Efficient cancer vaccines readily induce an MHC-I-restricted cytotoxic T lymphocyte (CTL) response by delivering tumor neo-antigens to the cytosol of dendritic cells (DCs). Nucleic acid adjuvants have been shown to further enhance CTL responses by triggering intracellular signaling pathways in DCs that are associated with activation, maturation and migration to the lymph nodes where priming of CTLs takes place. Studies show that DCs are present in high numbers in LNs relative to peripheral tissues such as the skin, suggesting that delivery of antigen and adjuvant to the LN might enhance vaccine efficiency. Studies also show that to effectively prime antigen-specific CTLs, both the antigen and adjuvant need to be co-delivered to the same DC.

Our optimized NP vaccine enables neo-antigens and adjuvants to be loaded on one delivery vehicle and co-delivered to DCs. Since particle size plays a major role in the efficiency and route by which these vaccines reach LNs, we strategically optimized the NPs to be ~50 nm in size with a slight cationic surface charge to improve accumulation in LNs from the injection site. Thereby, allowing the NP vaccine to reach the majority of DCs in the LN. Upon uptake by LN-resident DCs, the pH-responsive NP will respond to the decreased pH within endosomal compartments and disassemble allowing cargo to be released into the cytosol. Cytosolically delivered neo-peptides are subsequently loaded on MHC-I molecules and presented to CTLs. Thus, the optimized NP vaccine can potentially improve targeting of LNs, activation of LN-resident DCs, and enhanced induction of antigen-specific CTLs.
