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Topical immunization using nanoengineered genetic vaccines.

Cui Z, Mumper RJ.

Division of Pharmaceutical Sciences, College of Pharmacy, University of Kentucky, Lexington, KY 40536-0082, USA.

Abstract

DNA vaccines have been shown to elicit both broad humoral and cellular immune responses. Needle-free injection devices and the gene gun have been used to deliver these DNA vaccines to dendritic cells in the viable skin epidermis with some success. However, more cost-effective and dendritic cell (DC)-targeted immunization strategies are sought. To this end, a nanoengineered genetic vaccine for simple topical application was developed. Expressed beta-galactosidase was used as a model antigen. Plasmid DNA was coated on the surface of preformed cationic nanoparticles engineered directly from warm oil-in-water (O/W) microemulsion precursors comprised of emulsifying wax as the oil phase and CTAB as a cationic surfactant. Mannan, a DC ligand, was coated on the nanoparticles with and without entrapped endosomolytic agents, dioleoyl phosphatidylethanolamine (DOPE) and cholesterol. In-vitro cell transfection studies were performed to confirm transgene expression with these pDNA-coated nanoparticles. An in-vitro Concanavalin A (ConA) agglutination assay confirmed the presence of mannan on the surface of nanoparticles. The humoral and proliferative immune responses were assessed after topical application of these nanoengineered systems to the skin of shaved Balb/C mice. All pDNA-coated nanoparticles, especially the mannan-coated pDNA-nanoparticles with DOPE, resulted in significant enhancement in both antigen-specific IgG titers (16-fold) and splenocyte proliferation over 'naked' pDNA alone.

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