Polyethylenimine-Enhanced Alumina Nanoscale Adjuvant for Cancer Vaccine

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ABSTRACT

Aluminum oxide nanoparticles (Al2O3 NPs) have been shown to increase the efficiency of cell-mediated immune response. Specifically, CD8 and CD4 immune response is required for T cell activation by dendritic cells. These nanoparticles, when functionalized with peptides and other molecules, can be used as vaccine in cancer treatment. HPV-induced cervical cancer expresses E6/E7 antigens. E6/E7 proteins were attached using surface modification of the Al2O3 NPs; different types of molecules were used to see which adhered the highest amount of protein and produced the strongest cell response. Protein measurements were done using bicinchoninic acid assay (BCA assay) and spectrophotometry. CD8 and CD4 immune response was measured in vivo using flow cytometry. In vitro measurements of immune response were done using the TC1 tumor line. When coated on the nanoparticles and mixed with E6/E7 protein, the polymer polyethylenimine (PEI) proved to be most effective at strengthening the immune response in vaccinated mice.

Our findings in this study demonstrate the growing importance of applied physics in the fields of medicine and biology. Fabrication and characterization of nano-materials are important for improving vaccine delivery and ensuring effectiveness.

RESULTS

Modification of Alumina NPs with Polyethylenimine

Surface modification of Al2O3 NPs with PEI was accomplished via ultra-sonication. Diagram A is an illustration of the functionalization. Figure 1a is a transmission electron microscope (TEM) image of naked alumina. Figures 1b and 1c show that PEI is coating the Al2O3 NP. The electron beam from the microscope causes the polymer to form bubbles. Figure 1c is a high magnification of the sample, showing the lattice fringes of the polyethylenealine Al2O3.

PEI efficiently enhance alumina nanoscale adjuvant

Different molecules were analyzed for their efficiency at protein attachment (Figure 2a). Al2O3 NPs were coated with the polymer styrene maleic anhydride (SMA), PEI, the chemical aminophenol (AP), aminophenol cross-linked with SPDP (SPDP), and polyvinylpyrrolidone (PVP). Determining that PEI was the best candidate for improving antigen delivery, different forms and weights of PEI were tested in vivo. Mice were injected with five different samples: branched PEI at 25k Daltons (“Bz5000”) and 800 Da (“B800”), linear PEI at 25k Da (“Lz5000”) and 800 Da (“Lz800”), and E6/E7 (protein only). Flow cytometry determined that the branched PEI at 25kDa stimulated the most CD8 and CD4 immune response when re-stimulated with E6/E7 protein (figures 2b and 2c).

T CELL IMMUNE PROCESS

Antigen presenting cells (APCs) such as dendritic cells (DCs) process and present antigen to naive T cells via the Major Histo compatibility Complex (MHC). MHC class I activates CD4+ helper T cells which activate other immune cells against the antigen. MHCII activate CD8+ T cells which kill antigen-positive cancer cells.

REFERENCES


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