experimental study focused on the development of single dose vaccines based on biodegradable polymer microspheres. Tetanus toxoid (TT) is encapsulated in bioerodible polyanhydride microspheres. Polyanhydrides provide a hydrophobic environment for the stabilization of the protein until it is released. Polymer formulations used are copolymers of sebacic acid and 1,6-bis(*p*-carboxyphenoxy)hexane. The *in vitro* release kinetics is modulated by changing the copolymer composition. The *in vitro* release profile indicates that the formulations investigated can provide a sustained exposure to the antigen, obviating the requirement of multiple injections to obtain protective immunity. Mice (C3H/HeOuJ) were inoculated with the microspheres and bled weekly from the saphenous vein for 12 weeks. Antibody titers were determined by ELISA and were superior to equivalent single dose of unencapsulated protein. The vaccine efficacy is improved if the antigen is delivered along with a small bolus of free TT. The bolus alone is insufficient to stimulate a sustained immune response, but provides sufficient activation of the immune response pathway that the subsequent slow release from the microspheres is more effective.