Development of a Nanoparticle for Targeted Antigen Delivery as a Therapeutic Vaccination Platform

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A novel antigen-presenting cell (APC)-targeted immunomodulatory nanoparticle (NP) was developed as a vaccination platform, with potential uses such as cancer therapeutics. The nanoparticle encapsulates a plasmid encoding a fusion of DsRed2, a red fluorescent protein, and ovalbumin (OVA), a model antigen. The NP, a polyacrylamide hydrogel crosslinked with DNA oligonucleotides including aptamers (oligonucleic targeting ligands), was engineered with an innovative intracellular controlled release system, Dynamic Aptamers Release Targeting System (DARTS). Upon binding of one aptamer to its target, DC-SIGN (an APC surface receptor), the NP is designed to internalize by receptor-mediated endocytosis. This is followed by the binding of a second aptamer to Toll-Like Receptor 9 (TLR9), causing the destabilization of the complementary base pair bonds between the hybridized crosslinking strands and leading to NP dissociation and plasmid release. The aptamer is also a TLR9 agonist and can therefore act as an adjuvant. Plasmid was generated by inserting an OVA-encoding restriction fragment into a DsRed2 vector by subcloning. Nanoparticles (void and plasmid-encapsulating, NP-plasmid) were synthesized and analyzed by transmission electron microscopy. Size was monodispersed around 50 nm for void NPs and 200 nm for NP-plasmid. The presence of aptamer and plasmid DNA in NP-plasmid was confirmed by energy-dispersive X-ray spectroscopy and gel electrophoresis. Nanoparticle uptake to an antigen-presenting cell line was studied by confocal microscopy; dose- and time-dependent internalization was shown. The hydrogel nanoparticle and DARTS have many applications in controlled release drug delivery in addition to their role in this vaccination platform, a potential cancer therapeutic.

Awards Won:

Second Award of $2,000